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Born in the Ear Canal: Tick Larva on the Eardrumm

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Original Investigations

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Türk Otorinolarengoloji Arşivi

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Turkish Archives of Otorhinolaryngology
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Aims and Scope

The Turkish Archives of Otorhinolaryngology (Turk Arch Otorhinolaryngol) is the scientific, peer reviewed, open access journal of the Turkish Otorhinolaryngology Head and Neck Surgery Society. The journal is released at three-month intervals, in March, June, September and December, and one volume of the journal comprises four issues. The journal's publication language is English.

The aim of the journal is to publish qualified original clinical, experimental and basic researches on ear, nose, throat, head and neck diseases and surgery, reviews that contain sufficient amount of source data conveying the experiences of experts in a particular field, case reports and original images of rare clinical pictures which would shed light on the clinical practice and which were not previously published, letters from the readers and experts concerning the published studies, articles about general practice and subject of the journal with historical content, memories of scientific significance, educative and catechetical manuscripts about medical deontology and publication ethics.

Target audience of the journal includes academic members, specialists, residents and other relevant health care professionals in the field of ear, nose, throat, and head and neck disorders and surgery.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

Turkish Archives of Otorhinolaryngology is indexed in PubMed Central, Web of Science-Emerging Sources Citation Index, TUBITAK ULAKBIM TR Index, DOAJ, EBSCO, CINAHL and ProQuest.

Processing and publication are free of charge with the journal. No fees are requested from the authors at any point throughout the evaluation and publication process. All manuscripts must be submitted via the online submission system, which is available at www.turkarchotolaryngol.net. The journal guidelines, technical information, and the required forms are available on the journal's web page.

All expenses of the journal are covered by the Turkish Otorhinolaryngology Head and Neck Surgery Society. Potential advertisers should contact the Editorial Office. Advertisement images are published only upon the Editor-in-Chief's approval.

Statements or opinions expressed in the manuscripts published in the journal reflect the views of the author(s) and not the opinions of the Turkish Otorhinolaryngology Head and Neck Surgery Society, editors, editorial board, and/or publisher; the editors, editorial board, and publisher disclaim any responsibility or liability for such materials.

All published content is available online, free of charge at www.turkarchotolaryngol.net. Printed copies of the journal are distributed to the members of the Turkish Otorhinolaryngology Head and Neck Surgery Society, free of charge.

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Turkish Archives of Otorhinolaryngology
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Instructions to Authors

CONTEXT

The Turkish Archives of Otorhinolaryngology (Turk Arch Otorhinolaryngol) is an international, scientific, open access periodical published by independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Turkish Otorhinolaryngology Head and Neck Surgery Society, and published quarterly in March, June, September and December. The publication language of the journal is English.

The aim of the journal is to publish qualified original clinical, experimental and basic researches on ear, nose, throat, head and neck diseases and surgery, reviews that contain sufficient amount of source data conveying the experiences of experts in a particular field, case reports and original images of rare clinical pictures which would shed light on the clinical practice and which were not previously published, letters from the readers and experts concerning the published studies, articles about general practice and subject of the journal with historical content, memories of scientific significance, educative and catechetical manuscripts about medical deontology and publication ethics.

EDITORIAL AND PUBLICATION PROCESS

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal conforms to the Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

Originality, high scientific quality, and citation potential are the most important criteria for a manuscript to be accepted for publication. Manuscripts submitted for evaluation should not have been previously presented or already published in an electronic or printed medium. The journal should be informed of manuscripts that have been submitted to another journal for evaluation and rejected for publication. The submission of previous reviewer reports will expedite the evaluation process. Manuscripts that have been presented in a meeting should be submitted with detailed information on the organization, including the name, date, and location of the organization.

PEER REVIEW PROCESS

Manuscripts submitted to The Turkish Archives of Otorhinolaryngology will go through a double-blind peer-review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in their fields in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation processes of manuscripts submitted by editors or by the editorial board members of the journal. The Editor in Chief is the final authority in the decision-making process for all submissions.

ETHICAL PROCEDURES

An approval of research protocols by the Ethics Committee in accordance with international agreements (World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," amended in October 2013, www.wma.net) is required for experimental, clinical, and drug studies and for some case reports. If required, ethics committee reports or an equivalent official document will be requested from the authors. For manuscripts concerning experimental research on humans, a statement should be included that shows that written informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly. Information on patient consent, the name of the ethics committee, and the ethics committee approval number should also be stated in the Materials and Methods section of the manuscript. It is the authors' responsibility to protect the patients' anonymity carefully.

For photographs that may reveal the identity of the patients, signed releases of the patient or their legal representative should be enclosed, and the publication approval must be provided in the Materials and Methods section.

PLAGIARISM

The Turkish Archives of Otorhinolaryngology is extremely sensitive about plagiarism. All submissions are screened by a similarity detection software (iThenticate by CrossCheck) at any point during the peer-review and/or production process. Even if you are the author of the phrases or sentences, the text should not have unacceptable similarity with the previously published data.

When you are discussing others' (or your own) previous work, please make sure that you cite the material correctly in every instance.

In the event of alleged or suspected research misconduct, e.g., plagiarism, citation manipulation, and data falsification/fabrication, the Editorial Board will follow and act following COPE guidelines.

AUTHORSHIP

Each person listed as an author should fulfill the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE - www.icmje.org). The ICMJE recommends that authorship is based on the following four criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

2. Drafting the work or revising it critically for important intellectual content; AND

3. Final approval of the version to be published; AND

4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In addition to being accountable for the parts of the work he/she has done, an author should be able to identify which co-authors are responsible for specific other parts of the work. Also, authors should have confidence in the integrity of the contributions of their co-authors.

All those designated as authors should meet all four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who do not meet all four criteria should be acknowledged in the title page of the manuscript.

The Turkish Archives of Otorhinolaryngology requires corresponding authors to submit a signed and scanned version of the authorship contribution form (available for download through www.turkarchotolaryngol.net) during the initial submission process to act appropriately on authorship rights and to prevent ghost or honorary authorship. If the editorial board suspects a case of "gift authorship," the submission will be rejected without further review. As part of the submission of the manuscript, the corresponding author should also send a short statement declaring that he/she accepts to undertake all the responsibility for authorship during the submission and review stages of the manuscript.

DECLARATION OF INTEREST

The Turkish Archives of Otorhinolaryngology requires and encourages the authors and the individuals involved in the evaluation process of submitted manuscripts to disclose any existing or potential conflicts of interests, including financial, consultant, and institutional, that might lead to potential bias or a conflict of interest. Any financial grants or other support received for a submitted study from individuals or institutions should be disclosed to the Editorial Board. To disclose a potential conflict of interest, the ICMJE Potential Conflict of Interest Disclosure Form should be filled in and submitted by all contributing authors. The journal's Editorial Board resolves cases of a potential conflict of interest of the editors, authors, or reviewers within the scope of COPE and ICMJE guidelines.

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MANUSCRIPT PREPARATION

The manuscripts should be prepared in accordance with ICMJE-Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (updated in December 2019 - http://www.icmje.org/icmje-recommendations.pdf). Authors are required to prepare manuscripts in accordance with the CONSORT guidelines for randomized research studies, STROBE guidelines for observational original research studies, STARD guidelines for studies on diagnostic accuracy, PRISMA guidelines for systematic reviews and meta-analysis, ARRIVE guidelines for experimental animal studies, and TREND guidelines for non-randomized public behavior.

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at www.turkarchotolaryngol.net. Manuscripts submitted via any other medium and submissions by anyone other than one of the authors will not be evaluated.

Manuscripts submitted to the journal will first go through a technical evaluation process where the editorial office staff will ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the submitting author with technical correction requests.

Authors are required to submit the following:

- Copyright Agreement and Acknowledgement of Authorship Form, and

Instructions to Authors

- ICMJE Potential Conflict of Interest Disclosure Form (should be filled in by all contributing authors) during the initial submission. These forms are available for download at www.turkarchotolaryngol.net.

Preparation of the Manuscript

Title page: A separate title page should be submitted with all submissions and this page should include:

- The full title of the manuscript as well as a short title (running head) of no more than 50 characters,
- Name(s), affiliations, highest academic degree(s), and ORCID IDs of the author(s),
- Grant information and detailed information on the other sources of support,
- Name, address, telephone (including the mobile phone number), and email address of the corresponding author,
- Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria.

Abstract: An abstract should be submitted with all submissions except for Letters to the Editor. The abstract of Original Articles should be structured with subheadings (Objective, Methods, Results, and Conclusion). Please check Table 1 below for word count specifications.

Keywords: Each submission must be accompanied by a minimum of three to a maximum of six keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (https://www.nlm.nih.gov/mesh/MBrowser.html).

Main Points: All submissions except letters to the editor and clinical images should be accompanied by 3 to 5 "main points" which should emphasize the most noteworthy results of the study and underline the principle message that is addressed to the reader. This section should be structured as itemized to give a general overview of the article. Since "Main Points" targeting the experts and specialists of the field, each item should be written as plain and straightforward as possible.

Manuscript Types

Original Articles: This is the most important type of article since it provides new information based on original research. The main text of original articles should be structured with Introduction, Methods, Results, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Original Articles.

Statistical analysis to support conclusions is usually necessary. Statistical analyses must be conducted in accordance with international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). Information on statistical analyses should be provided with a separate subheading under the Materials and Methods section and the statistical software that was used during the process must be specified.

Units should be prepared in accordance with the International System of Units (SI).

Editorial Comments: Editorial comments aim to provide a brief critical commentary by reviewers with expertise or with high reputation in the topic of the research article published in the journal. Authors are selected and invited by the journal to provide such comments. Abstract, Keywords, and Tables, Figures, Images, and other media are not included.

Review Articles: Reviews prepared by authors who have extensive knowledge on a particular field and whose scientific background has been translated into a high volume of publications with a high citation potential are welcomed. These authors may even be invited by the journal. Reviews should describe, discuss, and evaluate the current level of knowledge of a topic in clinical practice and should guide future studies. The main text should contain Introduction,

Table 1. Limitations for each manuscript type

Type of manuscript	Author limit	Word limit	Abstract word limit	Reference limit	Table limit	Figure limit
Original Article	N/A	3500	250 (Structured)	30	6	5 or total of 10 images
Review Article	4	5000	250	50	6	10 or total of 15 images
Case Report	6	1000	200	10	No tables	4 or total of 8 images
Letter to the Editor	3	500	No abstract	5	No tables	No media
Clinical Images	3	500	No abstract	5	No tables	3 or total of 7 images

Clinical and Research Consequences, and Conclusion sections. Please check Table 1 for the limitations for Review Articles.

Case Reports: There is limited space for case reports in the journal and reports on rare cases or conditions that constitute challenges in diagnosis and treatment, those offering new therapies or revealing knowledge not included in the literature, and interesting and educative case reports are accepted for publication. The text should include Introduction, Case Presentation, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Case Reports.

Letters to the Editor: This type of manuscript discusses important parts, overlooked aspects, or lacking parts of a previously published article. Articles on subjects within the scope of the journal that might attract the readers' attention, particularly educative cases, may also be submitted in the form of a "Letter to the Editor." Readers can also present their comments on the published manuscripts in the form of a "Letter to the Editor." Abstract, Keywords, and Tables, Figures, Images, and other media should not be included. The text should be unstructured. The manuscript that is being commented on must be properly cited within this manuscript.

Clinical Images: This type of submissions should present a striking image that may challenge and inform readers and contribute to their education. Submissions can include high quality clinical images, radiology results or surgical images. Please check Table 1 for the limitations for Clinical Images.

Tables

Tables should be included in the main document, presented after the reference list, and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100 × 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

All references, tables, and figures should be referred to within the main text, and they should be numbered consecutively in the order they are referred to within the main text.

Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

References

Both in-text citations and the references must be prepared according to the Vancouver style.

While citing publications, preference should be given to the latest, most up-to-date publications. Authors are responsible for the accuracy of references If an ahead-of-print publication is cited, the DOI number should be provided. Journal titles should be abbreviated in accordance with the journal abbreviations in Index Medicus/MEDLINE/PubMed. When there are six or fewer authors, all authors should be listed. If there are seven or more authors, the first six authors should be listed followed by "et al." In the main text of the manuscript, references should be cited using Arabic numbers in parentheses. The reference styles for different types of publications are presented in the following examples.

Journal Article: Erkul E, Cekin İE, Kurt O, Gungor A, Babayigit MA. Evaluation of patients with unilateral endoscopic sinus surgery. Turk Arch Otorhinolaryngol 2012; 50: 41-5.

Book Section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.2290-308.

Books with a Single Author: Sweetman SC. Martindale the complete drug reference. 34th ed. London: Pharmaceutical Press; 2005.

Editor(s) as Author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.

Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92.

Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or Technical Report: Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Thesis: Yılmaz B. Ankara Üniversitesindeki öğrencilerin beslenme durumları, fiziksel aktiviteleri ve beden kitle indeksleri kan lipidleri arasındaki ilişkiler. H.Ü. Sağlık Bilimleri Enstitüsü, Doktora Tezi. 2007.

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Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

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Turkish Archives of Otorhinolaryngology
Türk Otorinolarengoloji Arşivi

Contents

What Has Changed in the Last Decade in the Turkish Archives of Otorhinolaryngology?

Original Investigation

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Abstract

Objective: The primary aim of the study was to perform sequential analyses together with a citation analysis on the characteristics of the studies published in the Turkish Archives of Otorhinolaryngology (TAO) in the periods of 2010–2014 and 2015–2019.

Methods: The studies published in the indicated periods were reviewed for study type, study topic, language and country of origin. Then, the citation analysis of the articles was performed through the Google Scholar and Web of Science (WoS) databases for the indicated periods. The estimated annual impact factors (EIF) of TAO from 2017 to 2020 were calculated by dividing the total number of citations performed in the projected year to the total number of citable articles published in the preceding two years.

Results: The total numbers of articles published from 2010 to 2014 and from 2015 to 2019 were 144 and 214, respectively. In 2010 to 2014, the most frequent study topic was head and neck with case reports ranking highest among study types. In 2015–2019, the most frequent study type had changed to original investigation and topic to general otorhinolaryngology. There was a remarkable increase in the total number of citations in 2015-2019 according to Google Scholar and WoS databases. Also, there was a remarkable increase in the EIF values for 2019 and 2020.

Conclusion: Although the increase in the number of citations and impact factor values cannot be appreciated as a single indicator for the success of a journal, the results of the presented study showed a promising advancement in the scientific quality of the TAO, driven by the inclusion of the journal to national and international indexes and by changing the language of the journal to English, as well as the well-orchestrated editorial efforts.

Keywords: Bibliometrics, publications, medical journalism, otorhinolaryngology, citation

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Introduction

Several studies in the literature that aim to ascertain the scientific status of a journal have mostly used citation analysis (1-5). The sequential analysis of a journal's publications with citations provides standard data regarding the publication trends with citation indicators of the journal, allows to evaluate the improvement of a journal in terms of scientific status and enables the editorial board to consider their publication

policies to augment the impact of a journal. It also enables to measure the effect of important experiences of a journal such as the inclusion of scientific indexes or change in publication policies.

The Turkish Archives of Otorhinolaryngology (TAO) is the scientific, peer-reviewed, open-access journal of the Turkish Otorhinolaryngology Head and Neck Surgery Society. TAO is the first Turkish otorhinolaryngology (ORL) journal that is in publication since November 1962 (6). The publication of the TAO represents a milestone in the Turkish ORL history and is regarded as a necessary step on the developmental path of the Turkish ORL literature. Professor Mehmet Hikmet Altuğ, the journal's first editor, expressed his visionary stance pertaining to scientific publishing in the first issue as: *"Our archive, we believe, fills a gap in a world getting smaller with radio, television, and everyday changing medicine,"* (7).

With the intense efforts of previous Editorial Boards along with the current successor, TAO was indexed by the TÜBİTAK ULAKBIM TR database, as well as two top international indexes—the Emerging Sources Citation Index (ESCI) and the PubMed Central in 2015. In the same period, also the journal's language of publication was changed to English. While such episodes that involve major changes can significantly affect the scientific status of a journal, the exact impact of these alterations should nevertheless be verified with a comprehensive analysis. Studies on this subject matter are rare in the Turkish otorhinolaryngological discipline (8-11). The primary aim of the presented study was to perform sequential analyses on the characteristics of the studies published in the TAO during the periods from 2010 to 2014 and 2015 to 2019. A comparison in terms of citation performance and characteristics was also performed for these periods.

Methods

The articles published in the TAO were initially reviewed through the archives of the journal for the periods from 2010 to 2014 and 2015 to 2019 in terms of study type (experimental study, clinical study, case report, review, letter to editor, clinical image, editorial article, historical article), study topic (otology, rhinology, head and neck, pediatric ORL and general ORL), language (Turkish/English) and country of origin. Subsequently, the citation analysis of the articles was made using the Google Scholar and Web of Science (WoS) databases based on the total number of citations, the mean number of citations per study, the mean number of citations per study type, the country of origin of the citations, the branch of the journals (ORL or other) in which they were cited, number of citations in TAO from the previous issues, WoS index types of citations, and the total number of citations with the mean per article for the studies published from Turkey and foreign countries. Google Scholar can count a paper multiple times, therefore duplications were reviewed and removed to obtain the accurate number of citations in the Google Scholar database analysis. WoS index types include Science Citation Index Expanded (SCI-E), ESCI and other WoS indexes (Conference Proceedings Citation Index-Science, Book Citation Index-Science). Our study was done in January 2021, hence, the analysis included citations made until this date and only articles written in English or Turkish were accepted as citation. However, due to the absence of citation reports of the articles published from 2010 to 2014 in the WoS database, only Google Scholar was used for the analysis of these articles. Then, the journals where the citations were published were analyzed manually to ensure the involvement of WoS indexes for this period.

Currently, the TAO is not indexed by Clarivate Analytics (previously the Thomson Institute for Scientific Information), therefore, no official impact factor was calculated for the journal. Nevertheless, the estimated impact factor (EIF) of a journal can be calculated by dividing the total number of citations made in the projected year to the total number of citable articles (original investigation, case report and review) published in the past two years. Because WoS databases started to include the articles published in the TAO after 2015, it was possible to calculate the EIFs only for the years 2017-2020. EIF was calculated manually according to the citations obtained from WoS databases.

Data analyses, including mean values and proportions, were calculated using Microsoft Excel 2010.

Results

The total number of articles published from 2010 to 2014 and from 2015 to 2019 was 144 and 214, respectively. Characteristics of articles published in the TAO from 2010 to 2014 and from 2015 to 2019 are shown in Table 1. From 2010 to 2014, the most frequent study topic was head and neck with the case reports having the highest rate among the study types. In 2015–2019, the most frequent study type had changed to original investigation and topic to general ORL. Of the original investigations 58 (98.3%) were clinical and one (1.7%) was experimental study in 2010–2014, whereas there were 116 (94.3%) clinical and seven (5.7%) experimental studies in 2015–2019.

From 2010 to 2014, the total number of citations was 75 for 122 articles according to the Google Scholar database with a mean of 0.61 (Figure 1). Twenty-two articles could not be retrieved from the database. Five of all citations (6.7%) were performed in other articles published in the TAO. While 20 out of 75 citations (26.7%) were of articles written in Turkish, the remaining 55 were (73.3%) of articles written in English. The total number of citations in the journals listed in WoS indexes was 31 (0.21 per study) (Table 2), of which 18 citations (58.1%) were in journals indexed in SCI-E and 13

citations (41.9%) in journal indexed in ESCI (Figure 2). Of the 31 citations, 13 (41.9%) were published in ORL journals, and 18 (58.1%) in other journals. While 16 citations (51.6%) were made by a group with a Turkish first author, 15 (48.4%) were cited by authors from other countries (Table 3). The numbers of citations made by Turkish authors indexed in ESCI and SCI were nine and seven, respectively.

According to the WoS and Google Scholar databases, the total numbers of citations for the 214 published articles in the period from 2015 to 2019 were 240 (mean: 1.12) and 398 (mean: 1.85), respectively (Figure 1). The characteristics of the citations are shown in Table 2. Of the 240 citations retrieved from the WoS, 77 (32.1%) were in ORL journals and 163 (67.9%) were in other journals. Fifty-eight out of 240 (24.2%) citations were made by a group with a Turkish

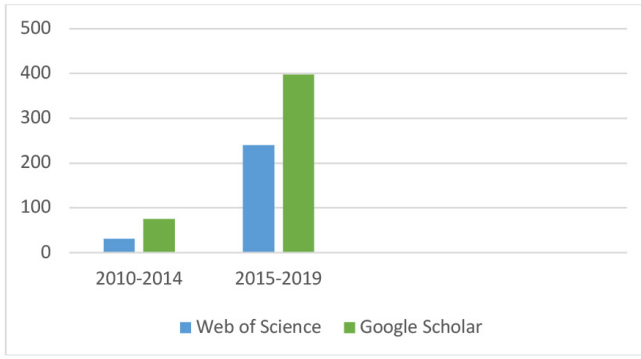

Figure 1. Total number of citations from 2010 to 2014 and from 2015 to 2019

Table 1. Characteristics of articles published in the TAO from 2010 to 2014 and from 2015 to 2019

Years	**2010–2014**		**2015–2019**	
Number of articles (n)	144	n (%)	214	n (%)
Study topic	Otology	27 (18.7)	Otology	45 (21)
	Rhinology	36 (25)	Rhinology	39 (18.2)
	Head and neck	41 (28.5)	Head and neck	49 (22.9)
	Pediatric ORL	7 (4.9)	Pediatric ORL	21 (9.8)
	General ORL	33 (22.9)	General ORL	60 (28.1)
Study type	Original investigation	59 (41)	Original investigation	123 (57.5)
	Case report	79 (54.9)	Case report	63 (29.4)
	Review	6 (4.1)	Review	11 (5.2)
	Letter to the editor	0	Letter to the editor	6 (2.8)
	Clinical image	0	Clinical image	3 (1.4)
	Editorial article	0	Editorial article	6 (2.8)
	Historical article	0	Historical article	2 (0.9)
Language	Turkish	72 (50)	Turkish	0
	English	72 (50)	English	214 (100)
Country of origin	Turkey	141 (97.9)	Turkey	187 (87.4)
	Pakistan	1 (0.7)	India	12 (5.6)
	Malaysia	1 (0.7)	Italy	2 (0.93)
	Bulgaria	1 (0.7)	Greece	2 (0.93)
			New Zealand	1 (0.46)
			England	1 (0.46)
			Spain	1 (0.46)
			Bosnia	1 (0.46)
			Egypt	1 (0.46)
			Brazil	1 (0.46)
			USA	1 (0.46)
			Portugal	1 (0.46)
			Japan	1 (0.46)
			Malaysia	1 (0.46)
			Serbia	1 (0.46)

TAO: Turkish Archives of Otorhinolaryngology, n: number of articles, ORL: Otorhinolaryngology, USA: United States of America

first author and 182 (75.8%) were made by foreign authors (Table 4). The total numbers of the citations according to the WoS indexes including the SCI-E, the ESCI and other indexes were 169 (70.4%), 67 (27.9%) and four (1.7%), respectively (Figure 2). While of the 58 citations performed by Turkish authors, 30 (51.7%) were in journals indexed in SCI-E, 28 (48.3%) were in journals indexed in ESCI. Also, nine of all citations (3.8%) were performed in other articles published in the TAO.

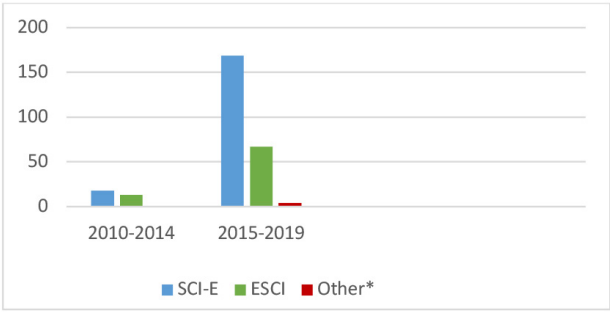

Figure 2. Distribution of the citations according to the WoS indexes from 2010 to 2014 and from 2015 to 2019

ESCI: Emerging Sources Citation Index, SCI-E: Science Citation Index Expanded, *Other: Conference Proceedings Citation Index-Science, Book Citation Index-Science

The EIFs that were manually calculated for TAO for each year from 2017 to 2021 are shown in Table 5. The highest EIF was found in 2020.

Discussion

The publish or perish concept is still valid in the academia, however, the growing body of scientific works is imposing to expand the area of publication (12). As a result, for-profit journals have increased their share in the domain and become a significant rival for not-for-profit journals. Community-based journals, including those published by scientific societies, however, offer clear benefits to the scientific community in that they are peer-approved and certified, accessible and supportive, agile and responsive, relevant, recognized, and targeted (13). As a follower of these universal concepts, the TAO has been endeavoring to improve the Turkish ORL literature nearly for 60 years, representing a substantial part of the Turkish Otorhinolaryngology-Head and Neck Surgery Society. To support the propitious attempts of the Turkish Otorhinolaryngology-Head and Neck Surgery Society aimed at serving for the development of community-based publishing in the Turkish ORL literature, we intended to carry out the present bibliographic study on the last decade of the TAO.

To our knowledge, the presented study is the first to conduct the sequential analysis of a Turkish ORL journal. According

Table 2. Characteristics of citations obtained from the WoS for the articles published in the TAO from 2010 to 2014 and from 2015 to 2019

	2010–2014			**2015–2019**		
Total citations (n)	**31**			**240**		
	Article (n)	**Citation (n)**	**Mean**	**Article (n)**	**Citation (n)**	**Mean**
Study topic						
Otology	27	8	0.29	45	54	1.2
Rhinology	36	8	0.22	39	45	1.15
Head and neck	41	8	0.19	49	46	0.93
Pediatric ORL	7	1	0.14	21	26	1.23
General ORL	33	6	0.18	60	69	1.15
Study type						
Original investigation	59	15	0.25	123	159	1.29
Case report	79	15	0.18	63	46	0.73
Review	6	1	0.16	11	16	1.45
Letter to the editor	0	0	0	6	12	2
Clinical image	0	0	0	3	3	1
Editorial article	0	0	0	6	4	0.66
Historical article	0	0	0	2	0	0
Country of origin						
Turkey	141	75	0.52	187	225	1.2
Foreign countries	3	0	0	27	15	0.55

TAO: Turkish Archives of Otorhinolaryngology, WoS: Web of Science, n: number of citations, ORL: otorhinolaryngology

to the results of the presented study, there was a remarkable increase in the number of citations in the period 2015–2019 compared to 2010–2014. There also was a remarkable increase in the EIF values for 2019 and 2020. Citations as a classical bibliometric tool still hold their position as a significant indicator for the scientific influence of a journal, despite its substantial drawbacks (3). Citations majorly measure the impact of a researcher as it pertains to other researchers without examining knowledge translation and reader uptake. Hence, its bibliometric significance seems to be an ongoing controversy and promotes the quest for alternative bibliometric indicators such as Altmetrics which measure

Table 3. Distribution of the citations obtained from the WoS according to the country of origin from 2010 to 2014

Country of origin	n (%)	Country of origin	n (%)
Turkey	16 (51.6%)	Oman	1 (3.2%)
USA	7 (22.6%)	Pakistan	1 (3.2%)
Ukraine	2 (6.5%)	Spain	1 (3.2%)
India	1 (3.2%)	Taiwan	1 (3.2%)
Egypt	1 (3.2%)		

TAO: Turkish Archives of Otorhinolaryngology, WoS: Web of Science, n: number of citations, USA: United States of America

Table 4. Distribution of the citations obtained from the WoS according to the country of origin from 2015 to 2019

Country of origin	n (%)	Country of origin	n (%)
Turkey	59 (24.58%)	Finland	2 (0.83%)
USA	41 (17.08%)	Germany	2 (0.83%)
China	19 (7.91%)	Indonesia	2 (0.83%)
Italy	14 (5.83%)	Israel	2 (0.83%)
South Korea	10 (4.16%)	Malaysia	2 (0.83%)
Iran	8 (3.33%)	Pakistan	2 (0.83%)
Saudi Arabia	8 (3.33%)	Belgium	1 (0.41%)
Brazil	6 (2.5%)	Czech Republic	1 (0.41%)
England	6 (2.5%)	French	1 (0.41%)
India	6 (2.5%)	Denmark	1 (0.41%)
Poland	5 (2.08%)	Hungary	1 (0.41%)
Romania	5 (2.08%)	Iraq	1 (0.41%)
Japan	4 (1.66%)	Mexico	1 (0.41%)
Taiwan	4 (1.66%)	Portugal	1 (0.41%)
Canada	3 (1.25%)	Russia	1 (0.41%)
Egypt	3 (1.25%)	Scotland	1 (0.41%)
Greece	3 (1.25%)	Slovakia	1 (0.41%)
The Netherlands	3 (1.25%)	Slovenia	1 (0.41%)
Switzerland	3 (1.25%)	Spain	1 (0.41%)
Australia	2 (0.83%)	Zambia	1 (0.41%)
Colombia	2 (0.83%)		

WoS: Web of Science, n: number of citations, USA: United States of America

Table 5. Estimated impact factor of the TAO for 2017–2020

Year	Citation (n)	Citable Article (n)	EIF
2017	13	72	0.1805
2018	5	73	0.0684
2019	33	84	0.3928
2020	65	86	0.7558

EIF: estimated impact factor, n: n: number of citations

the attention gathered by a work on the Web (14). However, it should be emphasized that new bibliometric indicators have also some disadvantages such as lack of standardization or control of scientific community. Therefore, editorial boards should primarily focus on the scientific merit of the submitted manuscripts and bibliometric indicators should be used as auxiliary tools for improving the scientific quality of the journal.

In the presented study, head and neck (28.5%) and rhinology (25%) were found to have the leading number of publications among the study topics in 2010 to 2014, whereas general ORL (28.1%) and head and neck (22.9%) had the highest number of publications in 2015–2019. However, in the context of the number of the citations, publications regarding otology (0.29) and rhinology (0.22) had the highest mean value of citations among the study topics in 2010–2014, whereas pediatric ORL (1.23) and otology (1.2) were the leading topics in terms of mean citation values in 2015–2019. In 2002, Fenton et al. (15) analyzed ORL citation classics from 1900 to 1999 and reported that otology/lateral skull base surgery (48.75%) and head neck surgery (33.75%) were the most frequent topics in the list. More recently, Coelho et al. (16) revisited the citation classics in ORL journals indexed in the WoS in 2014 and found that otology (51.7%) and head neck surgery (37.8%) were the leading topics. It should, however, be noted that the studies of Fenton et al. (15) and Coelho et al. (16) did not involve pediatric ORL as a topic. The results of the presented study showed that the citation trend shifted to pediatric ORL and otology in the TAO during 2015–2019. Like the presented study, Erdağ et al. (17) reported that otology and pediatric ORL were the most cited topics among the 100 most cited Turkish papers in the ORL journals of the WoS.

Reviews and original investigations were the most cited study types in the presented study with mean numbers of citations of 1.45 and 1.29 in 2015–2019, respectively. Original investigations and case reports, on the other hand, had the highest mean values of citations (0.25 and 0.18, respectively) in 2010–2014. As the second most published study type in the TAO in 2015–2019, case reports had 0.73 citation per study. Although the historical origin of the case reports dates to the BC era (18), the contribution of the case reports to the development of science have become a matter of debate especially in the last 20 years (19). Concerns related to the low evidence levels and the citation potentials of case reports are likely to be the most important factor for the editors' reluctance to publish a case report instead of more solid options, such as original investigations, reviews or meta-analyses, for improving the impact factor of a journal. Nevertheless, the benefits of case reports, such as informing the scientific community about new diseases or treatment methods should not be ignored. Furthermore, case reports have also become a significant contributor to initiate and/or improve the preparation of a scientific article for recruiters (20, 21). In the presented study, in contrast to the common beliefs concerning the low citation potential of a case report, we found that case reports published in the TAO in the years 2015 to 2019 had received considerable number of citations (46 citations for 63 article) which may support the ongoing significance of the case reports in the scientific publication.

Although there is no clear value regarding the exact rate accepted as a national bias of citation, improper national citations for improving a journal's impact factor may yield to ethical misconduct like those experienced in some Brazilian journals in 2012 (22). Also, encouraging the citation of a journal's own papers to artificially boost the impact factor of a journal may be considered as an ethical misconduct. However, citations to high-quality studies, whether national or self-citation to the journal's own papers, should not be subjected to ethical consideration, therefore, researchers should not hesitate, due to ethical concerns, to cite these papers. Erdağ et al. (10) reviewed the references of studies published in the 2015 issues of four Turkey-based ORL journals and found that 460 of 2,708 references (16.98%) had a Turkish first author. The authors also determined that 85 articles published in ORL journals indexed by SCI in the same period had a Turkish first author. In these articles, 271 of total 2,252 (12.03%) references were from Turkey and 18 of these were published in journals from Turkey. The data provided by Erdağ et al. (10) suggest that Turkish authors rather tend to cite national studies, both in their studies published in SCI-indexed ORL journals or national ORL journals. In the presented study, 58 out of 240 (24.2%) citations retrieved from the WoS databases for the articles published in the TAO in 2015–2019 were by Turkish authors, whereas 182 (75.8%) were by foreign authors. It is also worth noting that 30 out of 58 citations (51.7%) made by Turkish authors were in journals indexed in the SCI-E, whereas 28 (48.3%) were in journals indexed in the ESCI. Interestingly, there were only nine citations (3.8%) to TAO's own papers.

The presented study has several limitations. First, citation for an article is a dynamic and ongoing process and databases themselves have inherent limitations that may cause potential errors. Second, the bibliometric analysis of the citations regarding the period 2010–2014 was done only through Google Scholar databases since the articles published in the TAO were not listed in the WoS databases in this period. Twenty-two out of 214 articles published in the years 2010 to 2014 were not included in Google Scholar, therefore the citation analysis of these articles could not be done. Third, the TAO had no official journal citation report created by Clarivate Analytics, therefore, impact factors values were calculated manually.

Conclusion

Although the increase in the number of citations and in impact factor values cannot be appreciated as a single indicator for the success of a journal, the results of the presented study revealed a promising advancement in the scientific quality of the TAO, driven by the inclusion of the journal in the national and international indexes, the change in the language of the journal to English and the well-orchestrated editorial efforts.

Ethics Committee Approval: This study does not require the ethics committee approval due to the fact that the study is a citation analysis.

Informed Consent: This study does not require informed consent due to the fact that the study is a citation analysis.

Financial Disclosure The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

Main Points

- Turkish Archives of Otorhinolaryngology was first indexed in TÜBİTAK ULAKBIM TR, Emerging Sources Citation Index and PubMed Central after its publication language was changed to English in 2015.
- While the most frequent study type was case report and most frequent topic was head and neck in 2010 to 2014, these were original investigation and general otorhinolaryngology, respectively, in 2015 to 2019.
- According to Google Scholar and WoS databases, there was a remarkable increase in the total number of citations in 2015–2019.
- The presented study showed a promising advancement in the scientific quality of the TAO, driven by the inclusion of the journal to national and international indexes and by changing the language of the journal to English, as well as the well-orchestrated editorial efforts.

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Radiological Features and Pathognomonic Sign of Stapes Footplate Fistula in Inner Ear Malformations

Original Investigation

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Abstract

Objective: Some inner ear malformations may cause recurrent meningitis, which may be fatal. The etiology is usually a stapes footplate fistula which enables microorganisms to pass into the inner ear containing cerebrospinal fluid (CSF), causing repeated attacks of meningitis. Radiological signs of the fistula are not obvious and are not reported in detail in the literature. The aim of the study is to investigate the radiological features of stapes footplate fistula in inner ear malformations.

Methods: Radiological findings were analyzed for seventeen patients with inner ear malformations (IEMs) operated on because of recurrent meningitis. Using this information, images of 1,010 patients with IEMs were retrospectively reviewed to investigate the radiological findings of stapes footplate fistula and their relationship to IEMs. They were classified according to the Sennaroglu classification system, and according to different stages of stapes footplate fistula.

Results: In the case of a stapes footplate cyst, computerized tomography shows an opacity at the oval window. On magnetic resonance imaging, a fluid filled cystic structure continuous with and having similar signal characteristics to the CSF in the inner ear is a pathognomonic finding of a stapes footplate cyst. It is most commonly found in common cavity anomaly (18.2%); the second most frequent finding is incomplete partition type I (15%). And it can even be seen in cases of cochlear aplasia where only the vestibule is present.

Conclusion: If the history reveals recurrent meningitis, particular attention should be given to the oval window area, where an opacity, cyst or a leaking lesion should be looked for on the imaging. It is the responsibility of the otolaryngologist to notice these findings, and to operate on the patient to prevent further attacks of meningitis.

Keywords: Inner ear, stapes footplate fistula, congenital abnormalities, cochleovestibular anomalies, meningitis, diagnostic imaging, computerized tomography, magnetic resonance imaging

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Introduction

Meningitis is a serious disease that can be fatal. Recurrent meningitis is particularly important, because it means there is a condition that is predisposing the patient to meningitis once again (1). Inner ear malformations (IEMs) are one of the most important causes of recurrent meningitis; the disease is predominantly seen in children who have more attacks of acute otitis media when compared to adults (1, 2). It is the responsibility of the otolaryngologist to identify and treat the condition that causes recurring meningitis, in cases of IEMs, to prevent further complications.

In IEMs, the pathology causing recurrent meningitis is at the stapes footplate (2). Normally, the stapes footplate consists of a thin bone covered by the middle ear mucosa. During otitis media, the bony footplate provides a sufficient barrier to the medial spread of the microorganisms into the labyrinth. In the case of stapes footplate fistula, there is a bony defect at the stapes footplate, which is covered by a thin mucosal membrane or a cystic structure (2). This is not a true cyst, but a small, cerebrospinal fluid (CSF)-filled mucosal pouch in continuity with the vestibule. It is possible to have a leaking fistula as well. In the course of a middle ear infection, microorganisms pass easily through the thin membrane and defective footplate, and cause infection of the CSF immediately medial to the cyst; this results in meningitis.

Apart from being a fatal disease, in a case of single sided deafness, IEM on one side may cause meningitis and sensorineural hearing loss (SNHL) in the contralateral normal hearing side. The patient may become a candidate for a cochlear implant (CI), or even an auditory brainstem implant in cases of total ossification (Figure 1). Conditions predisposing the patient to recurrent meningitis must therefore be diagnosed and treated accordingly.

Until now, incomplete partition type I (IP-I) and cochlear hypoplasia type II (CH-II) have been regarded as the two subgroups of IEMs that may be associated with stapes footplate defect (2). Although the history may reveal recurrent meningitis and the radiologic examination demonstrates IEM, radiological signs of stapes footplate fistula are not very obvious and not well defined. Recently Mok et al. (3) published a case series showing the opacity of the cyst on computerized tomography (CT); however, a study investigating all IEMs from this perspective has not yet been done. As meningitis is a serious, life-threatening condition, it is important to know which anomalies can cause meningitis, and to define its non-obvious signs.

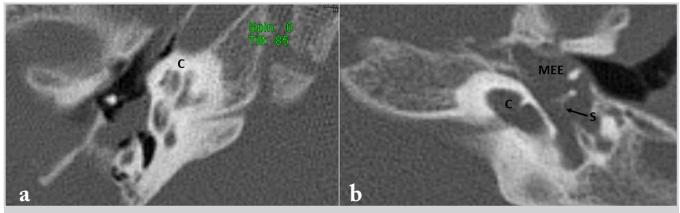

Figure 1.Cochlear hypoplasia type I (C) on the left side (a) causing meningitis and ossification on the normal hearing side on the right (b) C: Cochlea, S: Stapes, MEE: Middle ear effusion

Between 2008 and 2020, 17 cases of stapes footplate fistulas causing meningitis were operated on, and footplate defects were repaired; surgical decisions and choices of the side to be operated on were made based on imaging findings that were not very obvious. The surgical findings and outcomes of these cases are reported in a separate paper (4).

The first patient presented with a history of two attacks of meningitis after CI surgery. CT revealed fluid filling the middle ear and mastoid contralateral to the CI. Surgical indication and side selection were done according to middle ear effusion (not on the side with CI) and exploration of the middle ear revealed CSF leak and a footplate cyst. The second patient who had experienced two meningitis attacks had rounded soft-tissue density on the footplate area on the CT. This finding was thought to represent the cystic structure at the footplate, and surgery was planned accordingly. During her operation, a cyst was discovered at the footplate. From this moment on we started to look for soft-tissue density in the footplate area on CT, and for fluid (with similar intensity to CSF) filling the middle ear and the mastoid, in cases of meningitis in IEMs. More recently a cystic structure of similar characteristics, showing CSF filling the inner ear on the MRI, has also been used as an indication for middle ear exploration.

Surgical findings in these 17 patients were analyzed and reported in detail (4). The radiological findings in these patients were investigated retrospectively in 1,010 patients with IEMs; the radiological signs of stapes footplate fistula are reported in this paper.

Methods

Between 2008-2020, 17 patients who had recurrent meningitis with CSF fistula were surgically explored and the leak sites were repaired. The types of IEMs causing meningitis consisted of incomplete partition I (IP-I) and cochlear hypoplasia (CH) cases. The decisions for surgery and the choices of the side to be operated on were made if there was an effusion filling the middle ear, soft-tissue density at the oval window on CT, or a cystic structure at the oval window area on magnetic resonance imaging (MRI) (4).

Between 1998 and 2020, the author evaluated the images of 1,010 patients with IEM. They are classified according to the eight categories of the Sennaroglu classification system, which was finalized in 2013 and published in 2017 (5). In 2020, images of all 1,010 patients were evaluated once again in order to correlate the radiological signs of stapes footplate

fistula with the eight categories of IEMs. Institutional approval was obtained for this study (2020/17–21).

Based on surgical and radiological data, the stapes footplate fistula is classified as follows (Figure 2)(4):

1-Normal stapes footplate (Figure 2a): A thin and intact bony stapes footplate separates the middle ear and the vestibule.

2-Stapes footplate defect (Figure 2b): There is a defect in the stapes footplate covered by the middle ear mucosa.

3-Stapes footplate cyst (Figure 2c): There is a cystic structure originating in the vestibule, passing through the stapes footplate defect into the middle ear. This can vary in size.

4-Leaking stapes footplate fistula (Figure 2d): There is a defect in the stapes footplate and CSF is leaking from the vestibule into the middle ear and the Eustachian tube.

Based on the findings from IEM cases with meningitis that were operated on, the radiological findings in stapes footplate fistula can be classified as follows (4):

1-Normal stapes footplate: The oval window area is occupied by the stapes footplate which consists of a thin bone separating the vestibule from the middle ear (Figures 3a-b).

2-Stapes footplate defect: There is a bony defect in the footplate, covered by a thin mucosal lining, and without any cystic formation (Figure 3c). Although still a histopathological finding, it may be detected by the next generation CT devices.

3-Opacity at the oval window on CT: A round soft-tissue density at the footplate (Figures 3d-f) is an important sign of a stapes footplate cyst. It may be difficult to diagnose the opacity when there is middle ear effusion.

It is very important to differentiate the opacity at the oval window from an aberrant facial nerve and persistent stapedial artery (See, Discussion).

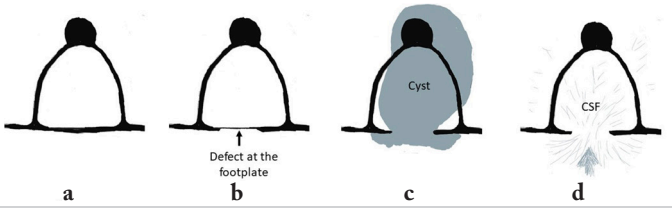

Figure 2. Classification of stapes footplate fistula: (a). Normal stapes footplate: Stapes has a thin and intact footplate, (b). Stapes footplate defect: Bony defect in the stapes footplate covered by middle ear mucosa, (c). Stapes footplate cyst: Cystic structure originating in the vestibule, passing through a stapes footplate defect into the middle ear, (d). Leaking stapes footplate fistula: There is a defect in the stapes footplate and CSF is leaking from the vestibule into the middle ear and from there into eustachian tube
CSF: Cerebrospinal fluid

4-Stapes footplate cyst on MRI: This is indicated if there is a fluid-filled cystic structure in the middle ear, continuous with and having similar signal intensity to the CSF in the inner ear (Figures 3e-g). Normally there should be no fluid-filled structure in the oval window area and the middle ear.

5-Fluid filling middle ear and mastoid: If there is fluid filling the middle ear and the mastoid, with a bright signal demonstrating similar characteristics to CSF, and fluid filling the inner ear in the CISS or FIESTA sequence on MRI (Figure 3h), this is an important sign of a leaking stapes footplate fistula. The fluid may extend via the Eustachian tube to the nasopharynx. Leaking CSF should be differentiated from fluid caused by otitis media with effusion, which has a different signal intensity on MRI (Figure 3i).

Results

The first patient with recurrent meningitis was operated on in 2008. She had bilateral IP-I anomaly and had CI surgery on the right side in 2005. On admission, she had contralateral effusion which was not present in her preoperative CT. It was therefore decided to operate on the left side. During surgery, the middle ear was filled with fluid, and there was a cyst at the footplate. Her preoperative CT demonstrated an opacity on that side that had not been noticed in 2005 at the time of her cochlear implant surgery. Therefore, as of 2008, we started to look for an opacity at the oval window area on CT in cases of meningitis in IEMs.

During surgery, there was a cyst at the footplate in nine children. Eight of these patients had a cystic structure on their preoperative MRI. The remaining patients had soft-tissue density on CT and normal findings on MRI. Therefore, if a cystic structure is present at the footplate on MRI, it can be accepted as pathognomonic for the stapes fistula cyst. Four of these patients had a CSF leak at the same time.

Twelve patients had leaking stapes fistula. One had normal CT and MRI, where the leak was encountered in the CI surgery. The remaining 11 patients showed fluid filling the middle ear and the mastoid on imaging. MRI was done on seven patients without prior CI surgery and demonstrated a fluid with similar signal characteristics to CSF. Three patients had prior CI surgery and underwent only CT scanning. CT at the time of admission demonstrated an effusion in the middle ear and the mastoid. The decision for surgery was made because of the effusion on CT, as MRI was contraindicated.

Five of the 11 patients with a leaking CSF fistula had opacity at the oval window in their original CT scanning even though there was no fluid filling the middle ear. This shows that there may be intermittent leaks from the cyst where the fluid hides the visualization of the cyst. They were all explored via an endaural approach to repair the footplate fistula.

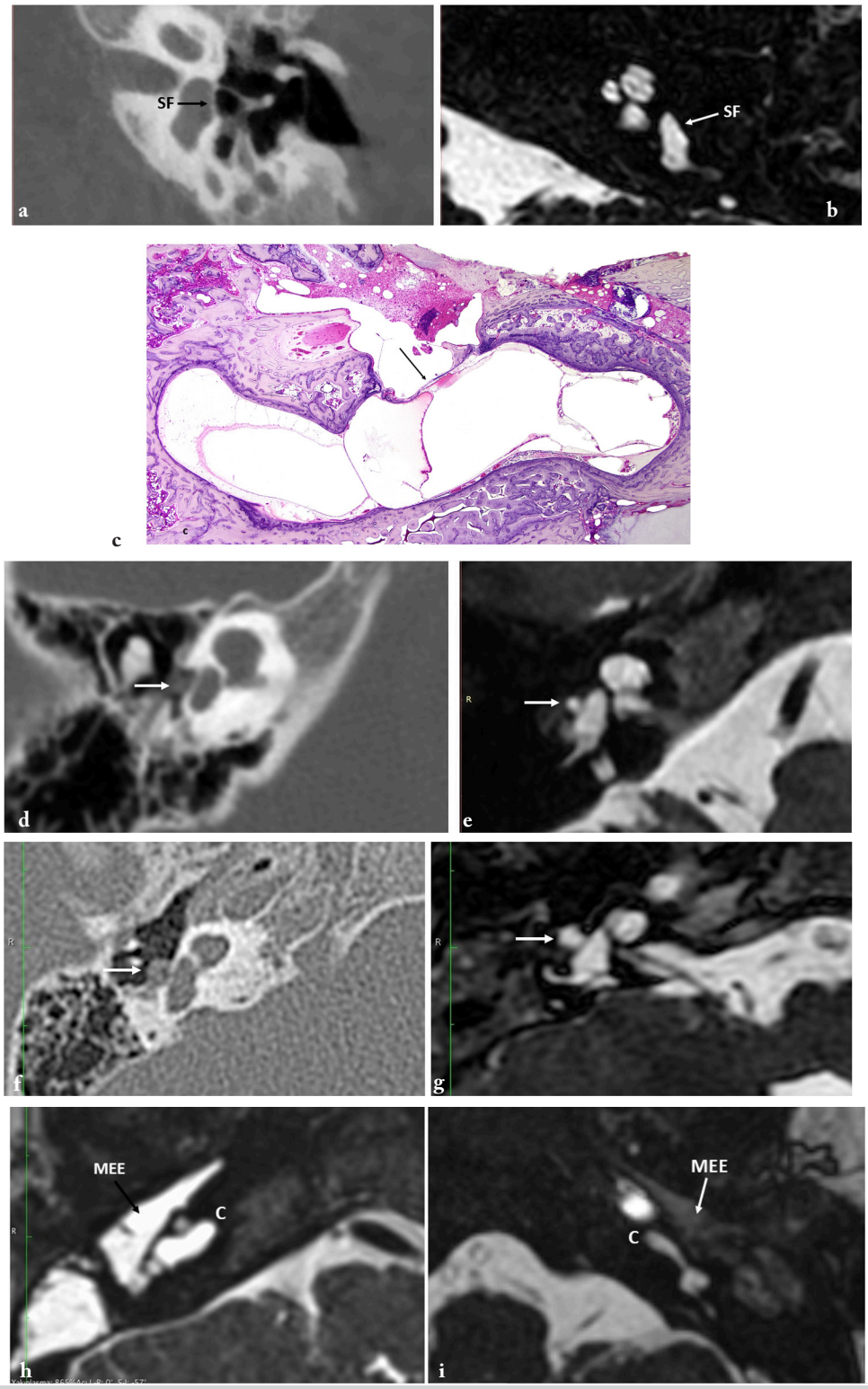

Figure 3 (a-b). Normal stapes footplate (SF) on CT (a) and MRI (b), (c). Stapes footplate bony defect covered by a thin fibrous membrane in a histopathological specimen (with Permission of the Massachusetts Eye and Ear Infirmary) (black arrow), (d-g). Computerized tomography showing a round soft-tissue density at the oval window (d-f) in IP-I cochlea. Corresponding magnetic resonance imaging demonstrates stapes footplate cyst (e-g), (h-i). Middle ear effusion (MEE). Leaking stapes fistula demonstrating MEE with a bright signal similar to cerebrospinal fluid filling the inner ear (h). Otitis media with effusion demonstrates different signal characteristics than CSF (i)
CT: Computerized tomography, MRI: Magnetic resonance imaging

Table 1. Percentage of inner ear malformations and stapes footplate fistula findings

Type of IEM	Number (right and left side)	Percentage within IEMs	Middle ear effusion (similar to CSF) on CT or MRI	Soft-tissue density at the oval window on CT	Oval window cyst on MRI	Soft tissue on CT and cyst on MRI present together	No with footplate fistula (%)
IP-I	221	10.9	7	28	29	23	**34 (15)**
IP-II	470	23.3	-	4	-	-	**4 (0.85)**
IP-III	64	3.2	-	-	-	-	-
EVA	68	3.4	-	-	-	-	-
CH-I	108	5.3	-	5	5	4	**6 (5.6)**
CH-II	114	5.6	3	5	2	2	**5 (4.4)**
CH-III	232	11.5	-	-	-	-	-
CH-IV	68	3.4	-	-	-	-	-
CC	121	5.9	-	17	18	13	**22 (18.2)**
CA	58	2.8	-	2	3	2	**3 (5.17)**
Total	**2,020**	**75.3**	**10**	**61**	**57**	**44**	**74 (3.6)**

Complete labyrinthine aplasia, rudimentary otocyst, cochlear aperture abnormalities and contralateral normal ears are excluded

IEM: Inner ear malfunction, CSF: Cerebrospinal fluid, CT: Computerized tomography, MRI: Magnetic resonance imaging, IP: Incomplete partition, EVA: Enlarged vestibular aqueduct, CH: Cochlear hypoplasia, CC: Common cavity, CA: Cochlear aplasia

The remaining five patients without a leaking fistula, showed rounded soft-tissue density on CT and a cyst on MRI in the oval window area. Two patients had CI surgery prior to experiencing recurrent meningitis. Both had opacity in the oval window on their original CT scanning, and this was the indication for exploration. A similar procedure was performed, with removal of the cyst and firmly packing the fistula.

In 2020, images of 1,010 patients with IEM (2,020 ears) were retrospectively evaluated to identify the relationship of stapes footplate fistula and different groups of IEMs. There were 538 females and 472 males. The frequencies of the radiological findings are summarized in Table 1. There were seven patients where the opacity at the stapes footplate was bilateral. Four of these cases were IP-I, and three were CC.

As can be seen in Table 1, stapes footplate fistula is most common in patients with CC (18.2%). IP-I is second in frequency (15%). Oval window fistula accounts for only 2% in CH. It is encountered only in CH-I and CH-II. No patient with CH-III and CH-IV had a fistula at the stapes footplate. Interestingly, stapes footplate fistula can also be seen in cochlear aplasia cases: when the cochlea is absent, the round window cannot be visualized; but the oval window is present, and it can have a fistula (Figures 4a-b). It is very rare but possible in IP-II as well, but no case of IP-III had a fistula at the oval window.

Usually, the defect at the footplate is small, and there is a cyst of 2-3 mm, slightly larger than the stapes (Figure 5a). In rare cases, the cyst may be very large, occupying the whole middle ear (Figure 5b).

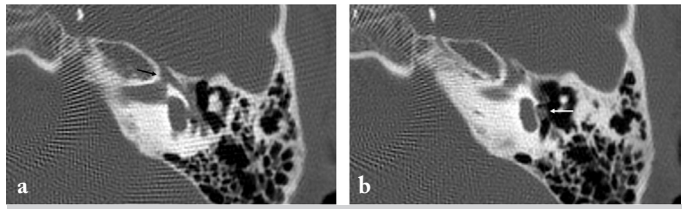

Figure 4. Cochlear aplasia with dilated vestibule (a) where labyrinthine segment of the facial nerve is at the location of the absent cochlea (white arrow). (b) Opacity is shown in the oval window area (black arrow)

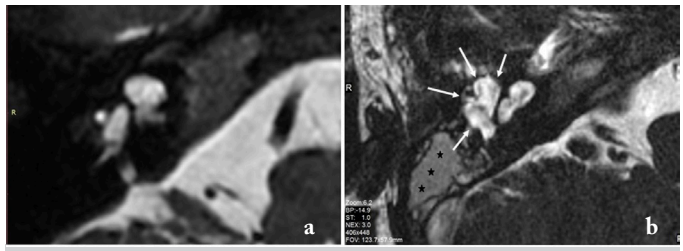

Figure 5. Different sizes of stapes footplate cyst; usually 2–3 mm cyst (a) is present at the oval window. Rarely a cyst filling the whole middle ear can be seen (b) (thin white arrows). Otitis media with effusion demonstrates different signal intensity (black stars) than CSF filling the cyst
CSF: Cerebrospinal fluid

Discussion

Recurrent meningitis in IEMs is a serious condition and has to be diagnosed and treated appropriately. It may be fatal, or cause hearing loss and ossification on the contralateral normal hearing ear in single sided deafness. Every effort must therefore be made to diagnose and treat the condition before it leads to meningitis.

Histopathology: In IEMs, the stapes footplate may have a defect which is covered by a thin membrane (Figure 3c). This defect has been reported mainly in IP-I and rarely in CH and CC (5-10). According to the database of Hacettepe University's Department of Otolaryngology, IP-I was found in 10.9% and CC in 5.9% of 1,010 patients with IEM. Therefore, CC is much rarer, and the histopathology of a true case of CC has not been reported. The presented study shows that the percentage of stapes footplate fistula is highest in the CC group. IP-I, CH-I, CH-II and CC are all endosteal developmental malformations (2). Therefore, a footplate defect is possible in all these cases.

One of the most interesting findings is the presence of a fistula in cochlear aplasia. When the cochlea is absent, the round window is absent, but the oval window is present. Three cases (5% of cochlear aplasia cases) demonstrated findings of stapes footplate fistula. All of these were cases of cochlear aplasia with dilated vestibule. When the vestibule is dilated, it is possible to think of an endosteal developmental abnormality. This supports the above explanation.

Pathophysiology: Normally, the oval window is occupied by the stapes footplate, which is a thin, bony structure with middle ear mucosa on top; it prevents the spread of middle ear infection into the inner ear and CSF-containing area. But if there is a stapes footplate defect or a cyst, this creates a defective area. In a case of acute otitis media, microorganisms can pass easily through the thin membrane into the CSF-containing area, causing meningitis. This condition is mainly seen in children who are more prone to acute otitis media than adults (2). If there is no middle ear infection, this defect may not be noticed at all throughout the life of the patient. Our patients with stapes footplate fistula had meningitis in spite of their having had a pneumococcus vaccination (4). Therefore, while vaccination is very important in patients with IEMs, it may not prevent meningitis in cases of stapes footplate cyst. None of the patients had meningitis after footplate repair; it is therefore important to diagnose and repair the footplate defect, even if it is asymptomatic.

Until 2014, high CSF pressure was held responsible for causing the stapes footplate defect in IP-I (1). Evaluation of IEMs in the Massachusetts Eye and Ear Infirmary revealed that it was possible to have a footplate defect even in the presence of a thin but intact modiolar base (Figure 3c) (2). This shows that it is not the CSF pressure causing the defect. Sennaroglu (2) explained this finding in terms of an endosteal developmental anomaly, which is the result of decreased blood flow from the IAC. This results in a very thin and defective endosteum (the innermost layer of the otic capsule) all around the cochleovestibular space, while the middle enchondral and outer periosteal layers are normal. The same explanation holds for CC, CH-I, and CH-II.

In IP-III there is a large defect at the base of the cochlea. These cases had a 100% risk of a CSF gusher during CI surgery, but none had a footplate fistula and recurrent meningitis. There is no histopathological specimen with IP-III, but it can be interpreted from the temporal CT scanning that there is a thick endosteal layer in IP-III, while the outer two layers of the otic capsule are missing. This causes stapes fixation without any fistula at the stapes footplate. Therefore, spontaneous stapes footplate fistula formation in IP-III has not been observed by our group or reported in the literature. This also highlights the fact that high CSF pressure cannot be held responsible for spontaneous stapes footplate fistulas.

The defect at the footplate is present at birth, but if there is no acute otitis media, the defect is not noticed, and patients live with it for the rest of their lives. In the event of a middle ear infection, it causes meningitis. If there is a bony separation between the IAC and the cochlea (preventing entry of CSF into the inner ear), the footplate defect may not be noticed at all during the patient's lifetime. A footplate fistula can only be noticed if there is a middle ear infection, which may cause meningitis when the infection passes through the thin membrane at the footplate, and into the CSF filling the cochlea.

We have seen patients with stapes footplate fistula who had meningitis despite having had pneumococcus vaccination. After the infection, the middle ear should be explored, and the fistula repaired. In all the cases that we explored the fistula was at the oval window. Once the fistula is repaired by a millimetric piece of fascia inserted into the vestibule in a dumbbell fashion, this provides a sufficient barrier, preventing the spread of microorganisms into CSF-containing areas, hence preventing meningitis.

Terminology: There are different terms used to describe this situation. As the pathology is at the stapes footplate, the best terminology appears to be stapes footplate fistula. A fistula is an abnormal connection between two spaces. Because it can happen even in cases of cochlear aplasia, "cochlear fistula" may not be an appropriate term. If there is continuous leakage, the term "leaking stapes footplate fistula" describes the situation correctly. On CT, we cannot differentiate the soft-tissue density, so the best terminology appears to be "round soft-tissue density at the stapes footplate." On MRI, if we observe a fluid-filled structure continuous with inner-ear fluid and CSF, it is termed "stapes footplate cyst." During surgery, the author removed the cystic structure from the footplate defect. However, a real cyst does not have any opening into any other surface, and therefore this pathology is different from a true cyst. Likewise, the term "cochleocelle" used by Mok et al. (3) may not be appropriate because the pathology does not originate from cochlea, and it can be observed even in the absence of a cochlea. One suggestion

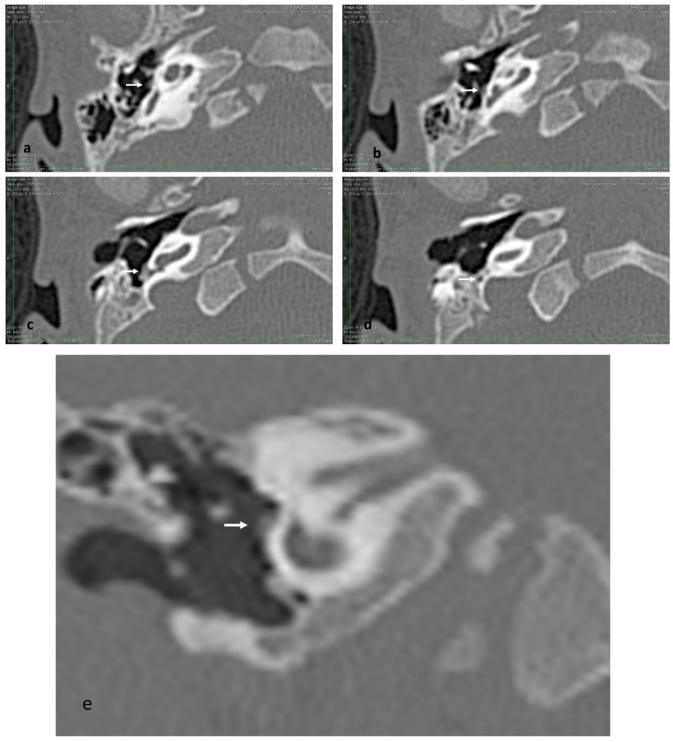

Figure 6. Aberrant facial nerve. Computerized tomography showing soft-tissue density (white arrow) around the oval window area (b) which can be followed proximally to the labyrinthine segment and distally to the mastoid segment on axial sections (a-d). On coronal section facial nerve (white arrow) is located inferior to oval window (e)

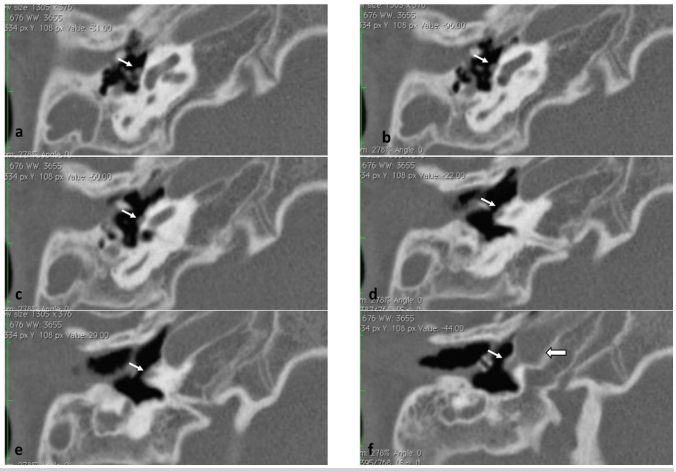

Figure 7. Persistent stapedial artery. Computerized tomography (a) shows a soft-tissue density in the left oval window area (thin white arrow). When followed distally it is located on the promontory and opens into carotid artery (thick white arrow) (a-f)

is to use the term "endosteocele;" this may be appropriate if we think of the origin of the cystic structure as the inner ear endosteum.

Imaging: Why is the sign on MRI pathognomonic? If we see a cystic structure in the oval window area in the middle ear, continuous with the vestibule and having bright signal on high-resolution T2 weighted images such as CISS or FIESTA sequences, this indicates that it is coming from the inner ear. If the fluid signal is widespread, it may be a leaking fistula. The soft-tissue density on the CT must be differentiated from an aberrant facial nerve and persistent stapedial artery.

It is very important that the otolaryngologist summarizes the patient's history in the request for imaging, particularly mentioning meningitis. If there is a history of recurrent meningitis, the stapes footplate area should be carefully evaluated on CT and MRI. If soft-tissue density or a cyst is noticed on imaging, it must be highlighted in the report. A previous study demonstrated that a slice-thickness of 0.5 mm for CT and MRI is appropriate to demonstrate the findings of stapes footplate cyst (4).

Radiological Signs of Stapes Footplate Fistula Necessitating Surgery: None of the patients who were operated on had a clear diagnosis of fistula before exploration. In cases of recurrent meningitis, the presence of the following points may be a sign of stapes footplate fistula necessitating middle ear exploration:

1. IEM of the subgroup: Common Cavity, IP-I, CH-I, CH-II, Cochlear aplasia

2. A round soft-tissue density at the oval window area on CT

3. Cystic structure in the oval window area on MRI

4.Middle ear effusion in the above IEM types, continuous and having a similar signal to the CSF-containing inner ear on MRI, which may extend through the Eustachian tube into the nasopharynx

As surgeons, we should not forget that if there is a suspicion of a CSF leak it is advisable to go ahead with surgery rather than to wait and see.

Special attention is necessary in patients with common cavity. In some of these cases, the vestibule is hypoplastic, and if the area is not evaluated with thin-section, high-resolution CT imaging, footplate cyst may not be demonstrated.

Differential Diagnosis: It is important to differentiate this condition from other pathologies at the oval window.

1. Aberrant facial nerve at the oval window. This has a characteristic finding on coronal CT (Figure 6e). There is no neural tissue at the usual location of the facial nerve, which is normally located inferior to lateral SCC, superior and lateral to oval window. When the soft tissue is followed proximally and distally on axial sections (Figures 6a-d) the canal for the facial nerve can be differentiated easily from the cyst which is located only at the oval window. In stapes footplate fistula,

facial nerve is at its usual location. In cases of aberrant facial nerve, there is no fluid signal indicating a cystic structure on MRI.

2. Persistent stapedial artery. There is a rounded soft-tissue density at the oval window. It can be followed distally until it is connected to the internal carotid artery (Figures 7a-f). If there is a stapes footplate cyst it cannot be followed proximally and distally as can be in the latter two situations.

Conclusion

In inner ear malformations, meningitis may be fatal but may also cause SNHL on the contralateral normal hearing side in single-sided deafness. Patients with single-sided deafness therefore need to undergo CT and MRI, for the purpose of carefully evaluating the footplate, and not missing an oval window fistula that may result in meningitis. It is very important to diagnose a stapes footplate fistula preoperatively. A cystic structure on MRI is pathognomonic, but a round soft-tissue density on CT should arouse suspicion: these are indications for middle ear exploration. Stapes footplate fistula is most common in common cavity and incomplete partition type I cases.

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Free Flap Reconstruction of the Head and Neck Region: A Series of 127 Flaps Performed by Otolaryngologists

Original Investigation

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Abstract

Objective: To determine flap success rate and complications in patients who underwent microvascular free tissue reconstruction after major head and neck ablative surgery and to report the improvement in the results.

Methods: Medical records of 124 patients who were operated on in 2012 to 2019 were retrospectively reviewed. Indications for different free flap types, success rates and re-exploration rates, donor site morbidities, and reasons for flap loss were analyzed. Patients were divided into two groups to identify the effects of the anticoagulant and the antiaggregant treatments on postoperative results.

Results: There were 127 flaps in 124 patients, including two different free flaps each in three patients that were harvested and used in the same surgical session. Of the total 127 flaps, 82 (64.6%) were radial forearm flaps, 39 (30.7%) were fibula flaps, and 6 (4.7) were rectus abdominis flaps. Four patients were re-explored for flap perfusion problems, and 18 patients were re-explored for hematoma drainage (n=22/124, %17.3). The rate of hematoma and re-exploration was higher in patients who received anticoagulant and antiaggregant treatments synchronously (p=0.02). Three flaps were lost, and the overall success rate was 97.6%. Two patients died from perioperative complications. No major complications were observed at the donor site; minor complications were observed in 30 patients.

Conclusion: The success rate for the 127 flaps in 124 patients were found comparable to those reported in the literature. These results show that successful outcomes can be achieved with experience and a head and neck team dedicated to improving the results in microsurgical reconstruction, and flap failure rarely occurs if perioperative care of the patients is given meticulously.

Keywords: Head and neck cancer, reconstructive surgery, microsurgical free flaps, otolaryngologists

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Introduction

Survival from head and neck cancers continues to improve with the help of early diagnosis and the advancement in treatment strategies (1). As a principle, the primary goal of the cancer treatment is to achieve good oncological control. This is followed by the goal of rehabilitating functional loss and cosmetic defects with utmost care. Cancer survivors can maintain their social and economic position as long as their quality of life is not significantly affected. Whilst being the anatomic region of the sense organs and the most important part of the body in a person's social interaction, the head and neck is also the region where significant functional and cosmetic loss occurs as a result of cancer treatment (2, 3).

There are local flaps, rotational flaps, and pedicle flaps described to be used for the reconstruction of the surgical defects after primary ablation or salvage surgery of the head and neck tumors. Free flaps, on the other hand, are considered as the gold standard in head and neck reconstruction surgeries since they supply multiple different tissues, such as skin, muscle, bone, and nerve, without limitation of transfer to the surgical resection site (4, 5). As a result, free flaps provide better cosmetic and functional outcomes. They also offer the advantage of allowing two surgical teams to work at the same time. Additionally, harvesting a tissue distant from the head and neck region can be advantageous in patients previously treated for head and neck cancer. In this study, the authors report their experience in free flap reconstruction, as well as their success rates, complications and perioperative morbidities.

Methods

In this study, the medical records of 124 patients who underwent free flap reconstruction by otolaryngologists following a major head and neck surgery in the period September 2012 through December 2019 were retrospectively reviewed. Of the 124 patients, 57 were female (45.9%), 67 were male (54.1%); their mean age was 45.9 (range: 14–72). All patients were evaluated by the tumor board consisting of head and neck surgeons, radiation oncologists, medical oncologists, a nuclear medicine physician, a radiologist, and a pathologist. The patients were informed about the possible surgical complications and postoperative morbidities, and informed consent was preoperatively obtained from all participating patients. The study was approved by the Institutional Ethics Committee of İstinye University Faculty of Medicine (decision no: 2/2021.K-02).

Ablative surgery and reconstruction were performed in the same surgical session in all patients. Three different types of free flaps were used: fasciocutaneous radial forearm flap (RFF), osseocutaneous fibula flap (FF), and musculocutaneous rectus abdominis flap (RAF). RFF and FF flaps were harvested under tourniquet from the extremities, and loop magnification (x2.5 or x3.5) was used in all. The Allen test, by which the patency of the ulnar artery is assessed, was done in all RFF patients; computerized tomography (CT) angiography of the lower extremities was done in all FF patients to exclude the presence of arteria peronea magna anomaly or atherosclerotic plaque.

The facial artery, lingual artery or superior thyroid artery were used for arterial anastomosis. Venous anastomosis was done to the thyroid vein or the thyrolingofacial trunk, or directly to the internal jugular vein as end-to-side anastomosis. Anastomoses were done under microscopic magnification with 9-0 or 10-0 polyamide suture with round needle. All patients were followed in the intensive care unit for one day to keep the blood pressure stabilized, and then transferred to the ward the next day. All patients were given anticoagulant treatment with enoxaparin sodium and some patients were also given antiaggregant treatment with acetylsalicylic acid.

The indications for the preference of free flaps, the success rate of different flap types, and the risk factors for flap loss were analyzed. The need for revision surgery, the morbidities of the donor site, and the postoperative complications that developed on the resection site were reviewed. Patient data were also analyzed by dividing the patients into two groups, as patients operated on in September 2012–August 2016 (group 1) and those operated on in September 2016–December 2019 (group 2), to identify the effects of the anticoagulant treatment on the postoperative results.

The statistical analyses were performed with the Statistical Package for the Social Sciences for Mac version 21.0 (IBM SPSS Inc.; Armonk, New York, USA). Fischer's exact test was used in analyses and $p<0.05$ was considered significant.

Results

Free flap reconstruction was performed during salvage surgery in only five patients (4%), of whom three had sinonasal malignancy (surgery+, RT+), and two had tongue cancer (surgery+, RT-). RAF was preferred to preserve the dura mater and to close the defect which resulted from craniofacial resection in two patients, and to close the total maxillectomy defect in one patient; RFF was used for the reconstruction of the tongue after subtotal glossectomy. Free flaps were preferred in the primary surgical treatment of the remaining 119 patients. The final pathological diagnosis of the patients are given in Table 1.

In total 127 flaps were used in 124 patients as three patients received synchronous two free flaps in the same surgical session. Of the 127 free flaps, 82 were RFF (64.6%), 39 were FF (30.7%), 6 were RAF (4.7%). The defects in the surgical resection sites and the flaps used for their reconstruction are listed in Table 2. In three patients with oral cavity cancer, reconstruction was achieved by double free flaps as FF and

RFF, which were designed for mandibular reconstruction in all three patients: reconstruction of the tongue in two patients and closure of the skin defect over mentum in one patient.

Recipient veins, donor arteries and type of the anastomoses were analyzed (Table 3). Except for one patient all anastomoses were done to the vessels on the side in which the flap was predominantly set. In one patient, RFF was anastomosed to the vessels on the contralateral side and then lost due to arterial insufficiency.

Anticoagulants and antiaggregants were routinely administered to all patients in group 1 (n=63) with the following doses: enoxaparin sodium 2x4000 IU, acetylsalicylic acid 1x100 mg. Because of the high rates of postoperative hematoma, antiaggregant treatment was abandoned in patients in group 2 (n=61) unless the patient had another disease that necessitated antiaggregants. Additionally, the dosage of enoxaparin was reduced to 6000 IU.

Complications

Four patients underwent surgical re-exploration because of flap perfusion problems (3.2%). In two FFs, the problem was venous insufficiency that developed in the postoperative 24 hours in both. In two RFFs, the problem was arterial insufficiency, which developed in the postoperative 24

Table 1. Final pathological diagnosis of patients

Histological type	Number of patients	Percentage (%)
Squamous cell carcinoma	100	80.6%
Osteosarcoma	7	5.6%
Ameloblastoma	5	4%
Adenoid cystic carcinoma	2	1.6%
Mucoepidermoid carcinoma	2	1.6%
Other*	8	6.5%

*Adenosquamous carcinoma (n=1), basal cell adenocarcinoma (n=1), giant cell bone tumor (n=1), esthesioneuroblastoma (n=1), Ewing sarcoma (n=1), hemangioma (n=1), ossifying fibroma (n=1) and aseptic necrosis of mandibula due to biphosphate usage (n=1)

n: Number

Table 2. Defects in the surgical resection sites, flaps used for their reconstruction, and failed flaps according to reconstruction site

	RFF	FF	RAF
Partial pharyngectomy	12		
Total laryngopharyngectomy	9		
Buccal region (mucosa or through and through defect)	12		
Total lower lip	1		
Tongue and oral base	47(2)*		1
Skin of submental and submandibular region	1		
Mandible		35(1)**	
Maxilla		4	3
Craniofacial resection			2

RFF: Fasciacutaneous radial forearm flap, FF: Osseocutaneous fibula flap, RAF: Musculocutaneous rectus abdominis flap

*Two flaps (RFF) used for tongue defect reconstruction failed

**One FF used for mandibulectomy defect failed

Table 3. Vascular anastomoses of flaps

Arterial anastomoses	Facial artery (n=111/87.4%)
	Superior thyroid artery (n=12/9.7%)
	Lingual artery (n=2/1.6%)
	External carotid artery – end-to-end (n=2/1.6%)
Venous anastomoses	Internal jugular vein – end-to-side (n=66/53.2%)
	Thyrolingofacial trunk (n=59/47.6%)
	Middle thyroid vein (n=2/1.6%)

hours in one patient and on the postoperative 14th day in another patient because of a salivary fistula to the neck. The anastomoses were explored, sutures were untied and washed with heparin and lidocaine solution. Only one flap (FF) survived; the other three flaps were lost (75%). These four patients were all in group 1, i.e., they were receiving high-dose anticoagulant and antiaggregant treatment. Including these four patients, 22 patients in total underwent surgical re-exploration (17.7%). The reason for re-exploration was hematoma in the neck in 18 patients, so the rate of hematoma was found to be 14.5%. Of these 18 patients, 12 were in group 1 (12/63, %19), and six were in group 2 (6/61, %9.8). The difference between these rates were found statistically significant (p=0.02).

Overall, only three flaps (1 FF, 2 RFFs) were lost among the 127 flaps; the success rate was found to be 97.6%. While these three losses were in group 1 (3 out of 65), there was no flap loss among the 62 flaps in group 2. The difference between these two groups regarding flap loss was not statistically significant (p=0.2445).

Morbidity and mortality

The donor site morbidities were analyzed; there was no healing problem on the donor site in 97 flaps (97/127; 76.4%). The donor site was repaired with split-thickness skin graft in all patients with RFF; partial graft necrosis occurred in 14 patients (%17.1) and defects closed by secondary intention in all 14 patients in two months after debridement. No motor or neurologic sequel of the forearm occurred in any of the patients. There was hematoma of the donor site in one patient and keloid, which required steroid injection, in another patient. In three of the FF cases, contracture of the toes with a configuration of dorsiflexion developed, but rehabilitation was achieved without sequel in two patients and with a partial sequel in one patient. Of the seven patients in whom the donor site was repaired primarily, three had necrosis of the skin in the peroneal region. In one of these patients the wound was left to healing by secondary intention after debridement. In the remaining two the findings in the crus were considered to be risky for compartment syndrome, because their legs were thick and fatty, so vacuum assisted closure was applied. Of the 32 patients whose peroneal skin were repaired with split thickness skin graft, nine had partial necrosis of the graft (28%) and the defect closed by secondary intention in two months after debridement in all. The defects were repaired primarily in the donor site of RAF; in one patient hematoma occurred in the first 72 hours and was controlled after changing the drain tube, and no abdominal hernia developed in any of the patients. While the overall average hospitalization time of the patients was 14.2 days, according to flap types, 13.4 days for RFF; 16.6 days for FF; and 10.3 days for RAF.

Two patients (1.6%) died due to perioperative complications. One of them had undergone craniofacial resection including resection of the dura and the brain parenchyma because of recurrence of esthesioneuroblastoma and the defect was reconstructed with RAF. She developed subdural hematoma on the 5th postoperative day. Despite craniotomy and drainage, she died on the 15th postoperative day because of parenchymal edema and herniation. The other patient had undergone subtotal glossectomy and reconstruction with RFF; she died due to a rupture of the innominate artery caused by a tracheostomy complication on the 14th postoperative day. There was no flap viability problem in these two patients.

Discussion

The first free flap reconstruction performed by otolaryngologists was reported by Panje et al. (6) from Iowa in 1976 for the reconstruction of the oral cavity. Today, microvascular surgery training has become a part of the head and neck surgery fellowship programs in most of the centers in Western countries, and head and neck surgeons perform microvascular reconstruction themselves (7, 8). This, however, is not the situation in Turkey, and there is not yet a fellowship program in otolaryngology. The otolaryngology residents cannot train in microvascular surgery during their 5-year residency program. Therefore, reconstruction of the head and neck region by otolaryngologists is being performed only in a few centers. In other centers, plastic surgeons take over the reconstruction stage of the surgery, or if this is not possible, local/pedicled flaps are preferred, which may cause a significant decrease in the quality of life of the patient in the rest of his/her life.

On the other hand, the duration of free flap operations is long, and they require two surgical teams working together for the ablation of the tumor and for the harvesting of the flap at the same time. Additionally, flap harvesting requires anatomical knowledge of a region different from the head and neck. These operations necessitate postoperative admission of the patients in the intensive care unit at least for one night, and require longer hospitalization times and higher healthcare costs (9). Whilst any kind of a defect in the head and neck region can be repaired by free tissue transfer, free flaps are not the first choice of the authors because of the mentioned reasons, and they opt for this type of flaps in cases of absolute indication. Reconstruction should be planned individually for every patient based on the three-dimensional anatomical features of the defect. If possible and sufficient, local flaps or pedicled flaps should be preferred since they are easier to perform and cause less morbidity in the early postoperative period.

There are numerous alternatives to free tissue flaps in the human body when perforator flaps are also included, however,

the most commonly used flaps in head and neck region are RFF, FF, RAF, anterolateral thigh, jejunum, iliac crest, and scapular free flaps (8, 10). It is assumed that the variety of flaps will increase as the experience of the microvascular surgeon increases. If, however, we look from the perspective of an otolaryngologist who is interested in head and neck reconstruction, the aim of the reconstruction should be to achieve the best functional result for the patient with minimal morbidity. The flaps described in this study were suitable and allowed the two surgical teams work together simultaneously. The other alternatives were not preferred because of different disadvantages such as: anterolateral thigh flap has a high rate of anatomical variations (11); jejunum flap requires intraabdominal intervention and participation of a general surgeon; harvesting the iliac crest flap has the risk of penetration into the abdomen; harvesting of the scapular flap requires prone positioning of the patient, and thereby does not allow for the simultaneous work of two teams. As demonstrated in our study, RF and FF meet the 90% of the free flap requirement for head and neck reconstruction, and together with the RAF, these three types of flaps fulfill the need. RFF is preferred when there is a need for fine tissue; the fascia and the skin are sufficient for the repair of the tongue (Figure 1a), the pharynx and the hypopharynx. FF is preferred when bone tissue is needed for the reconstruction of the maxilla and the mandible (Figure 1b). RAF is preferred when there is a need for bulky tissue for the restoration of the defects after total maxillectomy (Figure 1c) and total glossectomy.

FF, iliac crest, radial forearm osseocutaneous flaps and scapular flaps can be used for the reconstruction of the upper and lower jaws; in this series, FF was preferred because of the surgeons' experience. In patients with oral cavity cancer and accompanying infiltration of the skin, free tissue transfer may be indicated for not only the repair of the oral cavity structures but also for repairing the skin. With this indication, RFF and FF were performed in the same surgical session in one patient with mandibular involvement, and RFF was used for another patient without bone involvement. In cases of large skull base defects resulting from craniofacial resection, free flap reconstruction provides the tissue to restore the defect and separate the intracranial content from the nasal cavity (12). Therefore, RFF and RAF can be preferred for this purpose, and RAF was used in our series. In patients with advanced-stage hypopharynx tumors that require total pharyngectomy and end up with circular pharyngeal defect, the pharynx should be reconstructed by folding the flap tissue to form a tube as a neopharynx. An anterolateral thigh flap or RFF can be used for this purpose, while the jejunum flap is also an alternative. In our series, RFF was

Figure 1a. Reconstruction of the tongue with radial forearm flap

Figure 1b. Reconstruction of the mandible and floor of mouth with fibula flap

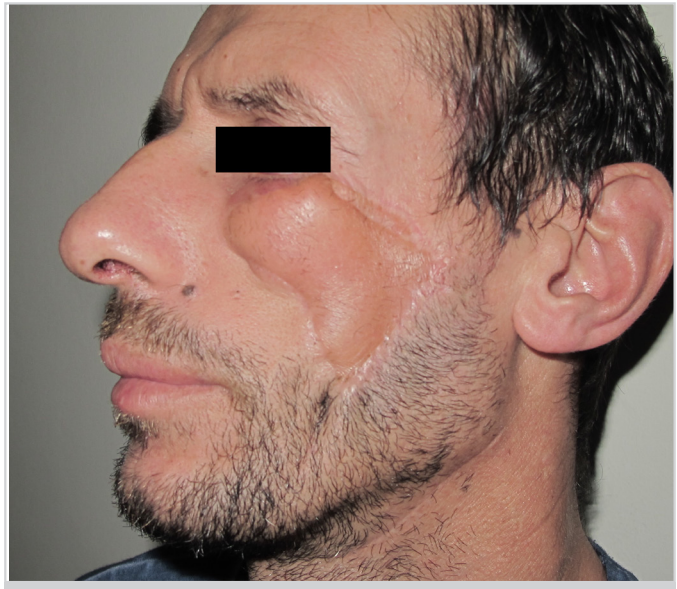

Figure 1c. Restoration of maxillectomy defect and skin defect with rectus abdominis flap

preferred, and we observed no stricture at the esophageal anastomosis line in any of the patients, and rehabilitation of swallowing was achieved in all. RFF can also be used for partial pharyngectomy defects, yet pedicled flaps are also suitable for this purpose. The fine structure of RFF, which enables it to be shaped easily, and better postoperative functional results are the reasons why it is preferred for the reconstruction of the partial pharyngeal defects (13).

In the postoperative period, a free flap surgeon should be prepared to deal with surgical field complications not only in the head and neck region but also in the donor site. No major complications developed in any patient in our series. In the literature, the most serious complication following RFF harvesting is insufficient arterial supply of the hand by ulnar artery (14). The deep palmar arch of the hand is mainly formed by the radial artery with the contribution of the ulnar artery, which mainly forms the superficial palmar arch. The anastomosis between them is tested by the Allen test (15). In a cadaver study, it was demonstrated that arterial supply of the hand by ulnar artery was insufficient in 12%, however, this study dates to 1961, and further studies are needed (14). The Allen test was performed in all 82 patients in our series and no insufficiency was observed in the test and neither did any postoperative ischemia occur.

FF is riskier for donor site complications. The arterial supply of the crus is from the popliteal artery which divides into two as anterior tibial artery, and the posterior tibial artery which gives rise to the peroneal artery that supplies the FF. In 5% of the general population, anterior and posterior tibial arteries can be hypoplastic, which leaves the arterial supply of the crus to be solely from the peroneal artery, and this variation of the arterial system is called peronea magna (16). Therefore, the arterial system of the lower extremities of patients who are planned to undergo FF harvesting should be evaluated radiologically to exclude the presence of peronea magna variation (17, 18); for this purpose, doppler ultrasonography, CT angiography, magnetic resonance angiography or conventional angiography can be used. Another benefit of radiological studies is the ability to recognize an occlusive atherosclerotic disease of the femoral arterial system. Atherosclerosis is more frequent in the lower extremities, and if we consider that a high percentage of head and neck cancer patients are smokers, we may estimate this risk to be higher in them (19). In our series, all patients were evaluated by CT angiography preoperatively; two patients were assessed to have peronea magna so cardiovascular surgeons performed peroneal artery bypass surgery, which was successful in both patients. Additionally, the planning of closure of the peroneal region should be done with care in patients with fatty crus. Harvesting of a RA flap may lead to the development of an abdominal hernia. During the closure of the donor site, the use of a mesh decreases the incidence of hernia formation (15). We did so in each RAF case, and no hernia was observed in the long-term postoperative follow-up.

Although free flap surgery has specific difficulties in the different stages of the procedure, including harvesting of the flap and flap inset, the most important stage that determines the success of the surgery is vascular anastomosis. The problems in anastomosis usually develop in the first 24 hours; the endothelization of the tunica intima is completed in the first 72 hours so complications related to flap vascularization rarely occur after 72 hours (20-22). The use of antiaggregants and anticoagulants to prevent the development of thrombosis until the completion of the endothelialization of the intima is usually considered useful, but is still controversial. In the literature, while some authors recommend their routine usage, some others recommend it only in patients with high risk of atherosclerosis or in those with previous flap failure (23-25). The most frequently used agents are acetylsalicylic acid, enoxaparin and dextran 40; however, none of them are proved to be clinically efficient in free flap survival (26-29). One fifth of the patients in group 1 were explored in the operating room because of development of a hematoma. This result led the authors to change the treatment regimen, after which the rate of hematoma decreased by half, and no flap loss occurred. However, it is not possible to speculate on the effects of anticoagulant and antiaggregant treatments on the flap success rate, because this was not a randomized study. Furthermore, the patients in group 1 were operated on at a time when the surgeons were relatively less experienced. Therefore, it can be recommended to surgeons who are at the beginning of their learning curve to use both anticoagulants and antiaggregants to take the highest precaution against flap failure. Large series in the literature report re-exploration rates of 8%–9% and flap success rates of 95%–100% (15, 22, 30). In our series flap success rate was 97.6%. At the beginning, the re-exploration rate was 17.7% and was decreased to 9.8% in the later period, which is comparable to the rates reported in the literature. The fact that there was no flap failure in group 2 can be explained by the authors' increased surgical experience. Although this decrease is attributed to the modification of the anticoagulation protocol, the effect of the increased experience of the surgeons cannot be denied.

Conclusion

Free flaps widen the limits of intervention in ablative surgery. Factors such as the requirement of education of microvascular surgery, long operating times, and detailed postoperative care of patients discourage the head and neck surgeon from performing microvascular reconstruction. As demonstrated in this study, however, free tissue transfer can be performed by otolaryngologist with the same success rates as reported in the literature, when the head and neck team is dedicated to achieving the best reconstruction methods. The

proficiency of the surgeon increases rapidly when the correct surgical steps are followed, and flap failure rarely occurs if perioperative care is given meticulously according to the recommendations.

Main Points

- Head and neck reconstruction following cancer surgery may be performed by otolaryngologists successfully with the same success rates as reported in the literature.
- Head and neck surgeons who plan to start with free flap surgery could concentrate on fasciocutaneous radial forearm flap and osseocutaneous fibula flap, which meet 90% of the free flap requirement for head and neck reconstruction.
- It is recommended to surgeons who are at the beginning of their learning curve with microvascular surgery to use both anticoagulant and antiaggregant therapies in order to take the highest precaution against flap failure.
- With the increase in surgical experience, anticoagulant and antiaggregant therapies may be reduced, unless the patients had another disease requiring continuous antiaggregant usage. This may reduce the risk of postoperative hematoma and the need for re-exploration.

Ethics Committee Approval: The study was approved by the Institutional Ethics Committee of İstinye University Faculty of Medicine (decision no: 2/2021.K-02).

Informed Consent: The patients were informed about the possible surgical complications and postoperative morbidities, and informed consent was preoperatively obtained from all participating patients.

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Effect of Korean Red Ginseng on Noise-Induced Hearing Loss

Original Investigation

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Abstract

Objective: Noise-induced hearing loss (NIHL) is one of the most important problems affecting both social and professional life of patients. There is no treatment method considered to be successful on the hearing loss that has become a permanent nature. Aim of this study is to evaluate protective effect of Korean Red Ginseng (KRG) against NIHL in an animal model.

Methods: Twenty-eight rats were separated into four groups [control saline (group I), control KRG (group II), saline + noise (group III), KRG + noise (group IV)]. Rats in the saline and KRG groups were fed via oral gavage with a dose of 200 mg/kg/day throughout for 10 days. Fourteen rats (group III and IV) were exposed to 4 kHz octave band noise at 120 dB SPL for 5 hours. Hearing levels of rats were evaluated by distortion product otoacoustic emissions (DPOAE) and auditory brainstem responses (ABR) at 4, 8, 12, 16 and 32 kHz frequencies prior to and on days 1, 7 and 10 after the noise exposure. Rats were sacrificed on 10th day, after the last audiological test. Cochlea and spiral ganglion tissues were evaluated by light microscopy.

Results: Audiological and histological results demonstrated that after noise the group IV showed better results than group III. In the noise exposed groups, the most prominent damage was seen at the 8 kHz frequency region than other regions. After the noise exposure, DPOAE responses were lost in 1st, 7th and 10th measurements in both group III and IV. Thus, we were not able to perform any statistical analyses for DPOAE results.

Conclusion: Our findings suggest that KRG seems to be an efficient agent against NIHL. There is need for additional research to find out about the mechanisms of KRG's protective effect.

Keywords: Noise, noise-induced hearing loss, antioxidants, treatment, ginseng, animal experimentation, audiology

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This study was presented at the 37th Turkish National Congress of Otorhinolaryngology-Head and Neck Surgery in Antalya on October 28th–November 1st in 2015, Antalya, Turkey and 12th European Federation of Audiology Societies, May 27th–30th, 2015, İstanbul, Turkey.

Introduction

Noise-induced hearing loss (NIHL) is one of the most important problems affecting both the social and the professional lives of patients (1-4). The mechanism of NIHL can be attributed to direct mechanical injury and indirect metabolic stress to the cochlea due to over production of free oxygen radicals (1, 2, 3, 5-9). Noise exposure damages different structural components in the inner ear such as hair cells, spiral ganglion, auditory nerve fibers (3, 5, 7, 9-11). These effects may evoke the formation of free oxygen radicals resulting in sensorineural hearing loss (5, 12). The risk of NIHL may be decreased by using hearing protection devices or by attenuating the environmental noise level. An alternative way to prevent or to cure NIHL may be the usage of antioxidants and pharmacological agents (6, 13).

Korean Red Ginseng (KRG) is used in traditional oriental cure with various beneficial effects for over 2,000 years (14-20). Saponin, also called ginsenoside, is a component of ginseng which is found to improve cardiac and immune functions (16-18). Cancer-protective, antihypertensive, anti-inflammatory, antidiabetic, antioxidant, anti-aging, and radiation protective properties of KRG have also been shown in recent studies (14, 16, 21-23). Saponin may inhibit lipid peroxidation and demonstrates antioxidative effects by reducing free oxygen radicals which are known to play a key role in NIHL. The aim of this study is to evaluate possible protective effects of KRG against NIHL.

Methods

Animals

Twenty-eight male Wistar albino rats were used in this study. Wistar rats were obtained from the Dokuz Eylül University, Department of Laboratory Animal Science. They were weighing between 250–350 g and any rat showing a sign of ear infection was excluded. Experimental protocol was approved by the Ethics Committee of Animal Care and Use of the Dokuz Eylül University (protocol number: 46/2014). This study was performed in accordance with guidelines established by the Ethics Committee of Animal Care and Use of the University. During the study, all measures were taken to minimize the pain or the discomfort of the rats.

Experimental Groups

In this study we used four groups, each consisting of seven rats. Group I (control saline group) was given 200 mg/kg/day saline by gavage for 10 days. Group II (control KRG group) was given 200 mg/kg /day KRG by gavage for 10 days. The KRG extract (dissolved in distilled water) used in the research was provided.

On the first day of the study, the animals in group III (noise exposed saline group) and IV (noise exposed KRG group) were exposed to noise. Group III (noise exposed saline group) was given 200 mg/kg/day saline for 10 days by gavage one hour after noise exposure. Group IV (noise exposed KRG group) was given 200 mg/kg/day KRG for 10 days by gavage following one-hour noise exposure. The researchers who performed the audiological tests and the histological examinations were blinded to the groups. The control group animals were placed the same cage for the same duration as the noise trauma animals, but without noise exposure.

Anaesthesia Procedure

A combination of 40 mg/kg ketamine hydrochloride (Ketalar, Parke-Davis, USA) and 5 mg/kg xylazine hydrochloride (Rompun, Bayer, Germany) were used for anesthetizing the animals prior to audiological procedures.

Noise Exposure

Rats were exposed to one octave-band noise centered at 4 kHz at 120 dB sound pressure level (SPL) for five hours in a room. Speakers (Spekon CT-51AS, China) by a noise generator and power amplifier (Konig PRO-2008S, Louisiana, USA) were used to produce the noise. Sound level calibrations were tested at different points of the room to ensure the stability of the stimulus.

Distortion Products Otoacoustic Emissions

Distortion Products Otoacoustic Emissions (DPOAE) were performed with the Otodynamics Echoport ILO-V6 Cochlear Emission Analyzer 5.61 (Otodynamics, London, UK), using neonate probe. The f2/f1 ratio was kept at 1.22. The levels of the stimulus were L1 (65 dB SPL) for f1 and L2 (55 dB SPL) for f2 frequency. The baseline hearing condition of rats was measured with DPOAE, and the signal-to-noise ratio (SNR) was measured at seven frequencies between 1 to 8 kHz.

Auditory Brainstem Responses

Auditory Brainstem Response (ABR) measurements were repeated prior to noise exposure (day 0) and on days 1, 7, and 10 after noise exposure. Intelligent Hearing Systems Smart-EP 10(lHS Corp, Miami, FL, USA) version was used for ABR analyses. ABR measurements were recorded by sub-dermal needle electrodes (Neuroline Subdermal, 12x0.40 mm, Ambu A/S, Malaysia). The positive electrode was seated on the vertex, the negative electrode was ventrolateral of the test ear and ground electrode was seated on the ventrolateral to the non-test ear. Tone-burst (TB) stimuli were at 4, 8, 12, 16, and 32 kHz with 1 ms rise-fall by a Blackman-window envelope in an alternated polarity. Acoustic signals were recorded by band pass filtered 30-3000 Hz, and A/D converted at sampling rate of 25 kHz. Analysis time was set

at 10 ms and artifact rejection level at 31.00 μV. The ABR waves were gathered with 1000 stimuli presented at the rate of 37.1/s. Wave II was followed to define the auditory thresholds.

Histological Examinations

Animals were sacrificed under ether anaesthesia after the final audiological tests. Bullas were extracted and fixed in 10% formaldehyde. Paraffin blocks were prepared after decalcification with 5% glacial acetic acid for three days. The organ of Corti and the spiral ganglions were evaluated by light microscopy using hematoxylin-eosin (H&E) and terminal deoxynucleotidyl transferase mediated dUTP nick-end labeling (TUNEL) staining.

Hematoxylin-Eosin Staining

Bullas were fixed in 10% buffered formalin (minimum of 48 h) for histological examination and placed in paraffin blocks. Paraffin blocks were placed in rotary microtome (Leica RM 2255, Wetzlar, Germany), and 3 μM thick parts were cut. After deparaffinization and hydration, sections were marked with hematoxylin-Eosin (H&E) (Surgipath, Bretton, Peter Borough, Cambridgeshire, UK). H&E-stained parts were used to evaluate the general morphology and histological changes of the Corti and spiral ganglion cells on light microscopy.

TUNEL Assay for DNA Fragmentation

The TUNEL method was used to identify apoptosis. Detection of DNA fragmentation in situ was visualized with the use of the ApopTag Peroxidase *in situ* Apoptosis Detection Kit (Cat. No. S7100, Merck, Darmstadt, Germany). The kit was used in accordance with the manufacturer's protocol. After fixation and washing, samples were incubated with terminal deoxynucleotidyl transferase (TdT) at 37 C for 1 h. Anti-digoxigenin-peroxidase was used for 30 min at room temperature and colored with diaminobenzidine. The cells were incubated with this method. The percentage of apoptotic nuclei was calculated as division of the number of counted apoptotic nuclei per total number of nuclei × 100%. All counting procedures were performed blindly.

Statistical Analysis

For statistical analyses SPSS 20.0 (Statistical Package for the Social Sciences, IBM Analytics, NY, USA) statistics software was used. Descriptive statistics were performed for nominal, ordinal and continuous (means and standard deviations) variables. For analyzing the significance of differences between the related and independent groups, non-parametric Kruskal-Wallis test, Mann-Whitney U test and Wilcoxon signed rank test were used. $p<0.05$ was accepted as the level of statistical significance.

Results

Audiological Findings

The baseline DPOAE and ABR results were not statistically different between the groups ($p>0.05$). ABR thresholds and DPOAE results of both group I and II did not show any significant changes in the measurements on days 1st, 7th and 10th ($p>0.05$). The DPOAE results of groups I and II are given in Table 1.

On the other hand, after noise exposure, ABR thresholds of the noise exposed groups were elevated (Figure 1). Mean TB ABR threshold of group IV was lower than that of group III at all frequencies on the 7th and 10th day measurements, but this difference reached statistical significance ($p<0.05$) only on the 10th day measurement at 8 kHz (Figure 1).

Table 1. DPOAE results (SNR) of group I and group II (mean ± SE)

Day	Frequency	Group I (dB SPL)	Group II (dB SPL)
Baseline	**1 kHz**	0.28±0.2	0.27±0.1
	1.5 kHz	5.34±1.3	5.09±1.4
	2 kHz	12.40±1.8	11.14±2.3
	3 kHz	19.60±2.0	19.58±1.9
	4kHz	25.31±2.0	27.04±2.2
	6 kHz	39.51±1.9	40.22±1.1
	8 kHz	43.97±1.4	42.54±1.1
1	**1 kHz**	0.1±01	0.87±0.4
	1.5 kHz	6.5±1.5	3.88±1.1
	2 kHz	11.3±1.5	9.19±1.5
	3 kHz	18.56±1.8	19.36±1.6
	4kHz	23.9±1.5	27.84±2.0
	6 kHz	38.1±2.05	39.14±1.1
	8 kHz	40.25±2.3	38.47±1.4
7	**1 kHz**	0.19±0.1	0±0
	1.5 kHz	3.80±1.2	3.63±1.1
	2 kHz	10.70±1.5	11.83±1.9
	3 kHz	24.95±2.1	24.00±2.4
	4kHz	32.95±1.7	31.9±2.5
	6 kHz	41.43±1.3	40.96±2.9
	8 kHz	42.40±1.8	43.97±1.44
10	**1 kHz**	0.53±0.4	0.12±0.1
	1.5 kHz	3.85±1.1	3.58±0.9
	2 kHz	9.57±1.2	9.99±1.6
	3 kHz	21.59±1.8	20.72±1.9
	4kHz	29.24±1.8	28.04±2.3
	6 kHz	39.20±1.3	40.16±0.9
	8 kHz	39.83±1.9	42.44±1.06

DPOAE: Distortion Products Otoacoustic Emissions, kHz: Kilohertz, dB SPL: Decibel Sound Pressure Level, SNR: Signal-to-noise ratio, SE: Standard error

After noise exposure, DPOAE responses had disappeared on the 1st, 7th and 10th days measurements in both group III and group IV. Thus, we were not able to compare the DPOAE results.

Histological Examination

Hematoxylin-Eosin Staining

H&E-stained sections taken through the organ of Corti and spiral ganglion cells showed normal morphology in both groups I and II. The organization of the Corti organ cells were disrupted in both noise exposed groups. However, the level of disruption was not so much in group IV (Figure 2). The observed disruption might be caused while taking sections by microtome. In both noise exposed groups loss of cells in spiral ganglion neurons were evident, but these pathological changes were less severe in group IV (Figure 3).

TUNEL Assay

TUNEL Assay showed that noise-induced apoptotic cell death was prominent in the organ of Corti and spiral ganglion cells. Group I and II showed lower TUNEL positive cells than both of groups III and IV. There were more TUNEL positive cells in Group III. The TUNEL results showed that the level of apoptosis was less in the noise exposed KRG group (group IV) (Figure 4). The most significant apoptotic changes were obtained in the spiral ganglion cells (Figure 4). The ratio of apoptotic spiral ganglion cells was decreased in the group IV (33%) in comparison to group III (92%) ($p<0.001$). The mean percentage of apoptotic cells in the organ of Corti were 67% and 28% in group III and group IV, respectively ($p<0.001$, Figure 5).

Discussion

The mechanism of NIHL is related to mechanical and metabolic damage. NIHL affects the biochemical systems in the inner ear, leading to necrosis and apoptosis. This change causes permanent hearing loss (21).

KRG extracts have recently been shown to have anti-apoptotic and antioxidant effects in various studies (15, 17,

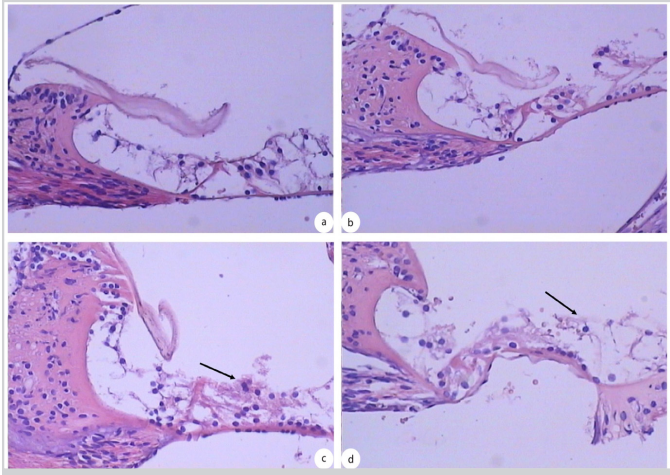

Figure 2. a-d. Hematoxylin-Eosin staining of organ of Corti (a. Group I, b. Group II, c. Group III, d. Group IV). The arrows show that the organization of organ Corti cells are disrupted (50 µm)

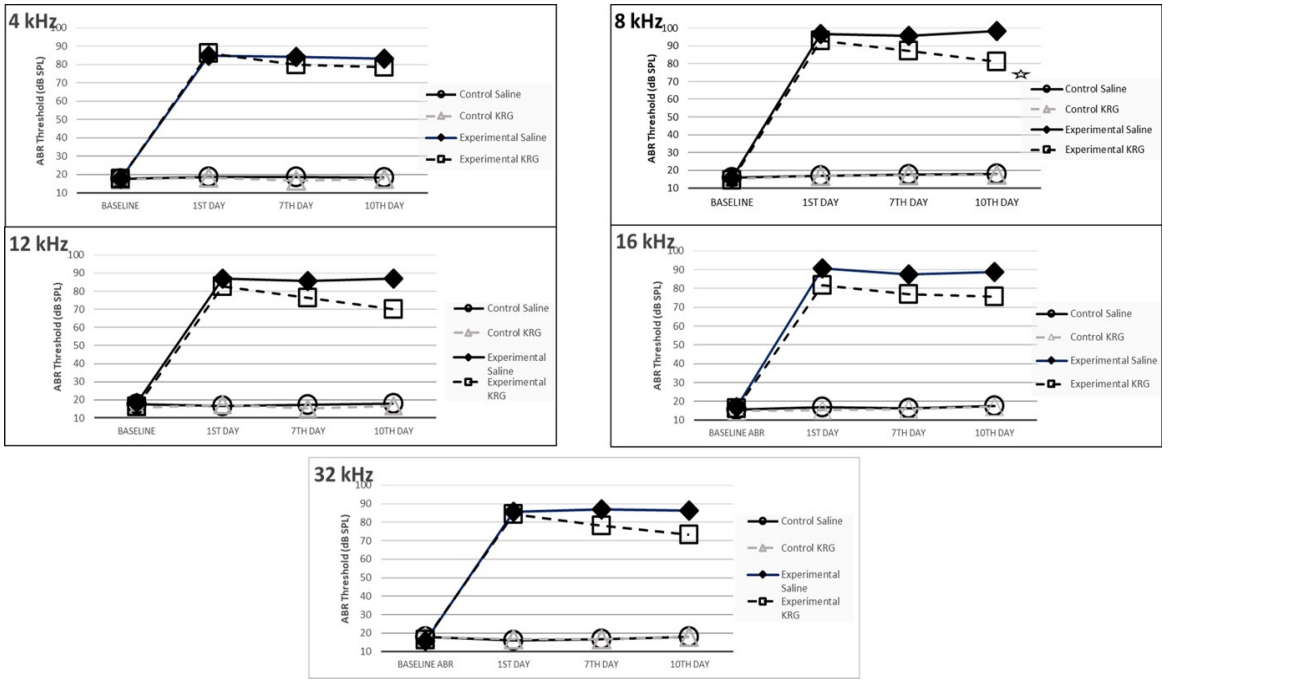

Figure 1. 4, 8, 12, 16, 32 kHz ABR thresholds shifts for all groups (☆= $p<0.05$)

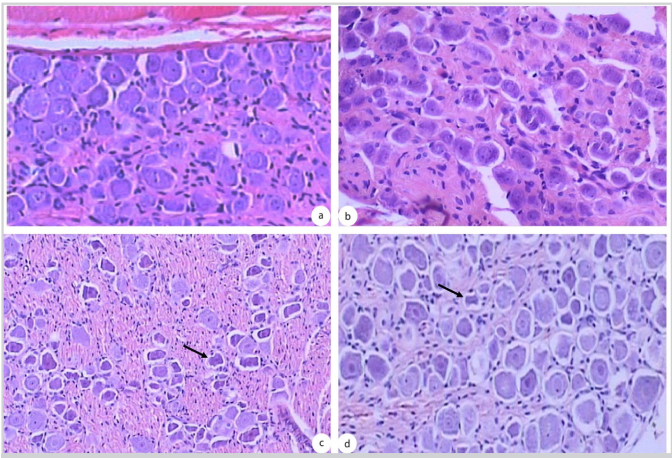

Figure 3. a-d. Hematoxylin-Eosin staining of spiral ganglion cells (a. Group I, b. Group II, c. Group III, d. Group IV). The arrows show the degeneration and picnotic changes in spiral ganglion cells (200 μm).

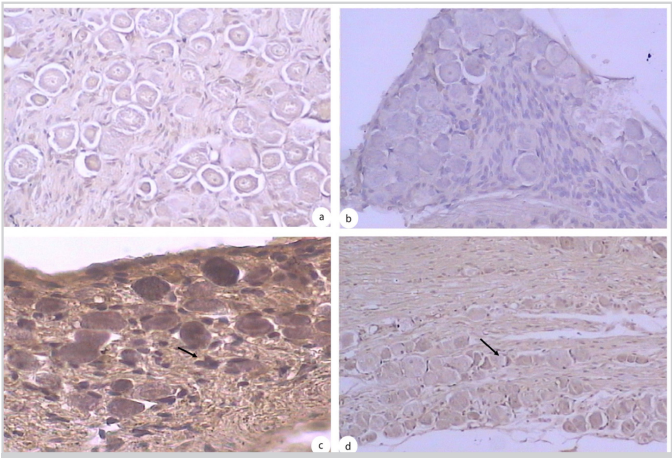

Figure 4. a-d. TUNEL staining of spiral ganglion cells in all groups (a. Group I, b. Group II, c. Group III, d. Group IV). Arrows shows TUNEL positive (apoptotic) cells (400 μm)

TUNEL: Terminal deoxynucleotidyl transferase mediated dUTP nick-end labeling

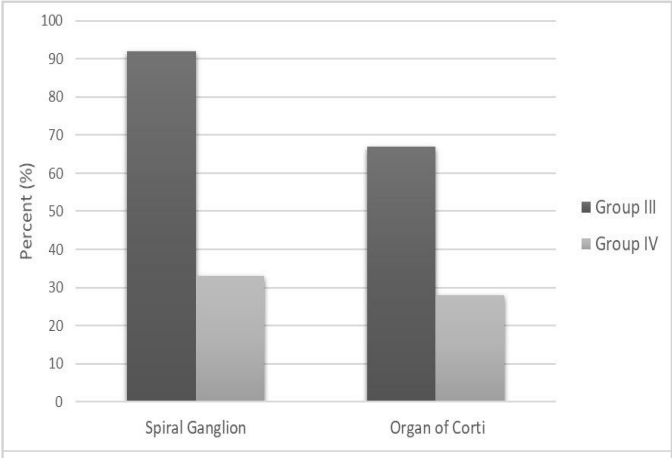

Figure 5. Apoptotic cell ratio in organ of Corti and spiral ganglion

19, 22, 23). Recently, some studies showed that KRG and ginsenosides (found in ginseng) have otoprotective properties against age-related hearing loss, gentamicin, 3-nitropropionic acid, cisplatin ototoxicity, and noise-induced hearing loss (15, 16, 18-21).

In the literature there were only two studies about the effect of KRG in NIHL. Kang and Chung (21), administered 200 mg/kg KRG orally for three days to mice, starting from one hour after the 110 dB SPL white noise (three hours). After noise exposure, the click ABR results of the KRG group were significantly better than the control saline group. On the 7th day, all groups returned to their basal hearing values and it was considered as a temporary threshold shift. The authors indicated that KRG had rapid recovery effect for temporary threshold shifts, and long-term results for permanent hearing loss might be better (21).

In our study, we investigated the effect of KRG on permanent NIHL and the wide hearing frequency range of the rats allowed us to evaluate the most affected high frequency region in NIHL. We used high frequency TB stimuli in ABR. To our knowledge, this is the first research using high frequency TB ABR on the effect of KRG for NIHL.

In their research, Hong et al. (24) tested various doses of 50 mg/kg and 100 mg/kg ginsenosides compounds, KRG and ginseng compounds 24 hours after the 120 dB SPL, 4 kHz, pure tone noise (2 hours) for seven days. The effects of KRG and ginsenosides compounds were evaluated by TEOAE, ABR and middle latency responses (MLR) after the 1st, 4th and 7th days. SNR was assessed in the TEOAE test, which was used to evaluate outer hair cell function. Significantly, better SNR responses were obtained in the group of ginsenoside compounds. The KRG group showed better ABR thresholds at 4, 6, and 8 kHz than the control group. It has been stated that KRG (100 mg/kg) and ginsenoside compounds have a protective effect for NIHL. In the study of Hong et al. (24) the ginseng compounds were administered for seven days and in our study the powder form of ginseng root was given for 10 days.

Choung et al. (15) reported the protective effects of KRG against gentamicin-induced ototoxicity, and Kang and Chung (21) also stated that, for NIHL, ginseng had reactive oxygen species repellent and apoptotic potency properties and might have a protective role in the ear. Kang and Chung (21) did not observe 8-oxoguanine as a ROS indicator after noise exposure. In our study, TUNEL (+) cells were less visible in group IV than in group III, especially in the spiral ganglion cells. This may be indicative of the protective effect of KRG in NIHL, as stated by referred studies (15, 21).

Fujita et al. (25) investigated the protective effect of the intravenous infusion of ginseng compound gRb1 on spiral

ganglion cells in the cochlear ischemia model of gerbils. In their study, with the application of gRb1 the ratio of TUNEL positive cells decreased from 25% to 5% and the authors concluded that gRb1 had otoprotective properties in cochlear ischemia model in gerbils (25).

In our study, antioxidant application was started within 1 hour after noise exposure since in daily life it is not always predictable when traumatic situations (such as in industry, armed forces, entertainment places, or unexpected bursts) will occur. We found a partial protective effect of KRG against NIHL which was prominent on 8 kHz.

According to some studies concerning NIHL, presbycusis, and ototoxicity, pathological changes firstly occur in the hair cells and the damage in the spiral ganglions neurons occurs after that (25, 26).

Our histopathological results showed that in Group IV, application of KRG had a significant protective effect on both hair cells and spiral ganglion neurons. Apoptotic cell ratio in hair cells and spiral ganglion neurons were 28% and 33% in Group IV in contrast to the higher apoptosis ratio in group III (67% and 92%, respectively). According to our histopathologic evaluations, KRG showed prominent protection in terms by preventing apoptosis. Although we saw some improvements on hearing levels with the KRG treatment, we think that this protection was not completely reflected in our audiological results. We think that other possible cellular death mechanisms like necrosis may be a possible explanation for these results. The primary limitation of this study is the fact that our DPOAE device was not able to measure higher frequencies above 8 kHz.

Conclusion

Our results have shown that there is a partial protective effect of KRG on NIHL. This protection was more prominent on 8 kHz and histopathologically more evident in both hair cells and spiral ganglion neurons. There is, however, need for further research to demonstrate the mechanisms of this protective effect, and to determine the optimal dose and the optimal timing for this protection on permanent noise-induced hearing loss models (impact sound, burst, repetitive, wavy).

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Informed Consent: Animal experiment study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: S.M.D., Y.O., S.A., H.E.E., S.G., Z.A., B.M., E.K., E.D., O.Y., G.K., Design: S.M.D., Y.O., S.A., H.E.E., S.G., Z.A., B.M., E.K., G.K., Data Collection and/or Processing: S.M.D., Y.O., S.A., H.E.E., S.G., Z.A., B.M., E.K., E.D., O.Y., G.K., Analysis and/or Interpretation: S.M.D., S.A., S.G., E.D., G.K., Literature Review: S.M.D., H.E.E., S.G., B.M., E.K., E.D., Writing: S.M.D., Y.O., S.A., H.E.E., S.G., Z.A., B.M., E.K., E.D., O.Y., G.K.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Animal Care and Use of the Dokuz Eylül University (Protocol number: 46/2014).

Conflict of Interest: No potential conflict of interest relevant to this article was reported.

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Main Points

- Noise exposure can damage hair cells, spiral ganglion neurons and result in hearing loss.
- Korean Red Ginseng attenuates hair cell and spiral ganglion neurons loss induced by noise exposure.
- Korean Red Ginseng may be a protective agent for noise-induced hearing loss.

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Allergy Practices in Otorhinolaryngology Residency Programs in Turkey: Quo Vadis?

Original Investigation

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Abstract

Objective: The aim of this study was to investigate how allergy practices in the otorhinolaryngology (ORL) residency departments in Turkey have changed over the last 20 years and to examine the current status in ORL residency training.

Methods: A 17-item questionnaire was developed following the study goals by a team experienced in allergy practices. The questionnaire was sent via e-mail to the program directors of all the 95 ORL residency departments in Turkey.

Results: A total of 60 (63.2%) program directors completed the questionnaire. We found that allergy testing and immunotherapy had been performed in 70% and 28.3%, respectively, at any time to date. The most common reason for discontinuing in allergy practices over time was "the changes introduced by the Turkish Social Security Institute as stated in the healthcare implementation communiqué" and "the difficulties in obtaining vaccine supplies from companies". Of all departments, allergy testing, immunotherapy, nasal smear, and nasal provocation tests were performed only by 35%, 8.3%, 28.3%, and 1.7%, respectively.

Conclusion: Allergy practices have been increasingly used, especially in the 2000s, but came to a standstill upon the changes introduced by the Turkish Social Security Institute as stated in the healthcare implementation communiqué. These findings suggest that allergy training, in the recent years, has remained in the background in ORL residency programs in Turkey. To achieve standardization in allergy training in ORL residency programs, professional associations and authorities should develop solutions in cooperation with legislators.

Keywords: Residency training, allergy, immunotherapy, skin prick test, otolaryngic allergy

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Introduction

Allergic rhinitis (AR) is the most common cause of chronic rhinitis in children and adults. It is estimated to affect approximately 20%-40% of the global population (1). Considering such comorbidities as nasal polyps, rhinosinusitis, otitis media, and Meniere's diseases, AR plays a central role in the clinical practices of otorhinolaryngology (ORL). It is estimated that approximately 50% of all patients presenting to ORL outpatient departments have allergic components (2). Therefore, otorhinolaryngologists should be provid-

ed with the knowledge of the diagnosis, treatment, and preventive medicine related to this patient group to a competent level during their residency training.

AR and otolaryngologic allergic diseases are a component of global ORL practices since the beginning of ORL residency training (3). In the United States, otolaryngic allergy education, including didactics and hands-on training, during ORL residency, has been mandated by the American Board of Otolaryngology and the Postgraduate Medical Education Accreditation Council (4). Also, the logbook, prepared by The European Union of Medical Specialist (UEMS) ORL Section, to provide standardization in ORL training programs in pan-Europe, aims to ensure ORL residents with the skills of allergy practice (5). Turkey is also a member of the Confederation of European Otorhinolaryngology-Head and Neck Surgery (ORL-HNS). However, there is currently a lack of sufficient data on AR diagnosis, treatment, and follow-up procedures in ORL residency departments, or the content of residency training in this regard in Turkey.

In Turkey, allergy practices have been performed since the 1970s, and interest in the approach has increased since the beginning of the 2000s (6). However, the reimbursement commission of the Turkish Social Security Institute (SSI), which is the most commonly used health insurance institution in Turkey, introduced changes to their scope with a healthcare implementation communiqué in 2013, by which allergy testing and immunotherapies performed by otorhinolaryngologists were excluded from the coverage (7). Allergy skin tests were included in the coverage again in 2016, but immunotherapies remained uncovered (8). It is unknown how these regulation changes have affected allergy practices in ORL residency programs or the education of the residents in Turkey.

In the present study, we investigate the changes in allergy testing and immunotherapy practices in the ORL residency training programs in Turkey over the last 20 years and examine the role of the current allergy practices in residency training.

Methods

A questionnaire was developed following the study goals by a team experienced in allergy-related practices (Figure 1). The questionnaire included 17 multiple-choice items, and comprised four parts, including demographic characteristics, allergy practices until today, current allergy practices, and resident training. In the questionnaire, some items could be responded to with more than one answer, while some items provided the opportunity to write comments.

The questionnaire was sent via e-mail to the department chairpersons and program directors of all the 95 departments currently providing ORL residency training in Turkey. The e-mail included a consent form explaining the purpose and the context of the survey. The research and a call for participation were announced through the networks used most commonly by Turkish otorhinolaryngologists (www.kanalkbb.com and www.kbb.org.tr). Reminder e-mails were sent every two weeks to the program directors that failed to respond. Data collection was completed in two months. The program directors who agreed to participate in the research completed the questionnaire online. Ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of Pamukkale University (no: 60116787-020/54426).

Results

Demographic Characteristics of ORL Residency Programs

A total of 60 (63.2%) program directors completed the questionnaire. The detailed demographic characteristics of the departments that participated in the study are presented in Table 1. Among the departments, 56.7% were public university hospitals, 35% were training and research hospitals, and 8.3% were foundation university hospitals. More than 70% of the departments had been providing ORL residency training for more than 20 years.

Previous Allergy Practices in ORL Residency Programs

Among the departments that participated in the study, allergy skin testing had been performed in any period in 42 (70%) of the departments, with the distribution of testing by the period provided in Figure 2. Allergy testing was performed in 31 (51.7%) departments until 2013, the year of the SSI payment cessation, while the number decreased to 10 (16.7%) after 2013. The most common reasons stated for discontinuing allergy skin testing practices were "the changes introduced by the Turkish SSI in their healthcare implementation communiqué" (43.3%) and "disallowance by hospital management" (21.7%) (Figure 3). Only nine (15%) departments had continued with allergy skin testing without interruption to the present day. The allergy skin testing methods most commonly performed by the departments were the lancet (43.3%) and the multitest (35%) epidermal prick test methods. According to the survey results allergy skin testing was never performed in 18 departments (30%).

Among the departments, immunotherapy practices had been performed in 17 (28.3%) in any period. There were 14 (23.3%) departments that had performed subcutaneous immunotherapy and 11 (18.3%) departments that had performed sublingual immunotherapy. The distribution of the departments by periods in which immunotherapy was provided is presented in Figure 2. The most common reason for discontinuing immunotherapy was importer-related problems in vaccine supply (Figure 3).

Allergy Practices in ORL Residency Programs

1. Which of the following best describes the institution to which your clinic is affiliated?
- o Public university hospital
- o Training and research hospital
- o Foundation university hospital

2. For how many years has your clinic been providing ORL residency training?
- o 1–5 years
- o 5–10 years
- o 10–20 years
- o 20 or more years

3. Has any allergy skin test been performed at your clinic at any time over the last 20 years?
- o Yes
- o No

4. If yes, in which of the following periods was skin testing for allergies performed? (You can mark more than one answer).
- o Not performed
- o Before 2000
- o 2000–2005
- o 2005–2013
- o 2013–2016
- o After 2016

5. If allergy test practices were interrupted in your clinic, what was the reason? (You can choose more than one answer).
- o Interruption in test material supply due to importing company
- o Lack of support by the hospital management
- o The departure of the responsible employee from the clinic
- o Non-payment for allergy testing by the reimbursement commission of the Turkish social security institute
- o Other .....

6. Which *in vivo* allergy test methods have been performed at your clinic to date? (You can mark more than one answer).
- o Epidermal test (Lancet)
- o Epidermal test (Multitest)
- o Intradermal test
- o Scratch test
- o Patch test
- o None performed

7. Have any immunotherapy practices been performed in your clinic at any time over the last 20 years?
- o Yes
- o No

8. If yes, in which of the following periods was the immunotherapy practice performed? (You can mark more than one answer).
- o Not performed
- o Before 2000
- o 2000–2005
- o 2006–2013
- o 2013–2016
- o After 2015

9. If immunotherapy practices were interrupted in your clinic, what was the reason? (You can mark more than one answer.)
- o Interruption in vaccination material supply due to importing company
- o Lack of support by the hospital management
- o The departure of the responsible employee from the clinic
- o Non-payment for immunotherapy practices by the reimbursement commission of the Turkish social security institute
- o Other .....

10. Which immunotherapy practices have been performed at your clinic to date?
- o Subcutaneous
- o Sublingual
- o Tablet
- o None performed

11. Is your clinic currently engaged in any allergy practices involving allergy testing or immunotherapy?
- o Yes
- o No

12. Is your clinic carrying out "nasal smear" assessments?
- o Yes
- o No

13. Is your clinic carrying out "nasal provocation tests"?
- o Yes
- o No

14.Are your allergy practices carried out by a full-time academician?
- o Yes
- o No

15. Do you have allergy nurses?
- o Yes
- o No

16. Do residents in your clinic's ORL residency program actively participate in allergy practices?
- o Yes
- o No

17. Which of the following practices do the residents in your clinic perform? Please mark which practices residents can perform.
- o Carry out and interpret allergy skin tests on patients
- o Interpret specific IgE allergy test (RAST)
- o Calculate immunotherapy doses using formulas
- o Administer immunotherapy injections

Figure 1. Allergy Practices in ORL Residency Programs
ORL: Otorhinolaryngology

Table 1. Demographic characteristics of residency programs

ORL residency training period	Public university hospital (n)	Training and research hospital (n)	Foundation university hospital (n)	Total (n, %)
1–5 years	1	1	1	3 (5%)
5–10 years	1	1	2	4 (6.7%)
10–20 years	4	3	2	9 (15%)
>20 years	28	16	-	44 (73.3%)
Total (n, %)	34 (56.7%)	21 (35%)	5 (8.3%)	60 (100%)

ORL: Otorhinolaryngology, n: Number

Only one (1.7%) department never discontinued their immunotherapy practices. According to the survey results, immunotherapy was never performed in 43 (71.7%) departments.

Current Allergy Practices of ORL Residency Programs

Among the departments, 21 (35%) were performing allergy skin testing at the time of the survey, while five (8.3%) of these were also performing immunotherapy. There were 17 (28.3%) departments carrying out nasal smear assessments, while nasal provocation tests were performed in only one (1.7%). It was stated that allergy practices were carried out by a full-time academician in 18 (30%) departments, while eight (13.3%) departments retained an allergy nurse. The distribution of allergy practices at the time of the survey is presented in Figure 4.

Allergy Practices Being Actively Performed by Residents

Among the departments participating in the study, 20 (33.3%) reported that they were actively performing allergy practices during residency training, while 40 (66.7%) departments reported that their residents were not receiving allergy practice training. It was also reported that residents were performing and interpreting allergy skin testing in 20 (33.3%) departments, interpreting specific Immunoglobulin E allergy tests in ten (16.7%) departments, performing immunotherapy injections in three (5%) departments, and were able to calculate immunotherapy doses using formulas in one (1.7%) department. The detailed allergy practices actively performed by residents are presented in Table 2.

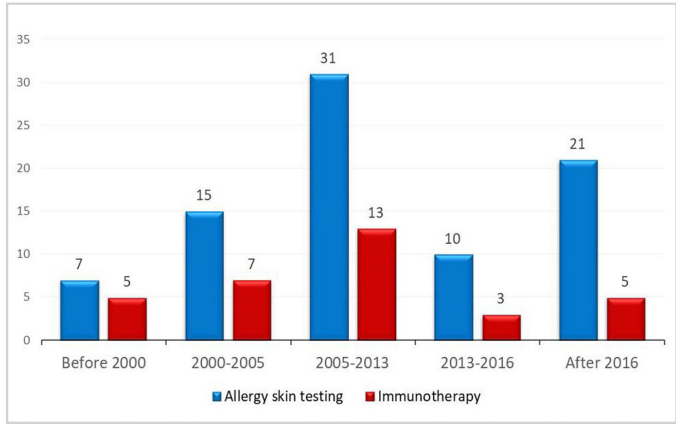

Figure 2. The number of residency programs performing allergy skin testing and immunotherapy according to time periods

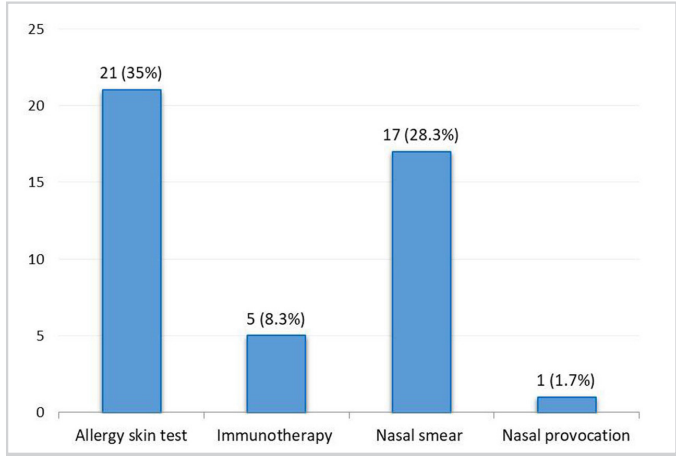

Figure 4. The allergy practices currently performed by the residency programs.

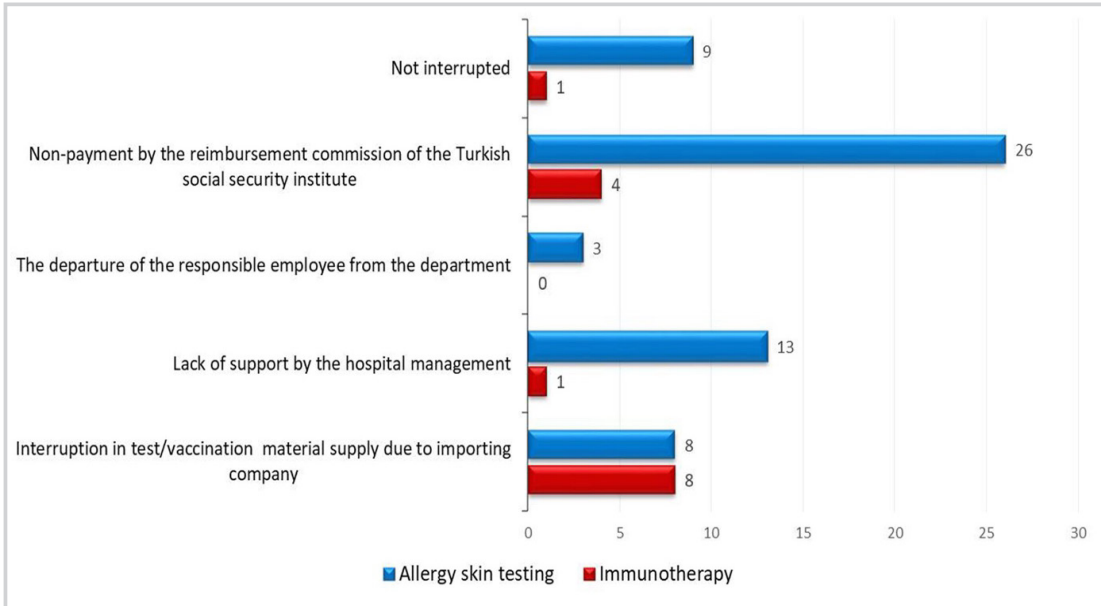

Figure 3. The reasons for the discontinuing allergy skin testing and immunotherapy practices

Table 2. The allergy practices actively performed by residents

	Public university hospital (n)	Training and research hospital (n)	Foundation university hospital (n)	Total (n, %)
Carry out and interpret allergy skin tests	11	7	2	20 (33.3%)
Interpret specific IgE allergy test	6	4	-	10 (16.7%)
Administer immunotherapy injections	2	1	-	3 (5%)
Calculate immunotherapy doses	-	1	-	1 (1.7%)

IgE: Immunoglobulin E, n: Number

Discussion

AR is a common condition all around the world, particularly in developed countries. It has a negative effect on life quality and is increasing in prevalence. Its prevalence is reported to be 20%–25% in Turkey (9). Given the high prevalence of AR and the frequency of comorbidities and complications, allergy practices have an important place in ORL procedures. In Turkey, the first national core program activities were initiated under the Turkish ORL-HNS Society in 2006, and a "Residency Core Training Program (RCTP)" containing all necessary knowledge and skills was prepared within the scope of this program that could be used as a guide by institutions providing residency training (10). The program recommended establishing an "allergy outpatient clinic" at every center providing ORL residency training. Moreover, it aimed to ensure that ORL residents gained the necessary skills to carry out allergy skin tests, nasal provocation tests, and nasal cytology and serological allergy tests. The RCPT was updated in the subsequent years, with "allergen-specific immunotherapy" added to the previous learning objectives. However, whether or not allergy education and training will be included in ORL residency programs in Turkey is uncertain. To our knowledge, this is the first study to evaluate allergy practices and education in departments that provide ORL residency training in Turkey.

Allergy skin testing and immunotherapy are the most important allergy practices in the diagnosis and treatment of allergic diseases (11). In the presented study, we found that the number of departments carrying out allergy skin tests in Turkey started to increase after 2000, rose to 31 after the RCTP was launched, but rapidly decreased to 10 after the change in Turkish SSI regulations in 2013. Likewise, the number of departments performing immunotherapy practices decreased from 13 to three following the change in SSI regulations. After otorhinolaryngologists were once more entitled to carry out allergy skin testing in 2016, an increase was seen in the number of departments performing allergy practices, albeit the numbers seen in the past have not yet been reached. These results show us that the official health policies in countries are very effective in resident training. The program directors of the departments also expressed the SSI regulation changes as the most important reason for discontinuing allergy skin testing practices. Besides, difficulties in obtaining vaccines due to importer-related problems were given as one of the leading reasons for discontinuing immunotherapy practices.

The literature contains few studies evaluating allergy practices in ORL residency programs. The study by Osguthorpe (12) in 1985 reported that only 8% of the ORL residency programs in the United States met the minimum criteria recommended by the American Academy of Otolaryngic Allergy. In the following years, the 2006 study by Lin and Mabry (3) reported a rate of residency programs that addressed active allergy practices in the United States of approximately 62%. Finally, the study by Bailey et al. (13) in 2014 found that this rate had increased to 73%. These studies suggest that allergy practices have witnessed a gradual increase in ORL residency programs in the United States. In the presented study, the proportion of departments with allergy programs, which peaked at 51% in the early 2010s, is only 35% today. Among the departments participating in the survey, the proportion of those that were performing allergy skin testing and immunotherapy practices at the time of the survey were 35% and 8.3%, respectively. The proportion of the departments carrying out nasal smear and nasal provocation testing practices, which, again, are very important in the differential diagnosis of AR among allergy practices, were approximately 28% and 1.5%, respectively, at the time of the survey. These findings suggest that allergy practices, in the recent years, have remained in the background in ORL residency programs in Turkey.

Allergy education in an ORL residency program should include hands-on training in addition to theoretical training. In the presented study, however, we found that residents were actively participating in allergy practices only in 33% of the residency programs in Turkey. Even though the theoretical and practical training issue in AR is broadly included in both the UEMS-ORL section logbook and the RCTP, it is understood that currently there are deficiencies in this regard in both university and training and research hospitals in Turkey. Given that allergy education is an inseparable part of the ORL residency program, arrangements should be made to increase the number of operational allergy laboratories in ORL residency departments.

Conclusion

In this study, we observed that allergy education in ORL training programs in Turkey has varied in both quantity and quality, over time and across institutions. Allergy practices were increasingly used, especially in the 2000s, but came to a standstill upon the changes introduced by the Turkish SSI in their healthcare implementation communiqué. We further concluded that import-related problems in accessing testing and vaccination materials in the recent years were an important factor in the lack of progress in allergy practices. These results show us that the official health policies in countries are very effective in resident training. To achieve standardization in allergy training in ORL residency programs, professional associations and authorities should develop short- and long-term solutions in cooperation with legislators. The priority, however, is to increase the number of operational allergy laboratories in the departments that provide ORL residency training.

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Ethics Committee Approval: Ethics Committee approval for the study was obtained from the Clinical Research Ethics Committee of Pamukkale University (no: 60116787-020/54426) on 08/08/2019.

Informed Consent: This is survey research and the survey was sent via e-mail to the department chairmen and program directors of all the 95 departments currently providing ORL residency training in Turkey. The e-mail included a consent form explaining the purpose and the context of the survey.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: E.M., C.O.K., B.T., Design: E.M., C.O.K., B.T., Supervision: E.M., C.O.K., B.T., Materials: E.M., C.O.K., B.T., Data Collection and/or Processing: E.M., C.O.K., Analysis and/or Interpretation: E.M., C.O.K., B.T., Literature Review: E.M., C.O.K., B.T., Writing: E.M., C.O.K., B.T., Critical Review: C.O.K., B.T.

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The Short-Term Effect of Eugenol on the Prevention of Experimentally Induced Myringosclerosis in a Rat Model

Original Investigation

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Abstract

Objective: The aim of our study was to assess the possible short-term effects of topical and oral eugenol on the suppression of experimentally developed myringosclerosis (MS).

Methods: Four groups of seven male Wistar albino rats were used in the study. The tympanic membranes (TMs) of all subjects were myringotomized, and group 1 was given no treatment (as control group), group 2 received saline, group 3 had received topical eugenol and group 4 received oral eugenol.

Results: In macroscopic evaluation the control and saline groups showed much more MS compared to the topical and oral eugenol groups which had statistically significantly less changes ($p<0.05$). Fibrosis and inflammation regarding the lamina propria (LP) of the eardrums of the topical and oral eugenol groups were significantly less than those of the control and saline groups ($p<0.001$). In microscopic evaluation, TMs were found to be thicker in the control and saline groups ($p<0.001$).

Conclusion: Our study showed that the application of topical and oral forms of eugenol reduced fibrosis and prevented the advancement of MS in the LP of the TMs in the short-term. More studies with different extracts are needed to investigate the efficacy of phytotherapeutic agents for preventing MS development following myringotomy.

Keywords: Tympanic membrane, myringosclerosis, antioxidants, eugenol, rats, animal experimentation

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Introduction

Myringosclerosis (MS) is the end-stage of the chronic inflammation, infection or injury in the tympanic membrane (TM) and usually seen following interventions such as ventilation tube insertion. It is represented by the hyaline degeneration of the elastic fibrils and calcification in the lamina propria (LP) of the TM (1, 2).

In pediatric patients, otitis media with effusion (OME) is a common disorder which often requires a procedure like myringotomy or ventilation tube placement on the TM between the external ear canal and middle ear (2). There is an increased possibility of MS in patients who had ventilation tubes placed (3, 4). Several studies reported that the incidence of MS was much higher in cases with a history of ventilation tube placement compared to without. These studies also reported the incidence in pediatric patients to range between 28 and 61% (5, 6).

Although the exact etiopathology of MS is unknown, hyperoxic conditions and increased oxygen-derived free radicals caused by trauma have been attributed to play an important role (7, 8). Setting out from this point of view, various anti-inflammatory and antioxidant agents have been used in experimental studies to reduce and prevent the effects of these free radicals (9, 10).

Eugenol ($C_{10}H_{12}O_2$ or $CH_3C_6H_3$) is a yellowish volatile essential oil secured from Eugenia caryophyllata leaves and buds which is primarily endemic in India, Madagascar, and Indonesia (11). Its anti-mutagenic, anti-inflammatory, analgesic, antimicrobial, and anti-carcinogenic effects have been shown in previous studies (12). The antioxidant efficiency of eugenol commixtures, which comes from their methoxy-phenolic formation, has also been reported in several experimental models (12). Eugenol is considered non-toxic, and safe by the U.S. Food and Drug Administration (13).

In our study, the purpose was to explore the possible effects of eugenol as an anti-inflammatory and antioxidant molecule on MS development in an experimental Wistar Albino rat model using otomicroscopic and histopathological methods.

Methods

Maintenance of Experimental Material

All methods used in this experiment met the ethical standards of the institution Sakarya University Animal Experiments Local Ethics Committee, (no: 04/03/2019-11) and complied with the ARRIVE protocol for animal experiments and were carried out according to the National Institutes of Health Protocol for the Use and Care of Laboratory Test Subjects (NIH Publications no: 8023, revised in 1978). Twenty-eight healthy male Wistar albino rats with a weight of 300–350 g were used in the experiment. All procedures were completed and all test subjects were cared for by the authors. Test subjects were kept in temperature-measured (23±2 °C) and humidity-measured (50±10%) chambers with factitious lighting from 8:00 a.m. to 8 p.m. and with free access to food and water They were given classic commercial rat food and fountain water and handled after seven days of segregation and acclimatization.

Experimental Design and Surgical Procedure

Intramuscular application of a combination of ketamine hydrochloride (50 mg/kg) (Ketalar® Eczacıbaşı Parke-Davis, İstanbul, Turkey) and xylazine hydrochloride (5 mg/kg) (Alfazyne® Alfasan International B.V., Woerden, Netherlands) was used to anesthetize the subjects. A warming blanket was used to maintain body temperature at 35 °C, and rectal temperature was continuously monitored during anesthesia. Otoscopic examinations were done to observe the ear canal and the TM. In the animal selection phase, rats with otitis media and/or externa, and rats with perforation and sclerosis in the eardrums were removed from the study. A perforation with a sterile pick was done in the posterior superior one-fourth of the TMs in both ears under the otomicroscope by the same author. Intratympanic bleeding was not observed during this procedure. Then all subjects were randomly partitioned into four groups of seven rats each.

Group 1: Control group, received no treatment, only myringotomy was performed.

Group 2: Subjects in this group received saline solution topically three times, immediately after myringotomy, at the 24th (day 1st) and 48th hours (day 2nd). A syringe was used to drop 0.1 mL saline solution into the outer ear canal.

Group 3: Immediately after myringotomy, subjects in this group were treated using a gelfoam fragment soaked in 0.1 mL eugenol (Eugenol ReagentPlus®, 99%; Sigma-Aldrich Chemical Co., Merck, Darmstadt, Germany). The solution was applied on the perforation of both TMs in each rat, at the 24th and 48th hours, and 0.1 mL eugenol was dropped into the ear canal with the help of a syringe with the second and third doses.

Group 4: This group received 50 mg/kg eugenol orally five times using the gavage method; immediately after myringotomy, at the 24th hour (day 1st), 48th hour (day 2nd), 72nd hour (day 3rd) and 120th hour (day 5th).

The oral doses of eugenol were specified based on the principles of previous experimental concepts (12).

Otomicroscopic Examination

On the 15th and final day of the experiment otomicroscopic examination was performed after all test subjects were euthanized and decapitated. The author evaluating and scoring the inflammation stage of the TMs was blinded to the animal groups. The rate of MS in the pars tensa of the eardrums was assessed semi-quantitatively and graded by the scoring system indicated by Mattsson et al. (14), as normal, mild, moderate, and severe. Normal: no distinguishable MS; *Mild*: white halo around umbo; *Moderate*: white halo around umbo and a white strip beside the handle of the malleus and

along the annulus; and *Severe*: converging whitish deposit forming a horseshoe pattern.

Temporal Bone Dissection and Histopathological Evaluation

Following otomicroscopic examination, temporal bone dissection was performed to access the tympanic bulla and the TM. A horizontal incision was made in the occipital area and the skin was lifted forward. The temporalis muscle and the periosteum were raised over the parietal bone, and then over the squamous part of the temporal bone. While retracting the auricle laterally, the cartilaginous outer ear canal was disconnected from the tympanic ring with a blunt dissection. The mastoid bulla was revealed when the elevation of the muscles in the subperiosteal plane was performed. At the next step, the squamous part was sectioned from the frontal, parietal, ethmoid, and palatine bones; the mastoid fragment was sectioned from the occipital bone; the petrous part was sectioned from the sphenoid bone; and the bulla was sectioned from the sphenoid and occipital bones. Finally, the temporal bone was sectioned from the surrounding muscle tissues and separated from the skull.

The temporal bones were fixed in 10% formaldehyde quick fix for 24 hours and then decalcified with formic acid for ten days. After the decalcification process, copies were separated into two fragments through a line that divided the perforation vertically up to the handle of the malleus. All slices were enclosed in paraffin, sectioned in 5 μm thickness, and stained with Masson's Trichrome and Hematoxylin & Eosin (H&E) staining techniques to assess fibrosis, inflammation, and thickness in the TMs of every subject. To examine the sclerotic changes and collagen fibrils in the connective tissue of the LP, Masson's Trichrome staining was performed. In H&E staining, calcification appeared as dark purplish pink color with irregularly bordered areas. With Masson's Trichrome technique, sclerotic areas emerged as blue spaces rather than white. The healed perforation areas where the most inflammation occurred were evaluated to measure the thickness of the TMs.

All samples were analyzed by a pathologist blinded to the groups. Micro calculations were done quantitatively on a high-resolution light microscope (Eclipse E200 Invert; Nikon, Tokyo, Japan) under 40x to 100x magnification. Severity of fibroblastic proliferation in the LPs and the degree of sclerotic lesions in the TMs were graded as follows: "0" if no distinguishable MS; "1" if mild; "2" if moderate; and "3" if severe. And the intensity of the inflammation was graded as: "0" if there was no inflammation; "1" if mild; "2" if moderate; and "3" if there marked inflammation and intense exudation and granulation.

Statistical Analysis

All data were analyzed with SPSS for Windows v22.0 (SPSS; IBM Co., Armonk, NY, USA). Descriptive statistics was used to determine mean, median (minimum-maximum), standard deviation, frequency distribution and percentage of individual and aggregate data. The Kolmogorov-Smirnov test was used to verify the normality of data distribution. In each group, mean thickness of the TMs was compared with one-way ANOVA and post hoc tests and otomicroscopic, inflammation and MS scores were compared with student's t-test. Categorical variables were evaluated with the chi-square test. A p-value <0.05 was considered statistically significant.

Results

Otomicroscopic Examination

On the final day of the experiment, it was observed that all TM perforations had improved and closed. More MS plaques were noticed in groups 1 and 2, whereas the TMs in group 3 (topical eugenol) and group 4 (oral eugenol) revealed significantly less or no sclerotic plaque (Figures 1a-d).

Figure 2 shows the calculations of MS degrees as assessed by otomicroscopy. MS degree was "moderate" or "severe" in 92.9% of the TMs in group 1 (control) and in 78.6% in group

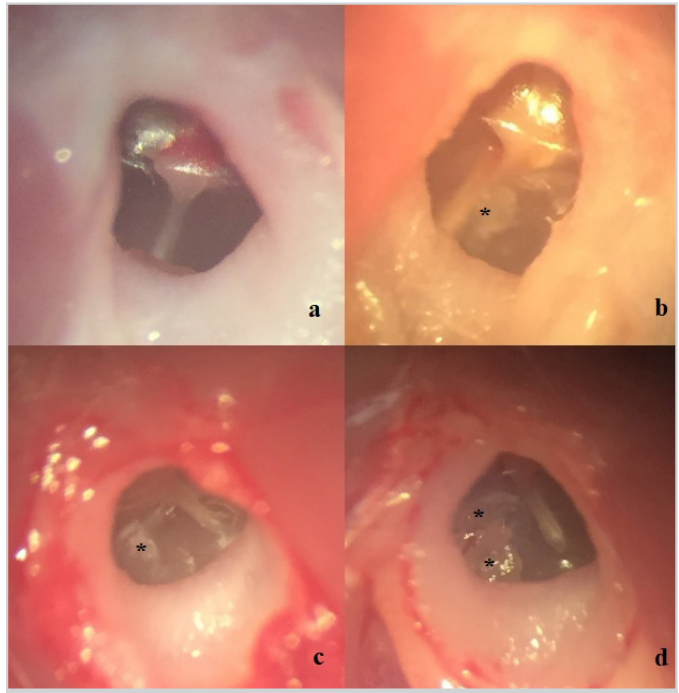

Figure 1. a-d. Otomicroscopic views of the TMs laterally on the final day of the experiment. a. Otomicroscopic view of TM from group 3 (topical eugenol), MS degree was normal. b. Otomicroscopic view from group 4 (oral eugenol), MS degree mild. Asterisk shows the white sclerotic plaques near the umbo and the healed myringotomy site. c. Otomicroscopic view from group 2 (topical saline solution), MS degree moderate. Asterisk shows the sclerotic plaques around the umbo, and adjacent to the handle of the malleus. d. Otomicroscopic view of TM from group 1 (no treatment-control group), MS degree severe. Asterisks show the dense sclerotic areas

TM: Tympanic membrane, MS: Myringosclerosis

2 (saline) but "none" or "mild" in 100% of TMs in groups 3 and 4. Sclerotic plaques were less in group 3 than in group 4 ("none" degree was 64.3% in group 3, 35.7% in group 4). The conclusions in the short-term were significantly more pronounced in groups 1 and 2 ($p<0.001$). There were no significant differences between groups 1 and 2 and groups 3 and 4 ($p=1$, $p=0.141$, respectively).

Histopathological Examination

In group 1, 12 (85.7%) TMs had moderate or marked (degrees "2" and "3") and two TMs (14.3%) had none or mild (degrees "0" and "1") inflammation. In group 2, 13 (92.9%) TMs had moderate or marked and one (7.1%) had none or mild inflammation. But in the topically treated group (group 3), 14 (100%) TMs had none or mild (2 TMs were "0" and 12 TMs were "1") and 0 (0%) had moderate or marked inflammation, and in group 4, 10 (71.4%) TMs had none or mild and 4 (28.6%) TMs had moderate or marked inflammation (Figures 3a-d). To summarize, inflammation in LP were significantly more severe in groups 1 and 2 compared to groups 3 and 4 in this short period (Figure 4) ($p<0.001$).

The extension of the fibroblastic proliferation and sclerosis in the short-term were less in the TMs of groups 3 and 4. Thirteen TMs (92.9%) in group 1 and all TMs (100%) in group 2 had degree "2" or degree "3" fibrosis. Conversely, in group 3, 12 TMs (85.7%) and in group 4, 11 TMs (88.6%) had degree "0" or degree "1" fibroblastic proliferation. There were significant differences among the groups in terms of fibroblastic proliferation and sclerotic plaques ($p<0.001$) (Figures 5 and 6a-d).

In the short study period, the thickness of perforated regions in groups 1 (control) and 2 (saline) were measured thicker than those of groups 3 (topical eugenol) and 4 (oral eugenol). The thinnest TMs were in group 3. Mean thickness of the TMs was 112.6±19.46 μm in Group "; 97.93±7.64 μm in group 2; 62.8±10.92 μm in group 3, and 80.36±7.66 μm in group 4 (Figure 7). In terms of the thickness of TMs, statistically significant differences were separately observed between groups 1 and 3 ($p<0.001$), groups 1 and 4 ($p<0.001$), groups 2 and 3 ($p < 0.001$), groups 2 and 4 ($p<0.001$) and groups 3 and 4 ($p<0.001$). There were no statistically significant differences between groups 1 and 2 in terms of mean thickness of TM ($p=0.075$).

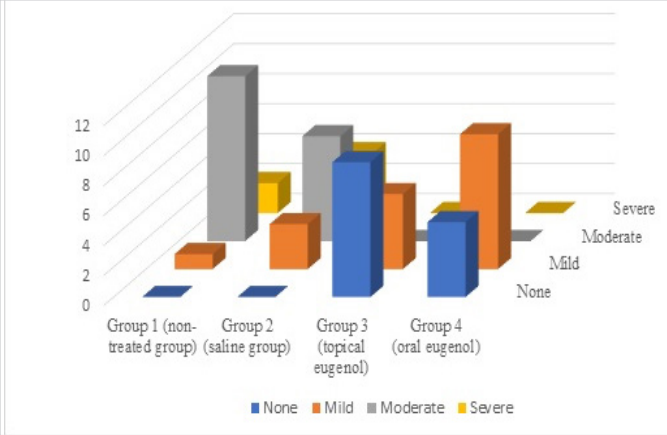

Figure 2. Graphical analysis of otomicroscopic grading of MS in tympanic membranes

MS: Myringosclerosis

Discussion

MS is defined as the reaction of tympanosclerosis localized to the TM. It is a frequent condition in OME, recurrent otitis media, chronic otitis media, and surgical interventions such as myringotomy and VT insertion (15, 16). Whilst there is no exact information on its etiology and pathogenesis, recent studies have emphasized that mechanical injury, intratympanic hemorrhage, foreign body reaction to VT, hyperoxygenation and oxygen-derived free radicals, and autoimmunity might be the key points in the occurrence of MS (15, 16). Mattsson et al. (14) indicated that after myringotomy procedure, the sclerotic changes

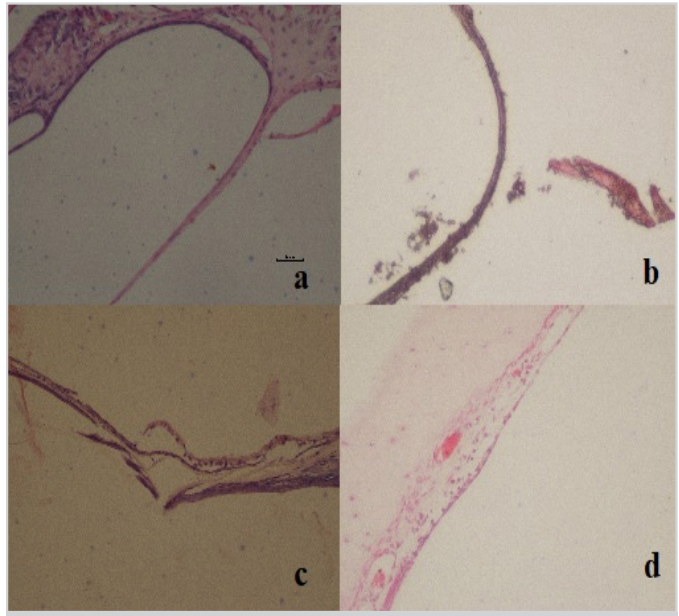

Figure 3. a-d. Light microscopic views of TM of rats (hematoxylin and eosin staining, all four photographs are at original magnification 200x). a. Photograph of pars tensa of a rat from group 3 (topical eugenol). There is no evidence of inflammation in LP of TM (Inflammation degree 0). b. Photograph of pars tensa of a rat from group 4 (oral eugenol). There is mild inflammation in the LP (Inflammation degree 1). c. Photograph of TM from group 2 (topical saline solution). Inflammation is more apparent, and the TM is comparatively thicker (Inflammation degree 2). d. Photograph of a rat from group 1 (no treatment-control group) showing extensive inflammation in the LP and thicker TM compared to other groups (Inflammation degree 3)

TM: Tympanic membrane, MS: Myringosclerosis, LP: Lamina propria

in pars flaccida of the TM evolved within nine hours and inflammatory response after 12-24 hours.

Whereas MS is identified histologically in 80% of cases after myringotomy it can be identified under otomicroscopy in only 40% of the cases. This suggests that the actual number of tympanosclerosis cases detected with otomicroscopy could be two-fold (6). To support this, in a study by Santos et al. (17), the sensitivity and specificity of otomicroscopy was found 80% and 75%, respectively. The authors concluded that histolopathological evaluation was a better method than otomicroscopy for diagnosing MS. Thickness, inflammation, and fibrosis can also be evaluated by the histopathological methods. Based on the results of our study, we also believe that the histological method is stronger than otomicroscopy for determining MS.

In the light of the literature, we preferred the myringotomy model to set up MS in our study. We sacrificed the subjects on the 15th day in order to see the potential defensive effects of the topical and oral eugenol on the evolution of MS with otomicroscopic and histopathological findings, considering

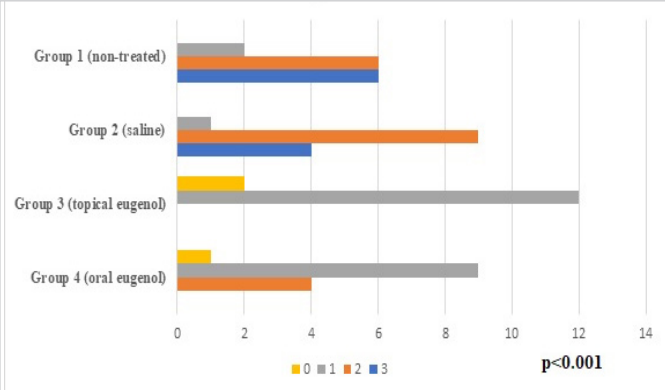

Figure 4. Graphical analysis of inflammation degrees in the LP of the TMs (results of hematoxylin and eosin staining)

LP: Lamina propria, TM: Tympanic membrane

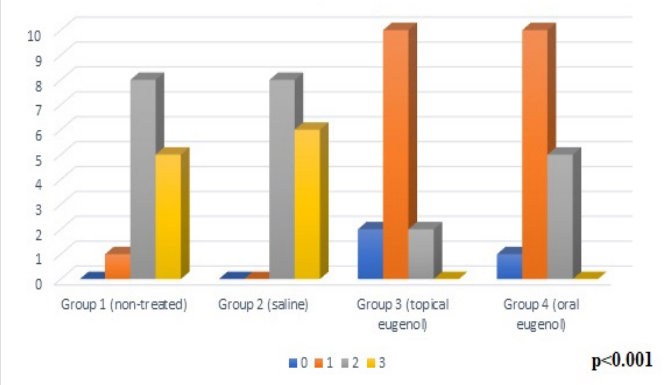

Figure 5. Graphical analysis of fibrosis degree in the LP of the TMs (results of Masson's Trichrome staining)

LP: Lamina propria, TM: Tympanic membrane

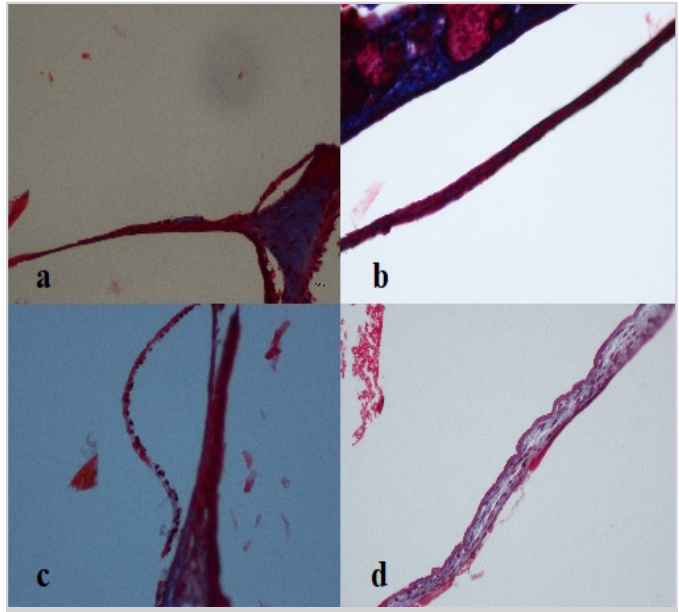

Figure 6. a-d. Light microscopic views of TM of rats (Masson's Trichrome staining, all four photographs are at original magnification 200x). a. Photograph of pars tensa of a rat from group 3 (topical eugenol). There is no evidence of sclerosis in LP of TM (fibrosis degree 0). b. Photograph of pars tensa of a rat from group 4 (oral eugenol). There is mild fibroblastic activity in the LP (fibrosis degree 1). c. Photograph of a TM from group 2 (topical saline group). Sclerosis degree is more apparent, and the TM is comparatively thicker (fibrosis degree 2). d. Photograph of a rat from group 1 (no treatment-control group) showing increased fibroblastic activity in the LP and thicker TM compared to other groups (fibrosis degree 3)

TM: Tympanic membrane, LP: Lamina propria

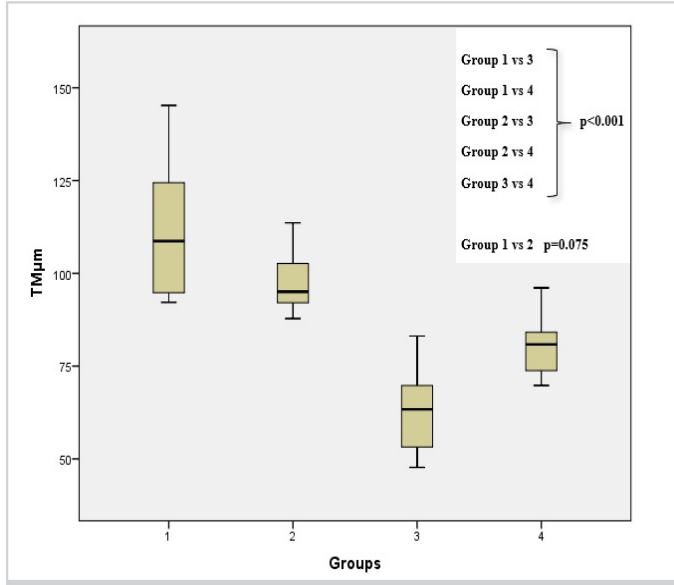

Figure 7. Mean, standard deviation, and statistical analysis of thickness of the TMs in µm (micrometer)

TM: Tympanic membrane

that it may have a preventive outcome in the first phase of MS development explained in the pathogenesis in the short-term period while experimental MS was forming.

Studies on this topic have focused on reducing or preventing MS by application of free radical scavengers, anti-inflammatory, and antioxidants agents. L-carnitine, selenium, Ginkgo biloba, ascorbic acid, N-acetylcysteine, zinc aspartate, vitamin C and E, N-nitro L- arginine methyl ester (L-NAME), Caffeic acid phenyl ester (CAPE), Hypericum perforatum, rosmarinic acid, montelukast, melatonin, dexamethasone and enoxaparin sodium have been used for this purpose in the current literature (1, 2, 6, 9, 15, 18-29). The effect of free radical scavengers is to arrest the formation of free radicals and active oxygen species, scavenging them, and repairing the damage. The aforementioned antioxidants, enzymes, and extracts were administered to the TMs of the myringotomized subjects, and the results indicated that the development of MS is inhibited or weakened with the therapy with antioxidants and free radical scavengers.

The antimicrobial, antimutagenic, analgesic, anticarcinogenic, anti-inflammatory, and antioxidant effects of eugenol, a yellowish fatty liquid obtained from the clove plant, are reported in the literature. It grows in the different parts of the world, especially in Indonesia, India and Madagascar (11). Some examples to the studies that have explored their effects are: a study by Islam et al. (30) reporting that eugenol strengthens the anticarcinogenic characteristic of cisplatin by limiting the Nuclear Factor kappa-B (NFkB) pathway when used together. The effect of eugenol counter to cisplatin-caused nephrotoxicity was studied by Rao et al. (31) and it was determined that eugenol protected against cytotoxic effects of cisplatin through free radical scavenging activities. Therapeutic action of eugenol against arsenic-caused cardiotoxicity was also investigated. Binu et al. (32) reported that in heart tissue, arsenic, by its cytotoxic effect, increased the levels of malondialdehyde (MDA)-a marker of lipid peroxidation; diminished grades of glutathione (GSH)-one of the important non-enzymatic endogenous antioxidant molecules. Also, they reported that when eugenol given orally at 5 mg/kg, antioxidant levels in tissues increased, membrane peroxidation was regulated, and thereby, heart rate was normalized. Additionally, MDA levels decreased, and GSH and Glutathione Peroxidase (GPx) levels increased as a conclusion of eugenol treatment. Consequently, they suggested that eugenol showed cytoprotective properties by preventing lipid peroxidation and by protecting non-enzymatic and enzymatic antioxidant pathways (32). Said and Rabo (33) in their experimental study, investigated the preventive effect of eugenol in aluminum-caused brain damage, and reported eugenol as a likely neuro-protective factor because of its anti-apoptotic and antioxidant characteristics. Martínez-Herrera et al. (34) used eugenol for gingival inflammation and reported that eugenol showed an anti-inflammatory effect even at low doses. Regarding the effects of eugenol on the ear, we can see that there are not many studies on this subject in the current literature. A study by Yadav et al. (35) in which the antibacterial activity of eugenol is mentioned reported that eugenol at sub-MIC (minimum inhibitory concentration) significantly decreased 88% *S. aureus* colonization in rat middle ear. A study about cisplatin-induced ototoxicity by Sakat et al. (12) on increased MDA levels and decreased GPx and superoxide dismutase (SOD) activities, reported that eugenol reduced these effects in the cochlea and prevented oxidative stress in the inner ear and exhibited otoprotective activity.

Eugenol has been approved by the US Food and Drug Administration to be used as an additive in the food industry, a natural antiseptic and analgesic in dentistry, and as scent in the cosmetics industry (11). Although it has been reported as safe, there are some publications in the literature regarding its toxic effect. In a case study, a two-year-old child who consumed 5-10 mL of clove oil was reported to develop impaired liver function and experience disseminated intravascular coagulopathy. Results showed similarities between paracetamol- and eugenol-poisoning in terms of hepatotoxicity (36). In an experimental study, intravenously infused 4 µL and 8 µL eugenol was reported to have caused hemorrhagic pulmonary edema and acute respiratory distress, and some of the damage was suggested to be prone oxidative stress (37). In an *in vitro* study, eugenol was administered to isolated rat hepatocytes for five hours, and toxic effects and cell damage were seen in more than 85% of the cells. Applying acetylcysteine to the same cell line showed prevention on cell death (38). Anesthetic doses of eugenol were studied on African clawed frogs by Goulet et al. (39) and injury in kidney and cell apoptosis and some morphological modification in renal cells were demonstrated. In another study, eugenol was given orally to the rats in different doses over a 15-day period, and some changes in blood chemistry, such as rise in total bilirubin levels, alanine aminotransferase, and aspartate aminotransferase were observed (40). In the literature, there is controversy about the potency of eugenol in inducing hypersensitivity and allergy. Several adverse effects have been reported after using dental products containing eugenol. Localized irritation of the skin, ulcers, tissue necrosis, allergic dermatitis, and even anaphylactic shock were also observed (41). Some studies, on the other hand, showed that clove oil or eugenol alone had low activity in stimulating these kinds of allergic effects (42, 43).

A limitation of our study may be that the absence of an audiological examination on the subjects. Because our focus was on the wound healing and anti-inflammatory effects of eugenol, otoacoustic emissions (OAE) and/or auditory brainstem response (ABR) were not considered in ototoxicity

evaluation. Further studies are needed to evaluate whether the eugenol has positive or negative effects on hearing.

Conclusion

There are many studies that have investigated the antioxidant and anti-inflammatory effects of eugenol, but to the best of our knowledge, this is the first study in the literature that has evaluated eugenol in preventing MS advancement (11). When the short-term otomicroscopic and histopathologic outcomes of the experimental study were examined, it was found that development of MS and thickness of TMs after myringotomy were significantly decreased in the topical and oral eugenol treatment groups, compared to the control and saline groups. In conclusion, both the topical and the oral administration of eugenol lowered fibrosis and restricted the advancement of MS. More studies with different extracts are needed to investigate the efficacy of phytotherapeutic agents in order to prevent MS developing after myringotomy.

Ethics Committee Approval: All methods used in this experiment met the ethical standards of the institution Sakarya University Animal Experiments Local Ethics Committee, (no: 04/03/2019-11).

Informed Consent: Animal experiment study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: O.K.E., H.E., Design: O.K.E., Supervision: M.G., Materials: O.K.E., S.G.E., Ö.B., H.Ç., H.E., Data Collection and/or Processing: O.K.E., S.G.E., H.E., E.M.G., Analysis and/or Interpretation: Ö.B., H.Ç., Literature Review: O.K.E., S.G.E., Ö.B., H.Ç., H.E., E.M.G., Writing: O.K.E., M.G., S.G.E., Ö.B., H.Ç., H.E., E.M.G., Critical Review: M.G., E.M.G.

Conflict of Interest: No potential conflict of interest relevant to this article was reported.

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Main Points

- Myringosclerosis is the end-stage of the chronic inflammation, infection or injury in the tympanic membrane.
- Possible preventive effects of the topical and oral forms of eugenol on myringosclerosis development were investigated in this experimental study.
- Otomicroscopic examination and histopathologic methods were used to evaluate the degrees of inflammation and fibrosis in tympanic membranes.
- It was demonstrated that the topical and oral utilization of eugenol lowered inflammation and fibrosis and restricted the development of MS.

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Evaluation of Speech Recognition Skills in Different Noises with the Turkish Matrix Sentence Test in Hearing Aid Users

Original Investigation

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Abstract

Objective: This study aimed to analyze the effectiveness of the Turkish matrix sentence test in evaluating the speech recognition performance of hearing aid users under different noise conditions.

Methods: Speech recognition performance of 42 individuals, 20 to 65 years of age (mean 49.1±14 years) with bilateral sensorineural hearing loss was measured in noise with the Turkish matrix sentence test without a background noise and with headphones. Additionally, the participants' speech recognition thresholds were measured with a matrix test while wearing their hearing aid under three different listening conditions in which the phases of speech and noise stimuli were changed with constant and fluctuating noise.

Results: Speech-recognition thresholds were better in fluctuating noise than in constant noise in all listening conditions, and this difference was statistically significant (p=0.02). In both types of noise, speech-recognition thresholds of bilateral hearing aid users (n=29) were lower (better) than those of unilateral hearing aid users (n=13) under three different listening conditions, but there was no statistically significant difference (p=0.67). Speech-recognition thresholds without hearing aids were statistically higher (worse) than those obtained with hearing aids (p=0.001).

Conclusion: Since the Turkish matrix sentence test gives useful results, this test can be used in the diagnosis, follow-up, and rehabilitation planning of hearing aid users. We observed that speech intelligibility was better, although there were differences among those with hearing loss when the speech test was conducted in fluctuating background noise with the Turkish matrix sentence test.

Keywords: Hearing loss, hearing aid, auditory rehabilitation, Turkish matrix sentence test, fluctuating noise, constant noise, speech audiometry

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Introduction

One of the most significant problems faced by individuals with hearing disorders is the impairment of speech perception in noise (1). The degree of speech perception may vary depending on the sound in the background, particularly on its temporal and spectral characteristics (2, 3). Hearing problems, including catching clues from speech context, can persist even with hearing amplification devices, particularly in challenging listening conditions, such as noisy and reverberant environments (4, 5). Tests involving speech recognition skills in different types of background noise should be applied when assessing the benefits obtained by patients from hearing aids equipped with complex signal processing algorithms (6, 7). The literature describes various methods for speech perception testing in different languages and presentation formats (including intermittent or continuous complex noise) (8-10). Assessment results vary according to the language or the procedures used in these tests. This led to the development of diagnostic tests such as the matrix sentence test and the hearing in noise test (HINT), which use different adaptive methods (noisy/noiseless conditions) and are suitable for many languages because they use the same syntactical structure (11-13). These sentence tests provide identical sentence-formation criteria for languages with low linguistic complexity. The vocabulary material used in these tests were selected to include phonetically balanced common words. The tests can be administered in a closed- or open-ended response format and in the native language of each patient (13, 14).

Various word lists can be created using different types of background noise (which either fluctuates according to the sentences used or maintains the same frequency distribution) to determine speech recognition scores through a matrix sentence test (7, 15). Constant speech noise and fluctuating filtered speech noise methods were developed to achieve adequate measurement accuracy in noise (15). Fluctuating filtered speech noise, which is used to evaluate hearing aid specifications, has been redesigned to evaluate the speech perception performance of individuals who have a hearing disorder and normal hearing sensitivity (6, 8).

The goal of the presented study was to analyze the effectiveness of the Turkish matrix sentence test (TMST) in different types of background noise when evaluating the speech recognition performance of hearing aid users.

Materials and Methods

This study was approved by Ankara Yıldırım Beyazıt University Ethics Committee (approval no: 55-14) and conducted according to the Helsinki Declaration. Informed consent forms were signed by all participants.

Participants

A total of 42 native Turkish speakers with bilateral sensorineural hearing loss and who had been using hearing aids for at least six months were included in this study. All participants were in the age range of 20–65 years (mean 49.1±14 years). They were divided into two groups: one with 29 individuals (12 females and 17 males) using bilateral hearing aids and the other with 13 individuals (five females and eight males) using unilateral hearing aids (Table 1). The air conduction hearing thresholds of the participants were tested with Sennheiser TDH 49 P supra-aural headphones using Otometrics Madsen Astera audiometry (Aurical Aud, Otometrics; Taastrup, Denmark) connected to a computer. Speech recognition scores were tested using a Turkish monosyllabic balanced word list, and individuals who scored higher than 70% were included in the study (16). All audiological tests were conducted in soundproof rooms according to international standards (17). To obtain speech recognition scores with hearing aids during the TMST, Oldenburger software program equipped with free-field speakers, which were calibrated to standards specified by the manufacturer and connected to the Otometrics Madsen Astera audiometry device (Hörtech, Oldenburg, Germany), was used for speech recognition scores with hearing aids.

Stimuli and Procedure

The TMST developed by Zokoll et al. (14) was used to evaluate the speech skills of participants when wearing a hearing aid in different types of background noise. Each sentence used in the TMST was created using words that are frequently employed in daily life. The test material included 20 randomly selected sentences from a list of 100 sentences and was presented in an electronic environment using the open-ended presentation model. The score was calculated as the percentage of words repeated by the participants. The software changed each subsequent sentence automatically, applying either the adaptive or the non-adaptive method as the number of correctly repeated words in the last sentence increased. The non-adaptive intelligibility scores of the

Table 1. Hearing levels of participants

	Age	Right PTA (dB HL)	Left PTA (dB HL)
Unilateral HA	53.4±15.2	39.4±9	35.2±11
Bilateral HA	47.3±13.2	52.4±8.1	52.2±7.9

HA: Hearing aid user, PTA: Pure tone average of 4 frequencies (500, 1000, 2000, and 4000 Hz)

TMST participants were determined as the percentage of the correct responses and compared with the speech recognition scores with headphones. The adaptive procedure was preferred in our study because it determines the signal-to-noise ratio automatically, and the test was started with a 0 dB signal-to-noise ratio at a constant 65 dB sound pressure level (SPL) with hearing aids. The difficulty level of the subsequent sentence was based on a correct understanding of 50% of the words in the current sentence (18).

In the present study, two different types of artificial noise (constant and fluctuating) were used. The first type of noise has the same frequency distribution as sentences with constant noise (Matrix noise) (8). The other noise is fluctuating, which has similar spectral and temporal characteristics with a speech and used in International Collegium for Rehabilitative Audiology (ICRA) (6, 19). To create the ICRA noise, four different speakers read the text followed by filtering with three bands (800 Hz low pass, 800–2400 Hz bandpass, and 2400 Hz high pass). The resulting signal was filtered with a 100 Hz high-pass filter to create the final ICRA 5 noise (19).

After adaptive TMST was performed in a quiet environment using Sennheiser HDA200 headphones, TMST was performed with hearing aids using a free field speaker at different azimuths (S_0N_0, S_0N_{90} and S_0N_{270}). In the first listening situation, speakers were placed in front and on the right side of the individuals, and speech and noise were simultaneously given through the speaker in front of the patient at the angle S_0N_0 (azimuth 0). In the S_0N_{90} listening situation, the speech stimulus was presented from the patient's face, while the noise stimulus was presented from the right side of the patient. In the S_0N_{270} listening state, after the patient was moved to face the speaker on the right, the speech stimulus was presented from the face of the patient and the noise stimulus was presented from the left side of the patient.

Statistical Analysis

Data analysis was conducted with IBM SPSS version 23.0 (Statistical Package for Social Sciences) (Armonk, NY: IBM Corp). The Mann-Whitney U test was used to compare two nonparametric variables. The nonparametric Wilcoxon test was used for comparing two dependent groups. The significance level was set as p=0.05.

Results

The mean right and left ear pure-tone air conduction of the participants was 50.43±8.6 dB HL and 50.15±8.4 dB HL, respectively (Table 1). The difference between the two ears of the participants was not statistically significant (p=0.12). The mean TMST non-adaptive speech intelligibility test score of individuals with hearing loss was 88.02±6.12% with headphones in quiet (65 dB SPL fixed speech level).

In fluctuating noise, the speech recognition thresholds of bilateral hearing aid users were lower (better) than those of unilateral hearing aid users under S_0N_0 and S_0N_{270} listening conditions, but there was no statistically significant difference between the two groups (p=0.67). In constant noise, the speech recognition thresholds were found to be better only under S_0N_{90} listening conditions for bilateral hearing aid users but not unilateral hearing aid users (p=0.023) (Figure 1). Bilateral hearing aid users showed a significant difference between their adaptive TMST scores obtained with and without hearing aids in constant noise under S_0N_{90} (p=0.001) and S_0N_{270} (p=0.001) listening conditions. In fluctuating noise, a statistical difference was observed between the results obtained under S_0N_0 (p=0.007) and S_0N_{270} (p=0.001) conditions.

The speech recognition thresholds of all participants were determined with and without hearing aids, and the scores obtained under fluctuating noise conditions were significantly lower than those obtained under constant noise conditions (p=0.02) (Table 2).

Table 2. Turkish matrix sentences test findings of individuals with/without hearing aid

		TMST value without HA			TMST value with HA			p-value
Listening conditions	**Noise type**	**Min**	**Max**	**Mean ± SD**	**Min**	**Max**	**Mean ± SD**	
S_0N_0	Constant	-5.80	10.70	-0.32±3.72	-5.90	5.10	-1.84±3.05	0.012*
S_0N_{90}		-9.20	6.60	-0.70±4.37	-10.90	4.00	-4.04±3.54	0.001*
S_0N_{270}		-13.30	6.20	-2.57±4.97	-15.00	6.00	-6.81±4.08	0.001*
S_0N_0	Fluctuating	-10.00	10.90	-1.80±4.98	-11.10	8.20	-4.21±4.54	0.017*
S_0N_{90}		-10.30	6.20	-2.63±3.79	-12.10	8.40	-2.80±5.69	0.67
S_0N_{270}		-9.70	6.50	-4.06±4.85	-15.50	6.40	-7.26±5.26	0.001*

TMST: Turkish matrix sentences test, HA: Hearing aid, S_0N_0: speech and noise from front (0^0 azimuth), S_0N_{90}: speech from front and noise from right (90^0 azimuth), S_0N_{270}: speech from front and noise from left (270^0 azimuth), Min: Minimum, Max: Maximum, SD: Standard deviation

Discussion

Speech tests are the primary tests used to diagnose hearing disorders and to evaluate hearing amplification process (20). Conventional speech recognition tests used in speech audiometry have limitations, dependent on the open response format, the practitioner, and the language. To resolve these limitations researchers developed matrix sentence tests that can be applied to many natural languages (13, 14). Matrix tests can be performed using different types of noise (21).

In the presented study, speech performances of hearing aid users were evaluated with two different types of noise (constant and fluctuating) by using the Turkish matrix sentence test (TMST). TMST scores of individuals with hearing aid were higher than the scores obtained without hearing aid in the free field in different azimuths (S_0N_0, S_0N_{90}, and S_0N_{270}) and different noises ($p<0.05$). This finding suggested that bilateral amplification is advantageous over unilateral amplification. Many studies in the literature indicate the benefits of bilateral amplification (22, 23).

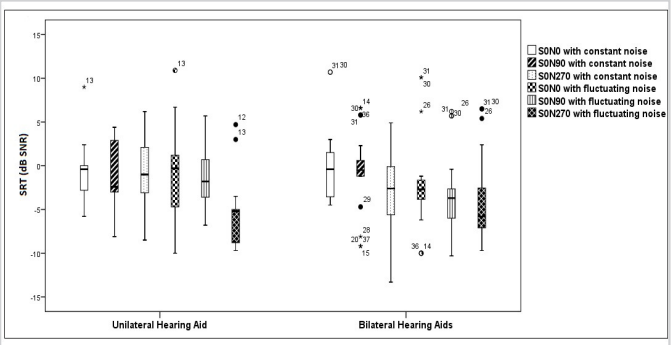

Figure 1. Turkish matrix sentence test results of bilateral and unilateral hearing aid users in different types of noise

SRT: Speech reception threshold, SNR: Signal-to-noise ratio

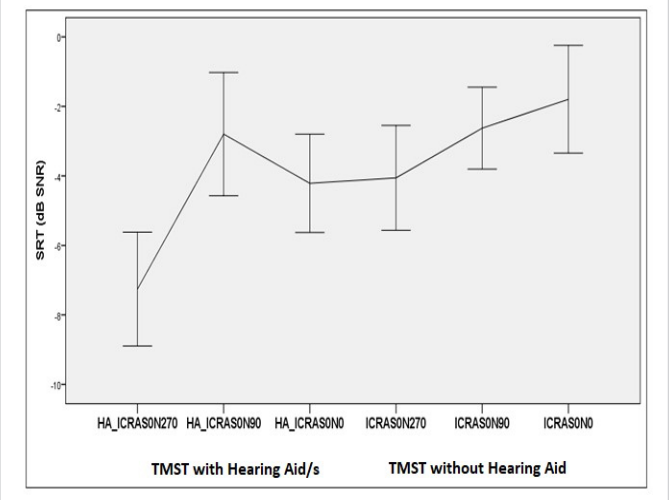

Figure 2. Turkish matrix sentence test results with/without hearing aid/s in fluctuating noise

TMST: Turkish matrix sentences test, SRT: Speech reception threshold, SNR: Signal-to-noise ratio

Ahlstrom et al.(24) used HINT in their study and reported that the use of hearing aids improved the audibility of speech and led to an increase in speech perception. Having used the matrix sentence test in their study, Gallo and Castiglione (25) reported that speech recognition skills were better in individuals who had a hearing aid in one ear and a cochlear implant in the other compared to those who used cochlear implant alone, and that the use of contralateral hearing aids (especially in bilateral amplification) positively affected the level of speech intelligibility.

The type of speech material and the features of the noise are essential factors affecting speech intelligibility, regardless of the signal-to-noise ratio (SNR) (26). In the presented study, we obtained lower scores in fluctuating noise than in constant noise, and this finding is comparable to the results reported by Kollmeier et al. (13). Noise differences may have different effects on speech intelligibility. Although there were individual differences, it is indicated that the speech intelligibility of listeners with normal hearing is increased when fluctuating noise (such as ICRA noise) is used instead of constant noise (2, 8). There were individual differences in our study, as well, and we thought that these differences might be due to the educational levels and lack of attention of the individuals. These factors are the limitations of our study.

In other studies, it has been stated that the speech-recognition threshold in fluctuating noise was 10 dB lower than noise with headphones in matrix test (8, 27). The advantage of the fluctuating noise depends on the duration of low-level intervals found in the noise (28, 29). We found the highest TMST score with the hearing aid in our design (free field) for fluctuating noise (Figure 2). In our study, it was found that the most effective noise used in the TMST test was constant noise, and this finding was consistent with the work of Wagener et al. (30). The highest (worst) thresholds were measured when speech and noise sources were in the same phase (S_0N_0), and the lowest (best) thresholds were observed when speech and noise were in different phases (S_0N_{90} or S_0N_{270}). In our study, the most significant change (better level) in speech reception threshold (SRT) value for those with hearing aids was observed in S_0N_{90} and S_0N_{270} conditions regardless of the noise type (Figure 2 and Figure 3), and this finding is consistent with the study of Freyman et al. (31). When speech and noise sources are presented to the listeners separately, delayed reflections from each source may affect the interaural time and level differences associated with that source (31). SRT difference between S_0N_0 and S_0N_{90} conditions shows the level of intelligibility (32, 33). If speech intelligibility in noise is spatially measured

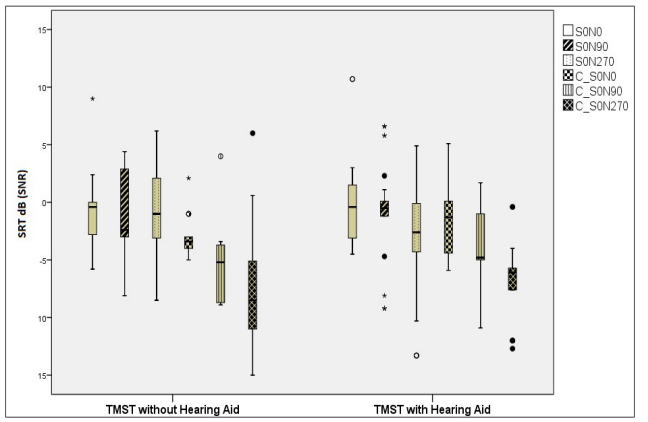

Figure 3. Turkish matrix sentence test results with/without hearing aid/s (HA) in constant noise

SRT: Speech reception threshold, SNR: Signal-to-noise ratio

with the binaural method, due to the azimuth difference, changes of more than 10 dB can be detected in people with normal hearing (34). In our study, different levels of speech recognition in two different noise types (between S_0N_0 and S_0N_{90} and between S_0N_0 and S_0N_{270}) and lower level of SRT in the TMST with hearing aids suggested that using hearing aids positively contributes to spatial speech perception skills.

As a result, since fluctuating noise does not completely mask speech and speech-like sounds, it can be a useful type of noise that can be used in the evaluation and follow-up of the auditory rehabilitation process compared to constant noise.

Conclusion

TMST is a useful test for evaluating the speech recognition level of hearing aid users. That better matrix sentence test levels were found in bilateral hearing aid users under different noise and listening conditions compared to unilateral hearing aid users showed that the latter group could improve speech intelligibility in noise by using interaural difference cues with bilateral amplification. Because fluctuating noise resembles environmental sounds in daily life, it could provide useful information in assessing speech perception skills of hearing-impaired individuals. Using speech recognition levels in determining spatial perception provides convenience in the clinical examination of various types of hearing aid users.

Ethics Committee Approval: This study was approved by Ankara Yıldırım Beyazıt University Ethics Committee (approval no: 55-14).

Informed Consent: Informed consent forms were signed by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Conception: B.Ç., Supervision: S.T.Y., Data Collection and/or Processing: B.Ç., Analysis and/or Interpretation: B.Ç., Literature Review: B.Ç., Writing: B.Ç., Critical Review: S.T.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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Main Points

- The Turkish matrix sentence test is a useful tool for assessing the speech recognition of individuals with hearing loss.
- The Turkish matrix test can be used to monitor the auditory rehabilitation process in individuals with hearing loss.
- Turkish matrix sentence test gives more reliable and more precise results in evaluating hearing aid performance under constant noise compared to other noise types.
- It is important to pay attention to the localization difference in device adaptation when evaluating the speech recognition skills of individuals with hearing loss with the Turkish matrix sentence test.

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Vestibular Illusions and Alterations in Aerospace Environment

Review

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Abstract

As the aerospace industry has grown rapidly over the years, aviators and astronauts have been exposed to some abnormal physiological changes arising from the dynamics of the aerospace environment. The vestibular system, encoding linear and angular movements of the head, is one of the main affected systems in which those abnormal changes can occur during flight. Despite the intricate and solid organization, vestibular units are such delicate structures that they can easily be deceived by aerial dynamics and gravity changes. Therefore, it is of vital importance for the continuity of flight safety to be aware of the detrimental alterations and impairments regarding the vestibular system and its reflex pathways. The aim of this paper was to present a review about how a healthy vestibular system is negatively affected within the aerospace environment and how some vestibular disorders become exaggerated or impaired during aviation and space activities.

Keywords: Aviation, illusion, vestibular sense, acceleration, microgravity, otorhinolaryngology, physiology

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Introduction

Flying and exploring space have always been desired by mankind throughout history. Since the early days of aviation, great improvements have been made in the maneuverability and technological capabilities of aircrafts in correlation with developments in the aerospace industry. However, it has been seen that exposure to high altitude, excessive acceleration forces and microgravity cause some detrimental and extraordinary effects on human physiology.

Gravitational acceleration on the surface of the Earth is approximately 9.8 m/s^2 and this is denoted as 1 G. In a terrestrial environment under 1 G, the human body is well adapted to maintain the perception of the correct orientation carried out by visual, vestibular and somatosensory systems in splendid harmony. Conversely, during flight, the sensory systems have been shown to be poorly suited to the

abnormal situations and this harmony can easily succumb to misperception. This may occur in various ways depending on input misinterpretations from inadequate or conflicting orientational cues and some specific illusions which are generated in manned aircrafts during flight. Any vehicle that uses the air to gain support and provide stability for flying is called an "aircraft" and this term refers to all kinds of air vehicles such as airplanes, helicopters, gliders, hot-air balloons, blimps, etc. In aviation, there are different types of air vehicles with different flight principles. Among the most common manned aircrafts, airplanes and gliders refer to fixed-wing aircrafts and helicopters refer to rotary-wing aircrafts. We live in a world of three dimensions, so the aircrafts move around three axes of rotation. The rotational movement of an aircraft around the longitudinal axis is called roll, around the vertical axis is called yaw, and around the lateral axis is called pitch (Figure 1). The maneuverability (the ability to change the speed and flight direction around these three axes) and the stability (the ability to withstand a disturbing force and restore the initial flying position) of aircrafts are determined by structural and aerodynamic factors; therefore, it may be said that the type of an aircraft, its stability and maneuverability affect which types of the illusions are experienced to what extent.

The gravitational force decreases with altitude. For example, at an average altitude of 400 km where The International Space Station maintains an orbit around the Earth, the gravity is approximately 90% of what it is on Earth's surface (a microgravity environment). In orbital spaceflights, when the spacecraft enters the orbit with a speed of about 17,500 miles per hour at that altitude, the curved path of the spacecraft becomes parallel to the curvature of the Earth and there begins a continuous free-fall of the whole spacecraft (with its crew and anything inside). Within a constant angular momentum, the Earth's gravitational force and constant speed of the spacecraft are balanced, and this continuous free-fall creates a condition of floating and weightlessness. This condition is also called "microgravity" (1×10^{-6} G) and this term is generally used instead of weightlessness (1). The same microgravity conditions can also be created on Earth via parabolic flights, drop tower and skydiving activities. As in flight, deteriorations in orientation and conflicts between vestibular, visual, and proprioceptive systems also occur when exposed to microgravity (2).

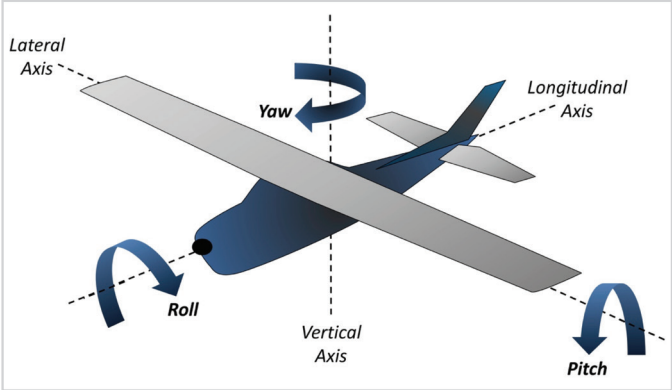

Figure 1. Axes of an aircraft

Spatial disorientation (SD) in aviation is defined as a pilot's erroneous perception of the position or motion of the aircraft with respect to the surface of the Earth or to any kind of aircraft flying nearby. During flight, nearly all pilots are confronted with inconspicuous but influential SD-related conditions and illusions which cause deprivation on multiple sensory and perceptual processing affected by operational circumstances. These undesirable illusions and misperceptions play a part in jeopardizing flight safety, causing near misses and accidents. In many studies, the rates of SD in aircraft and helicopter accidents have reached up to 30% with fatality rates up to 80% (3-5). Vestibular illusions may also have an important place in accidents attributable to SD. In some studies, illusions derived from the vestibular system were found to be contributing factors in SD-related accidents with rates up to 41% (6, 7).

SD-related illusions—mostly vestibular—are usually defined as "vertigo" among the pilots in practice. The term "Pilot's vertigo" has also been included in the aviation literature from the early days. Vertigo is a symptom which describes the sensation of spinning or moving and is associated mostly with the pathology of the vestibular system, whereas vestibular illusions during flight occur because of a physiological mechanism of a healthy vestibular system. Although not as much as SD, the term "vertigo" is still used among the pilots today and aeromedical specialists are able to understand what is meant. Moreover, describing a flight-related misperception as a vertigo episode may be useful in understanding the type of the vestibular illusion experienced (8).

In comparison to other clinical disciplines, otorhinolaryngology is thought to be more related with many main topics of aerospace medicine, such as the effects of partial pressure changes of gases and vestibular responses encountered during flight and high-altitude exposure (9). The developments in military and civil aviation activities, space missions, and adaptation processes to microgravity, have continued at an increasing rate, and thus the vestibular system, its flight-related alterations and some of the vestibular disorders have become more significant in the realms of both otorhinolaryngology and aerospace medicine. In this paper, it was aimed to analyze the main vestibular misperceptions that occur in subjects with a healthy vestibular system and some vestibulopathies which are affected or aggravated by exposure to the aerospace environment.

Interactions of the Vestibular System with Acceleration, Gravity and Eye Movements

The vestibular system plays an important role in providing balance and positioning. Gravitational and motional inputs, which originate from linear and angular acceleration forces, are transformed into orientational information by the vestibular system. Although the role in maintaining spatial orientation is not as great as the visual system, vestibular functions significantly predominate, especially in conditions of visual impairment such as flying in cloud or at night. The vestibular system also constitutes some main reflex pathways which enable gazing and retinal image stabilization during head and body movements (10).

During flight, aviators are exposed to several acceleration forces-commonly used as G forces in aviation—many of which are not encountered on the Earth's surface. These forces are generated in various directions and amplitudes that cause some physiological responses, and thereby affect their performance. When exposed to a high +Gz force (inertial force acts from the head towards the feet during an inside loop maneuver or a sharp banked turn), the blood pools in the lower parts of the body and this causes a sudden and critical reduction in cerebral blood flow which may result in tunnel-vision (loss of peripheral vision), gray-out (progression of the peripheral vision loss towards the center accompanied by dimming of color), black-out (complete vision loss) and eventually G-LOC (G-induced loss of consciousness). When exposed to -Gz force (inertial force acts from the feet towards the head during an outside loop maneuver), the blood pools in the upper parts of the body and this causes an increased pressure and vascular congestion in the head which may result in edema of the eyelids, subconjunctival hemorrhage, red-out (reddening of the vision), mental confusion and eventually unconsciousness. Besides these circulatory changes, G forces have also other systemic effects such as respiratory deteriorations and musculoskeletal hazards (11). The vestibular system is very sensitive to acceleration forces, so little amounts of these forces can cause considerable alterations. Semicircular canals and otolith organs are affected differently by these forces which occur with speed changes (acceleration or deceleration) and various maneuvers (roll, pitch, bank, spin, etc.) of the aircraft. During the takeoff and landing phases in flight or in launched aircraft, linear speed changes occur and primarily affect otolith organs. With spin, banking or coordinated turns, angular acceleration occurs, and this primarily affects the semicircular canals. When exposed to angular acceleration, because it has the same density as endolymph, the cupula moves together with the endolymph flow, but when exposed to linear acceleration, endolymph motion is not generated, and thus the cupula remains steady and does not produce any signal. In space, microgravity causes impairment in the sensitivity of otoliths, but has no significant effect on the semicircular canals (12, 13).

As the head is exposed to rotation with constant angular acceleration, the affected semicircular canals in the plane of the rotation begin to turn (Figure 2). At the very beginning of the turn, the canal walls also move in the same direction as the turn, but the endolymph itself lags behind due to inertia, then moves in the opposite direction of the turn and this fluid movement deflects the cupula to the same direction of the turn, causing a sensation of turning in the same way of the initial rotation. If this initial turn becomes prolonged with constant angular velocity for a period of 5–20 seconds, inertial endolymph flow ceases and can no longer generate a flow force to deflect the cupula. Within this period, the cupula gradually reverts to its central position because of its gelatinous structure, and no sensation of turning is perceived despite the persisting angular rotation. When the

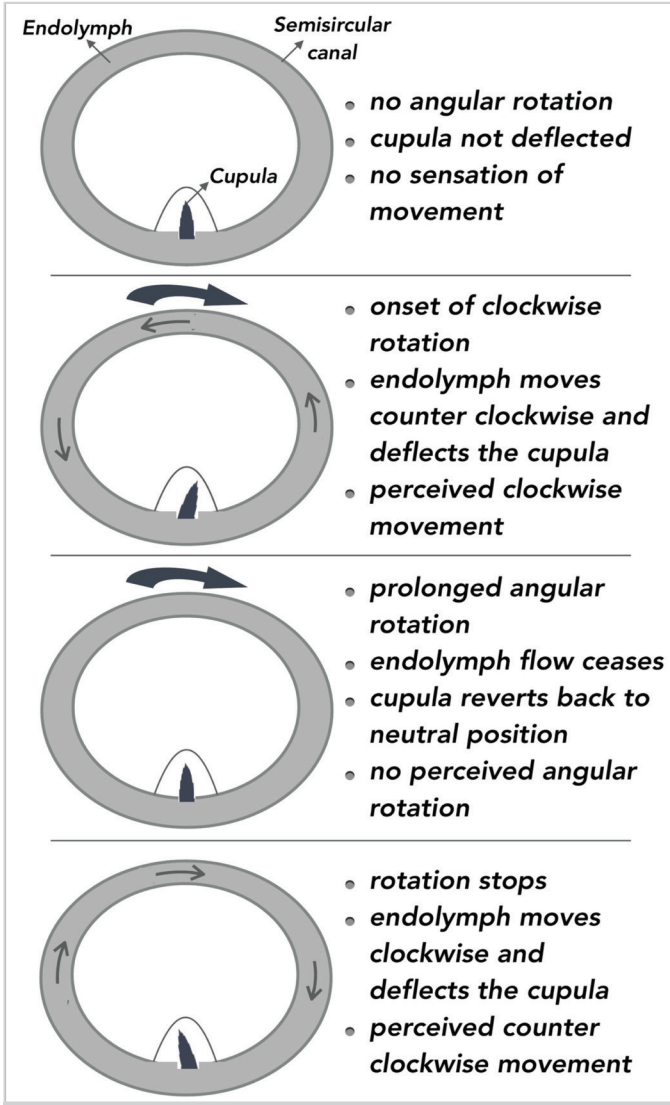

Figure 2. The response of the semicircular canals to sustained angular acceleration

rotation stops, the canal walls also accompany this angular deceleration, but endolymph flow continues to move because of inertia, deflecting the cupula to the opposite direction, and thus, once more a sensation of turning occurs (10, 14, 15).

To be able to perceive an angular acceleration, the constant rotation rate in a significant time must exceed a specified threshold. The threshold value of approximately 2.5°/second of the semicircular canals, below which angular rotations are not perceived is called Mulder's law (15, 16). In flight conditions, this approximate value may tend to be higher than measured due to excessive stress and work overload and cause the pilots to misperceive the critical angular maneuvers of the aircraft (15).

If exposed to a forward linear acceleration while the head is in a vertically fixed position relative to the Earth, otoconia located on top of the gelatinous membrane of the utricular macula moves backwards because of inertial force. This inertial force bends the cilia of the hairy cells backward and a sensation of tilting backwards is perceived (Figure 3). When the forward linear acceleration ceases, forward inertial force causes otoconia to move and bend the cilia in the same direction as the deceleration, and thus, a sensation of tilting forward is perceived. Similar linear perceptions are encountered when the saccular macula is affected by vertical (upward or downward) linear accelerations (10).

To maintain exact visual acuity during head movements, the image must be formed accurately on the retina. The vestibulo-ocular reflex (VOR), one of the main vestibular reflexes, maintains gaze stabilization for fixating the retinal image during head movements and linear or angular acceleration exposures (17). The VOR, generated by angular acceleration which results in response to the stimulation of the semicircular canals, is called angular VOR. The VOR, generated by linear acceleration and resulting in response to the stimulation of the otolith organs, is called linear VOR. Nystagmus and ocular counter-rolling are the two VOR responses contributing to retinal stabilization. Optokinetic movements which consist of fast and slow phases causing optokinetic nystagmus are other mechanisms providing retinal image stabilization during rotational head movements (10, 15).

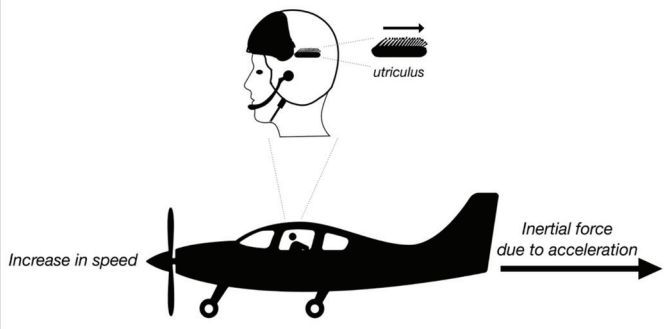

Figure 3. The response of the otolith organ to linear acceleration

Exposure to repetitive vestibular, especially angular, stimulations may have the effect of reducing the duration and intensity of misperceptions. There are also some significant differences in the maintenance of postural control between the pilots with a range of flying experience with different aircraft (18). Several studies have found that fighter pilots who are experienced and have more flying hours tolerate vestibular misperceptions better than those with fewer flying hours and less experience. The duration of nystagmus was also found to be decreased in experienced pilots after administration of some angular motions and Coriolis stimulus (19, 20). Such a habituation process to angular motions has not been observed in cases of exposure to linear motions (21).

Vestibular Illusions in Flight

Especially when flying without any external visual reference, the vestibular system predominates and causes rapid decrements in maintaining spatial orientation, which may create some specific illusions. Such illusions are so convincing that even seeing the flight instruments may not be enough to overcome these persuasive misperceptions. Coriolis, Graveyard spin and Leans illusions are some of the main specific illusions generated by the effects of angular accelerations on semicircular canals (14).

In flight, Coriolis illusion occurs with head movements during constant angular rotations. When exposed to a prolonged angular rotation for some time, endolymph flow of the semicircular canals aligned with the rotation axis ceases and the cupula becomes neutralized. From that time onwards, there is no sensation of turning. If the pilots move their heads on any plane (forward, backward, sideways, etc.) not aligned with the rotation axis, the state of balance is disrupted, and other semicircular canals are inserted into the axis of rotation (Figure 4). Which canals are affected depends on the direction of the moving head. Consequently, this disequilibrium in related semicircular canals activates the endolymph flow, the flow deviates the cupula and initiates an unbearable sensation of tilting, spinning or rotating in various directions (10, 15).

This illusion may occur with any kind of head movement resulting from checking the flight instruments, flight plan or the wings, reaching to the cockpit panel for any reason, following the leader aircraft, etc. Coriolis illusion is very common, especially in jet pilots. It was reported in a study that Coriolis illusion was experienced by 39% of pilots, many of whom were F-4 fighter jet pilots (22). This illusion is experienced not only by jet pilots, but also by helicopter and transport aircraft pilots. In an SD survey study conducted by the United States Air Force, Coriolis illusion was found to

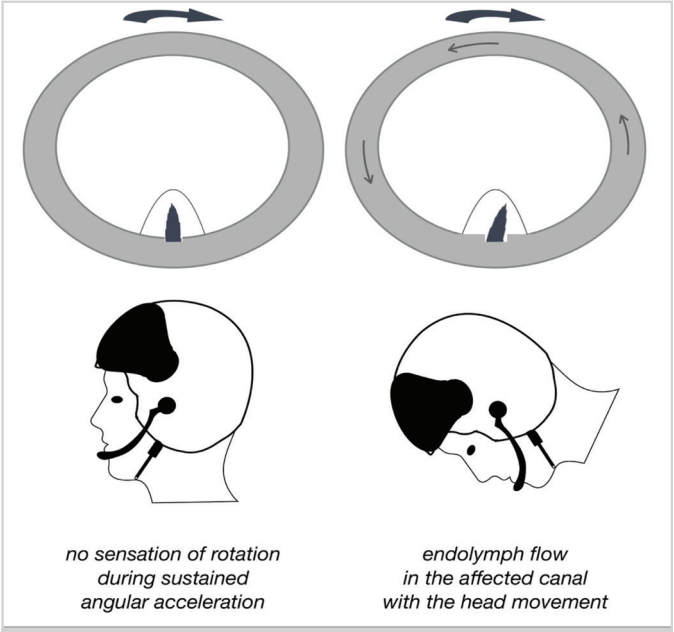

Figure 4. Mechanism of the Coriolis illusion

be experienced by 62.2% of jet pilots and 42.6% of helicopter pilots (23). Helicopter pilots stated that they experienced this illusion severely in night vision goggles (NVGs)-aided flights because of the limited 40° vision field, so NVGs hinder peripheral vision. Therefore, the pilots have to execute rapid head movements in order to view larger areas. It has also been stated that using NVGs caused increased sensitivity to vestibular misperceptions related to rotational motions (10).

The false sensation of rotation generated just after the cessation of constant angular acceleration encountered during a spin or a coordinated turn of banking maneuver is called somatogyral illusion. A typical example of this illusion is graveyard spin. In flight, spin is a dangerous maneuver in which the airplane follows a steep downward path in a stalled condition. Spin-like maneuvers can be executed unintentionally (because of pilot error, mechanical error or any kind of in-flight incident causing stall) or intentionally (in flight training or in procedure turns).

When an airplane enters into a spin, sudden changes occur in attitude (Figure 5). Besides perceiving many signs (an aerodynamic buffet—vibration caused by aerodynamic excitation—or a warning from the stall warning device) of the stall condition in an equipped airplane, the pilot also senses the direction of the bank correctly through the semicircular canals. If the rotation continues and angular acceleration becomes prolonged, inertial endolymph flow of the affected canals gradually ceases, the cupula returns to its neutral position and creates a sensation of level flight in 5–20 seconds. If the pilot decides to exit the spin, he or she recovers the aircraft to the opposite direction of the initial turn and brings it to a level flight position by some recovery maneuvers (neutralizing the controls, lowering the nose,

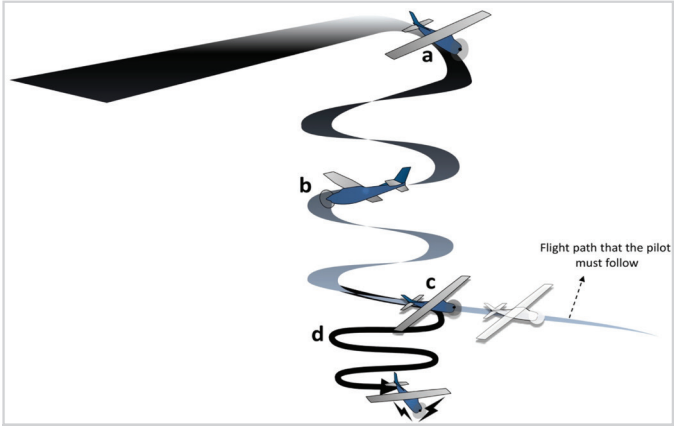

Figure 5. Mechanism of the graveyard spin. a. The pilot enters into a spin and the sensation of banking is perceived, b. The sensation of level flight is created after the angular rotation becomes prolonged, c. The pilot initiates the recovery maneuver to exit the spin, d. The pilot succumbs to the illusion and re-enters the initial spin position

building up airspeed while adding power, etc.). During these maneuvers, initial angular rotation stops, and endolymph starts to flow, and deflects the cupula to the same direction as the recovery position of the aircraft. At that time, although the instruments show level flight, the pilot perceives a sensation of banking in the direction opposite the initial rotation. If the pilot relies on this misperception, especially when there is no continuous external visual reference to maintain orientation, in order to dispel the sensation of banking he or she, because of the false sensation, may attempt to correct the aircraft in the same direction of the initial rotation, but, in fact, the aircraft erroneously re-enters the initial spin position. When the sensation of banking in the direction opposite the initial rotation occurs, without succumbing to this feeling the pilot must rely on the flight instruments and wait patiently until the sensation dissipates (10, 14, 15).

Various combinations of gravitational force and linear forces produce a resultant force called gravito-inertial force (GIF). GIF affects the otolithic membranes in different directions and these effects cause somatogravic illusions. Somatogravic illusions are false sensations of tilting, generated when various linear accelerations are encountered during takeoff and landing phases, or even in coordinated turns in flight. Nose-up Illusion, nose-down illusion, G-excess illusion and inversion illusion are the main somatogravic illusions caused by the effect of the GIF on the otolith organs (10, 24).

Nose-up illusion is a false sensation of pitch-up caused by forward acceleration during the takeoff or acceleration of the aircraft. During takeoff, if the aircraft accelerates forward with 1 G until the desired speed is reached, 1 G of inertial force acting backwards combines with the gravitational force (1 G) and produce a GIF. This resultant GIF acts on the otolithic membranes and creates an illusory sensation of having pitched-up at 45° (Figure 6). In the absence of

external visual cues, even if the flight instruments show slight pitch-up, the pilot may succumb to this misperception and attempt to push the stick forward in order to level the aircraft, or rather to correct the false sensation of climbing. If the altitude is low, this maneuver can result in controlled flight into terrain (CFIT), the inadvertent flying of an airplane under the control of the pilot who is unaware of the impending collision into the ground, water or an obstacle (24). Catapult launch entails a high risk of nose-up illusion because during this type of launch, the pilot is exposed to a rapid and a high acceleration force (generally 3–5 Gx in 2–4 seconds). This rapid and excessive acceleration may cause a sudden attempt to push the stick forward and consequently, a direct CFIT into the sea (15). Glider pilots also experience this illusion because the methods (winch, auto-tow, bungee launch, etc.) used in ground launching and aerotowing require rapid and excessive acceleration to gain as much height as possible in short distances.

The false sensation of pitch-down caused by the inertial force resulting from a sudden linear deceleration is called nose-down illusion (Figure 7). This illusion occurs with the reducing speed of the aircraft by lowering flaps, decreasing power, etc. It is not as dangerous as nose-up illusion, but if the pilot is deluded by this false sensation, he or she may want to correct the false sensation by pulling the stick and may inadvertently cause the aircraft to stall (24).

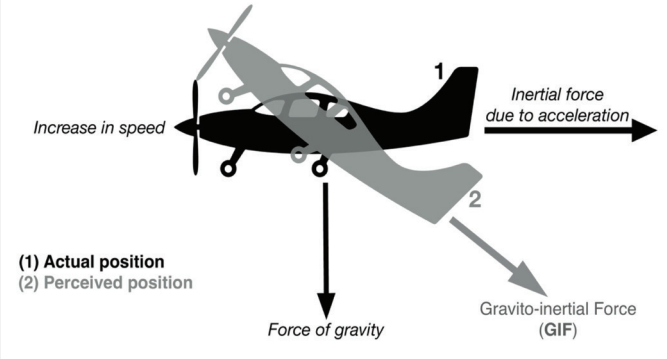

Figure 6. Nose-up illusion

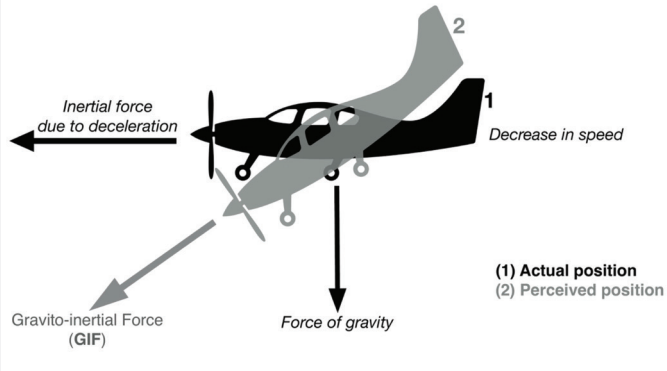

Figure 7. Nose-down illusion

During some specific maneuvers in flight, the direction of the GIF continually changes and creates an unending illusion. Inversion illusion is that kind of an illusion experienced while an airplane in a steep climb gradually levels off. As the pilot levels off the airplane, the speed spontaneously increases and consequently -Gz (centrifugal force) and backward inertial force combine and produce a GIF. As the direction of the GIF gradually changes and acts on the otoliths, the pilot begins to feel an excessive sensation of inverting backwards (Figure 8). To overcome this misperception, he or she pushes the stick and unintentionally contributes to the illusion by increasing both -Gz and +Gx. If the vision is degraded, the situation progressively worsens, and the airplane may enter a steep dive or even stall (25). It has been reported that this illusion is also experienced by the pilots in parabolic flights, in which microgravity is created for about 22 seconds (26).

G-excess illusion mostly occurs as a result of head tilts in various directions under excessive G forces. For example, if the pilot tips the head backwards under +Gz load (>1 G), otolithic membranes are deflected with a much greater acceleration force. Therefore, a more intense perception of body tilt is experienced, and the pilot may attempt to attenuate this exaggerated sensation of backward tilting (10).

G-excess illusion is also frequently experienced during banking maneuvers. In a sharp coordinated or a procedure turn, the amount of +Gz force is usually greater than 1 G. As there is exposure to a high G load, if the head is turned inside of the bank, the pilot perceives as if the aircraft is underbanked because the GIF produced by combinations of +Gz load and gravitational force acts on the otolith organ and deviates it backwards (Figure 9). If the pilot, especially when flying in adverse weather conditions, is deluded by this false sensation of underbanking they may attempt to increase the bank angle and inevitably the aircraft stalls (10, 24).

This illusion is commonly experienced in formation flights in which multiple aircrafts fly together as a single aircraft

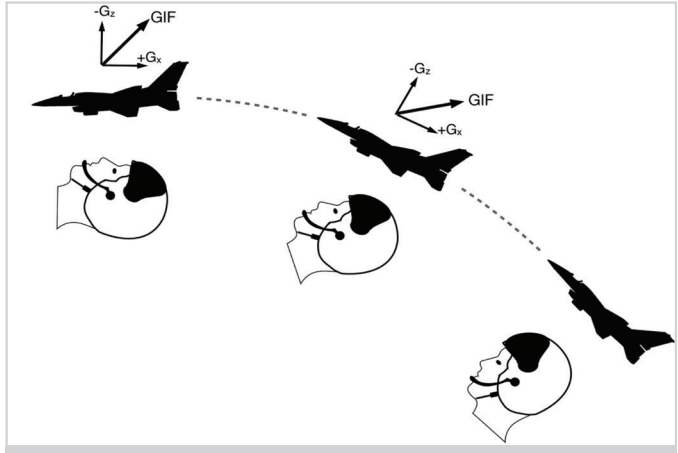

Figure 8. Inversion illusion. The pilot's head depicts the sensation of inverting backwards

at a constant angle under the command of a flight leader. The head of the pilot following the leader usually moves in order to observe the leader continually and correctly. The movement of the head is executed in various directions in accordance with the leader's maneuvers and may cause G-excess illusion in case of a sudden visibility loss. Coriolis illusion, which is generated with the head movements, is also experienced during formation flights (24).

One kind of misperception experienced during vertical linear accelerations is called elevator illusion. When an aircraft abruptly accelerates vertically upward mostly because of an updraft (a strong rise of warm and moist air), a sudden increase in +Gz load acts on the otoliths, creates a misperception of being in a climb and therefore, the pilot may attempt to descend. This kind of misperception is also experienced by glider pilots while using updrafts to gain lift and altitude (14).

The most common vestibular illusion experienced during flight is the Leans illusion (24). It is mostly experienced when exposed to a prolonged rotational banking below the threshold rate of 2.5°/sc (Mulder's constant). If the pilot unknowingly begins to rotate the aircraft around the roll axis at a subthreshold rate, no endolymph flow is generated, and the cupula remains stable in its resting position. Throughout the rotation period, the pilot perceives the aircraft to be in wings-level flight, while, in fact, it is banked. If the pilot notices this involuntary banking and abruptly corrects the bank position at a suprathreshold rate, he or she perceives a false sensation of banking in the direction opposite to the initial rotation although the aircraft is straightened and leveled. The pilot, if experienced and aware of the illusion, may lean towards the direction of the initial bank, tending to align his or her body vertically while forcing him or herself to rely on the flight instruments and waiting for the unbearable sensation of banking to dissipate. Otherwise, if the pilot succumbs to this false sensation of banking, he or she may attempt to correct the aircraft in the same direction

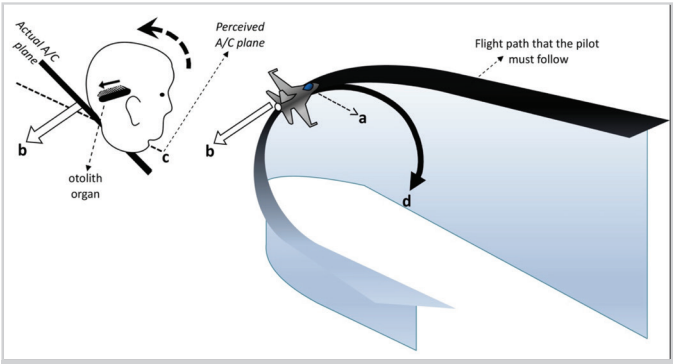

Figure 9. The mechanism of the G-excess illusion. a. The pilot looks to the inside of the turn, b. Gravito-inertial force (GIF) acts on the otolithic membranes, c. The pilot feels a false sensation of underbanking, d. The pilot may attempt to increase the bank angle

of the initial bank but, in fact, the aircraft may erroneously re-enter the initial banking position (Figure 10). Lack of somatosensory feedback also play part in loss of awareness of the aircraft's banking position and lowering the nose of the aircraft gradually accompanies this inadvertent bank. Therefore, it will be appropriate to increase speed to tilt the airplane's nose up and maintain a constant altitude during a banked turn (10, 24).

This illusion occurs insidiously when flying without any external visual reference. Moreover, it is very convincing, and thereby poses a high risk if not noticed at the right time. In many studies, Leans illusion has been found to be the most convincing illusion among the pilots of many types of aircraft (7, 27, 28). Among these studies, Sipes and Lessard (7) stated that Leans illusion was experienced by 94% of the pilots. In another study, the most common type of illusion was found to be the Leans illusion at a rate of 47.2% (22).

Visual Correlations of Vestibular Illusions in Flight

In certain periods of linear and angular acceleration exposures, some visual illusions co-occur with some vestibular illusions. These visual illusions are oculogyral and oculogravic illusions elicited by somatogyral and somatogravic illusions, respectively. Oculogyral and oculogravic illusions may exacerbate the effects of these vestibular illusions and make the illusions more intense. Post-rotatory nystagmus, counter-rolling and oculomotor reflexes play a role in these kinds of visual illusions (29).

Oculogyral illusion is the visual component of somatogyral illusion. As the pilot executes a maneuver to exit a prolonged

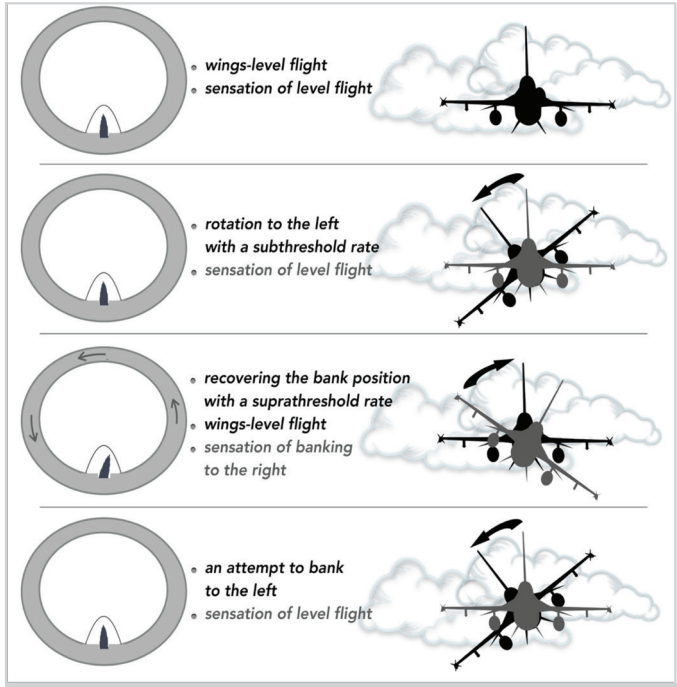

Figure 10. The Leans illusion

spin or a procedure turn, initial angular rotation stops, endolymph starts to flow and deflects the cupula to the same direction as the exit. At the time when the pilot perceives a sensation of banking in the direction opposite the initial rotation, any stationary objects or lights (cockpit instrument lights, etc.) within the pilot's visual field also appear to move in conjunction with the pilot's misperception. Oculogravic illusion is the visual component of somatogravic illusion. Any stationary objects or lights within the pilot's visual field appear to move in conjunction with the pilot's misperception. For example, these lights or objects appear to move upwards during the nose-up illusion or downwards during the nose-down illusion (24).

Other Vestibular Alterations Occurring During Flight and Afterwards

Apart from SD-related misperceptions, there are also various abnormal conditions which occur during or after the aerial or space flights. One of these conditions is airsickness which is a common type of motion sickness (MS) in aviation, especially among student pilots. Presence of a functional vestibular system is the main condition for the development of MS. It is hypothesized that during flight, exposing to linear and angular motions create conflict between the combined signals from vestibular, visual and proprioceptive systems and this sensory conflict leads to a mismatch between these signals and neural memory which contains individual balance information encoded thus far (30). Cold sweats, weakness, loss of appetite, nausea, fatigue and vomiting are the main symptoms. Desensitization therapy (repetitive exposure to provocative maneuvers in SD-training devices or in real flights) and relaxation methods (breathing exercises) are commonly used to alleviate the symptoms.

Another different form of MS is space motion sickness (SMS) in which weightlessness is the main precipitating factor. SMS usually occurs in the first two or three days in space and for several days up to seven after return to Earth, and it has been reported to have been experienced by 60%–80% of astronauts. Symptoms are similar to those seen in airsickness. There are some theories explaining this situation. According to the fluid shift theory, headward fluid shift caused by microgravity increases intracranial pressure. This increased pressure reverberates to the inner ear, and thereby alters the response of the vestibular receptors. The sensory conflict theory is another theory assuming that the harmony of the four main sensory inputs (otoliths, semicircular canals, visual and proprioceptive systems) in the perception process deteriorates under microgravity and these inputs may conflict with each other. Pharmaceuticals are commonly used in the treatment of SMS (1).

The vestibular and other related effects which emerge during aerial flights, air travel or space flights may also continue afterwards. Sometimes, when exposed to high amounts of negative and positive acceleration forces during flights involving aerobatic or dog-fight maneuvers, the pilots may have difficulty maintaining balance. This condition, which is defined as G-induced vestibular dysfunction (GIVD), occurs as a result of high G forces that are difficult to tolerate. These forces probably cause canalithiasis or cupulolithiasis. Detached otoconial debris moves to any canal and initiates the symptoms; it is therefore important to identify the affected canal to be able to achieve treatment success. Dizziness, unstable gait, nausea, loss of balance, and a sensation of spinning are the common symptoms and can last for days or even months. According to an informal survey conducted in 1998 during the World Aerobatics Championships, more than 75% of the pilots declared that they had experienced at least one GVID episode (31).

Mal de Debarquement (MdD) is another condition in which the vestibular system is affected especially after long cruises, air, space and even ground travel. It usually causes balance problems such as turning, shaking or wobbling sensations and may also be accompanied by impaired perception, fatigue, insomnia, anxiety and headache symptoms. Generally, 72% to 80% of these symptoms last less than 48 hours. Conditions in which the symptoms last from three days to years can be defined as Mal de Debarquement Syndrome (MdDS) (32, 33). MdDS is a rarely seen condition and the underlying mechanism is unknown. The symptoms can temporarily diminish by 80% during exposure to movements that cause MdD (cruise, flight, etc.) and again intensify after the exposure ends. This change is useful in diagnosis. There are various studies indicating that MdDS has some connections with MS, increased motion, and visual sensitivity (34, 35). In a study, 20 patients with MdDS were examined with positron emission tomography to determine the changes in brain metabolism. Increased metabolic activity was determined in the left entorhinal cortex (the region located in the medial temporal lobe, which controls memory, sense of place and direction and maintains communication between the hippocampus-neocortex) and the amygdala region, and increased interaction between the entorhinal cortex and the vestibular region (36). In another study, in which 29 patients with MSDS were examined, gray matter changes were observed in the visual-vestibular regions (37). There are also some studies suggesting that people with MdDS may have VOR incompatibilities (38, 39). Modulation of the VOR is one of the treatment options in MdDS.

Initial presentations of some pathologies that do not show any symptoms under normal conditions and have not been detected in routine examinations may emerge with the flight. Superior semicircular canal dehiscence (SSCD) is one such conditions in which symptoms occur due to the hydroacoustic transition to the inner ear through a defect overlying the superior semicircular canal. The disease involves

vestibular and auditory findings and patients often feel dizziness, drowsiness, hyperacusis, autophonia, conductive hearing loss, tinnitus, or ear fullness (40). Dreibelbis and Organ (41) reported a 30-year-old male trainee pilot suffering from recurrent attacks of dizziness. At first all these attacks were considered to be associated with air sickness. As the patient stated a sensation of spinning and hearing sensitivity, computed tomography (CT) scan of the temporal bones was taken, and it revealed a bone defect in the left superior semicircular canal (SSC). The patient refused to have surgery and was obliged to leave the flight training. As can be seen from that example, SSCD can emerge with a predisposing factor such as flight and can have a negative effect on flight careers. In another report, a 71-year-old female who experienced dizziness during an intercontinental flight and sudden hearing loss during landing was examined two days after the flight and found to have sensorineural hearing loss in the right ear and left lateralization in the Weber test. Epidural air over the right frontal lobe and bone defect in the SCC were also observed on cranial CT. Steroid treatment was administered for 14 days, after which CT scan and audiogram were repeated. Results showed that hearing functions had returned to normal, and the gas formation had disappeared (42). As in this case, although rare, pneumolabyrinth due to SSCD may occur during flight. These patients are advised not to travel by air before the gas formation has been completely resorbed.

Besides providing balance and positioning, the vestibular system is involved in different physiological changes induced by various acceleration forces. There are different vestibular-related physiological effects including the vestibulo-cardiovascular reflex (entails some changes in arterial blood pressure), vestibulo-sympathetic reflex (causes alterations in sympathetic system functioning), vestibulo-spinal reflex (maintaining postural steadiness), etc. For example, some vestibular illusions not only cause misperception in pilots, but also affect some physiological parameters and these effects may intensify the illusory sensations. Flights that are endangered by such exacerbated misperceptions may end with pilot incapacitations and even loss of lives. In a study in which heart rate, heart rate variability, electrodermal responses and respiratory rates were analyzed before, during and after Coriolis illusion stimulations in a flight simulator, heart rate and electrodermal response were found significantly increased during the period of the disorientation. However, these increased parameters returned to normal after cessation of the illusion (43).

There are also various findings about the interactions between vestibular dysfunction and some metabolic activities in microgravity. As previously mentioned, microgravity causes impairment in the sensitivity of otoliths, but has no significant effect on semicircular canals. With the decrease of gravitational input, otoliths become weightless and cannot provide information about the position of the head. A significant correlation has been found between decreased otolith functions and blood pressure imbalance (44). In addition, changes in otolith functions continue for a while after returning to Earth. Orthostatic hypotension has been reported in 40% of astronauts when they return to Earth (45). In addition to myocardial atrophy, reduction in circulating blood volume and baroreflex effectiveness are considered to be causes of orthostatic imbalance, and vestibular dysfunction also plays a role in this condition (44, 46-49). The vestibular system has many effects on dietary habits, bone and muscle metabolism and body temperature in addition to maintaining balance and orientation (50-52). Further research is ongoing about the vestibular system which has been found to have many effects on various metabolic functions.

Conclusion

SD has long been, and remains, a many-faceted problem in aerospace environment and requires a multi-pronged assessment. Awareness of SD among pilots has gradually increased with the developments in SD training programs. Theoretical background of SD is taught to pilots in lectures on visual and vestibular physiology, misperceptions and examples of SD-related incidents and accidents. In advanced SD training devices, veridical ground-based flight profiles are used to execute SD trainings in a safe environment. In these trainings, a wide range of real flight disorienting illusions are demonstrated. It is also told how to cope with vestibular illusions and alterations by teaching some critical methods such as minimizing head movements, waiting patiently until the sensation of angular rotation dissipates, etc. These training devices are also used in MS desensitization treatment.

There is a great danger if the control and the position of the aircraft depends on the erroneous perceptions of the pilot, and if not corrected, an accident is inevitable. Despite the technological developments that allow the pilots to use the latest generation aircrafts with high-tech equipment in all flight conditions, flight safety can easily be negatively affected due to the alterations caused by the vestibular system. It can be obviously seen that the vestibular system will continue to push our limits with various systemic and reflex responses as long as the human body is exposed to gravitational and inertial forces of different intensity and directions in the aerospace environment, or on any planet in the future. Therefore, it is important to be always aware of this fact in operational flights and aeromedical trainings.

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Main Points

- When a pilot with a well-functioning vestibular system is subjected to acceleration forces in different intensity and directions during flight, it is inevitable to experience illusions and misperceptions.
- Besides providing balance and orientation, the vestibular system has different effects on many physiological mechanisms.
- The effects of hypergravity and microgravity on the vestibular system and the pathological conditions caused by these effects constitute the joint field of study for otorhinolaryngology and aerospace medicine.

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Born in the Ear Canal: Tick Larva on the Eardrum

Case Report

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Abstract

We report the case of a 54-year-old woman who presented to the ear, nose, and throat (ENT) outpatient clinic with hearing loss, tinnitus, and fullness in her right ear. In the first clinical examination, a pouch hanging in the anterior upper quadrant was detected in the tympanic membrane of the right ear. A tick larva was found in the cyctic lesion located on the tympanic membrane. Our case was unique due to this unexpected diagnosis.

Keywords: External ear canal, tympanic membrane, foreign body, ticks, larvae, case report

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Introduction

In the ear, nose, and throat (ENT) practice, foreign bodies in the external auditory canal (EAC) are commonly seen. Beads, plastic toy parts, pebbles, corn kernels, toy parts, candle wax, food, paper, button batteries, cotton, metal balls, pen tips, and erasers are known aural foreign bodies (1, 2). Sometimes live foreign bodies, such as flies and ticks, can also enter the EAC. While vector-borne infections are among the leading causes of both human and animal diseases, ticks are one of the most critical vector groups. Ticks can mediate some diseases (Crimean-Congo hemorrhagic fever, Lyme disease) as vectors and cause some complaints (earache, fullness, hearing loss, tinnitus, painful otitis externa) when they settle in the EAC (3).

Case Presentation

A 54-year-old woman was admitted to the ENT outpatient clinic with tinnitus, humming, fullness, and hearing loss in her right ear. The patient did not have any problems with her right ear until an ache, followed by complaints like fullness, increasing hearing loss, tinnitus emerged abruptly. In the first clinical examination, a pouch hanging on the anterior upper quadrant was detected in the tympanic

membrane of the right ear. The pouch was a 5x4 mm cystic bag filled with fluid in constant motion (Figure 1).

The patient's medical history revealed that she was diagnosed with glomus jugulare in her left ear and was treated with radiotherapy. Deafness was found in the left ear after radiotherapy and the patient had not been followed-up in the past two years. The left EAC and tympanic membrane were found normal in otoscopic examination.

In addition to the constantly moving fluid in the pouch, there was an increase in the vascularization of the rest of the tympanic membrane, and its color was matte. Minimal fluid (air-fluid level) existed behind the tympanic membrane. Audiometric analysis revealed a conductive hearing loss in the right ear, audiogram, air 46 dB, and bone 16 dB. In the left ear, air 97 dB and bone 74 dB were found (sensorineural hearing loss associated with the glomus tumor and radiotherapy). In the tympanometric assessment, there were type B and A tympanograms respectively for the right and left ears.

The patient was hospitalized with otitis media and a preliminary diagnosis of tumor of vascular origin attached to the eardrum in the middle ear or epidermoid cyst of the tympanic membrane. The patient was given antibiotic (ampicillin/sulbactam) and topical nasal decongestant (oxymetazoline hydrochloride) as treatment. The temporal bone was scanned with computed tomography to evaluate the middle ear structures and the examination revealed no pathology. The complaints of the patients did not decrease but increased in the 48 hours after the treatment was started. In examination, the sac was enlarged and pronounced. On the third day of hospitalization, severe tinnitus and ear pain emerged in the patient's right ear. Otoscopic examination revealed that the cystic pouch on the tympanic membrane had burst, and an arthropod was moving in the EAC. The arthropod was carefully removed from the EAC and placed in a glass jar (Figure 2). The patient's tympanic membrane was intact, and all complaints, tinnitus, humming, and hearing loss regressed.

Figure 1. Tick larva on the eardrum

The tympanic membrane was normal two days after the arthropod was removed. New audiometric analysis revealed normal hearing in the right ear with type A tympanogram. The patient was referred to the department of infectious diseases for Crimean-Congo hemorrhagic fever. All the hematologic and biochemical examinations were normal.

The arthropod was sent to the departments of parasitology and medical microbiology of the Veterinary Faculty for parasitological analysis. Parasitological analysis defined the arthropod as a tick due to its specular formation and four pairs of legs (Figure 3). The tick was in the latest stage of the first nymph (the juvenile stages of life) and nearly past the second nymph stage without bloodsucking. After its subtype was defined, the tick was released to the natural environment and no more examinations were performed.

Discussion

Foreign bodies in the EAC are not rare entities among otolaryngologic diseases. It is especially common in pediatric age groups. Unlike children and mentally disabled people, most normal adults know the etiology of the foreign body and consult a doctor without complaints arise. Such cases can remain asymptomatic, or cause earache, otitis externa,

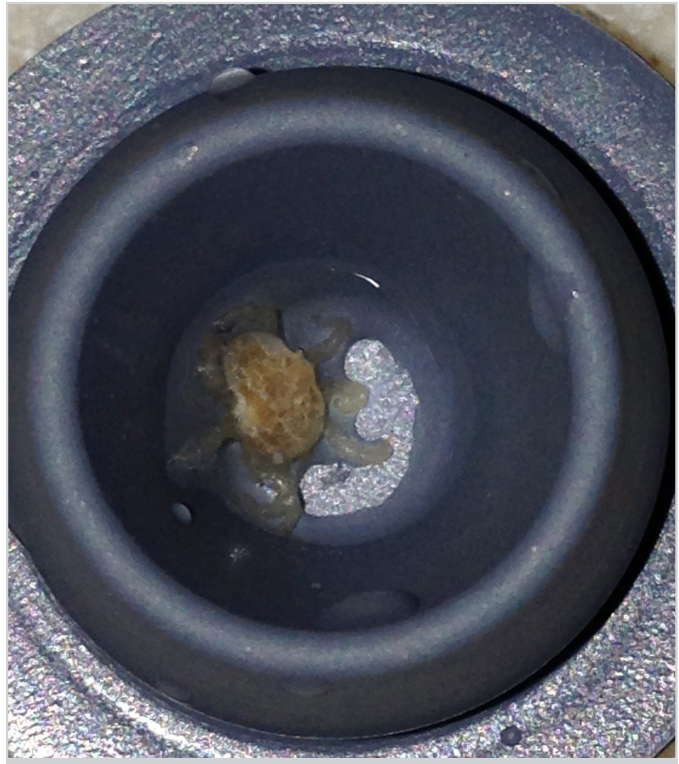

Figure 2. The young larva, which has just come out of the pouch, was taken to a transport container

Figure 3. Image of nymph not yet fed under a magnifying glass

purulent drainage from the affected ear, hearing loss, hyperacusis, itching, fullness, tinnitus, or feeling of a foreign body in the ear (4).

Sometimes they can lead to more severe complications such as advanced sensorineural hearing loss, suppurative labyrinthitis, and osteomyelitis (5). A wide variety of foreign bodies, such as beads, batteries, fruit seeds, paper, grass have been removed from the ear canal. Although rare, pests such as ticks, flies, and ants can also enter the EAC. It should be noted that ticks, as was the case of our patient, can release their larvae in the external ear canal. The EAC is an ideal place for ticks to suck blood or leave their larvae. When clinicians identify the presence of tick larva, they should not try to pull it with tools like punch forceps, but gently cut the cyst wall and try to remove the content without damaging the eardrum.

Spinose ticks, which consume blood while in the external ear canal, can cause irritation, inflammatory reaction, tissue necrosis, and bacterial infection. It is reported that a four-year-old female child had difficulty chewing and swallowing, hoarseness, hypernasal speech, and hypersalivation because of an oropharyngeal muscle weakness as a result of tick bite. Muscle weakness was seen due to the passage of neurotoxins secreted by the tick along the esophagus (6).

When tick eggs grow in the place they are laid, they can resemble a cyst. In our case, that the tick larva was attached to the eardrum led us to consider tympanic membrane cysts in differential diagnosis. Most of the cysts defined in the middle ear contain cholesteatoma and are associated with a history of infection or with iatrogenic effects (7). The presence of epidermal/epithelial inclusion cysts on the tympanic membrane is defined as a possible iatrogenic lesion that occurs only after myringoplasty or infection (8–10). In our case, however, we report that it can also occur due to tick larvae. We hope that this first-ever report about an unusual entity, which may go unnoticed due to its rare characteristics, will provide a key to clinicians when examining patients presenting with similar complaints.

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Main Points

- The appearance of ticks in the external ear canal is a common clinical condition.
- Tick larva on the eardrum, however, is a rare entity mimicking a membrane cyst or middle ear pathology.
- It can be confused with a tympanic membrane cyst and should be kept in mind in diagnosis, as we found in our case.

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Symptomatic Solid Ectopic Cervical Thymus in a 2-Month-Old Infant: Case Report

Case Report

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Abstract

Ectopic cervical thymus (ECT) is a rare pediatric pathology usually with an asymptomatic course. In fewer cases, the patient may present with dyspnea, hoarseness, stridor, dysphagia and pain. The mass may present in cystic or solid forms. Solid forms are rare, constituting only 10% of all ECT cases and these are mostly symptomatic. We aimed to present the case of an infant with ECT in the submandibular region that led to shortness of breath. ECTs in the submandibular region are mostly solid and larger in size, and therefore, likely to result in compressive symptoms. In this case report, we tried to cover the important aspects of the diagnosis of ECT, its treatment, and discussed the results with a literature review. We additionally aimed to emphasize the importance of considering pediatric ECT in the differential diagnosis of pediatric neck mass as well as considering surgical excision to prevent serious consequences.

Keywords: Thymus, ectopic tissue, neck, tumor, pediatric, case report

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Introduction

The thymic primordium originates from the third pharyngeal pouch during embryogenesis. It disassembles from the pharynx and migrates to the mediastinum, which is its final position in the body (1). During migration, the thymus tissue can be trapped in different locations in the neck region and results in an ectopic cervical thymus (ECT).

ECT is a rare condition and is generally asymptomatic. In some cases, however, ECT may present with symptoms of mass compression and results in asphyxia or death (2). Additionally, in rare cases, Horner's syndrome can occur (3). Symptomatic ECT patients are usually in the pediatric age group, and it is difficult to differentiate from other pediatric neck masses. Radiological imaging studies can be of tremendous help in distinguishing the condition from other neck mass pathologies.

In this case report, we share a pediatric patient with ectopic thymus who

presented with shortness in breath. The histopathologic evaluation revealed the solid variant. The aim of this report is to share a rare pediatric neck mass, discuss imaging findings that are useful in differential diagnosis and the management of this pathology.

Case Presentation

A 2-month-old male baby was admitted to our clinic with swelling in the right submandibular region and a history of shortness of breath for one week. On physical examination, the patient was found healthy except the mass. The lesion was 4x4 cm in size and mobile, not fixed to the surrounding tissues.

Neck doppler ultrasonography (USG) was performed to evaluate the size of the mass and its relation to the adjacent vascular structures. The Doppler USG revealed a well-circumscribed, homogeneous, solid mass lesion in the right submandibular region pushing the submandibular gland anteriorly and the major vascular structures medially, as seen in Figure 1. The mass was in the same echo with the thymic tissue and showed significant vascularization with no evidence of invasion to the adjacent structures. In contrast-enhanced magnetic resonance imaging (MRI) of the neck, a soft tissue intensity lesion of approximately 5x4x3cm was observed in the right submandibular region (Figure 2). When the patient was evaluated together with the MRI and USG findings, the senior author, who is an experienced head and neck radiologist considered the mass as an ectopic thymus because it had the same intensity as the thymus tissue found in the superior-anterior mediastinum. The fine needle aspiration biopsy (FNAB) performed on the patient had not contributed to a definite diagnosis.

The mass was totally excised by dissection from the surrounding tissues under general anesthesia, as shown in Figure 3. The patient did not have any postoperative complications and was discharged.

The diagnosis of the solid form of the ectopic thymus tissue was confirmed in the histopathology report. On the first week of postoperative follow-up, the wound was seen to heal optimally, and the patient's shortness of breath disappeared.

Discussion

The ectopic thymus can be found in different locations in the neck region as a result of the incomplete descent of the thymic primordia from the 3rd–4th pharyngeal pouches to the mediastinum. Lesions that remain in the submandibular region during migration are rarely encountered, compared to lesions located in other cervical areas, and tend to be

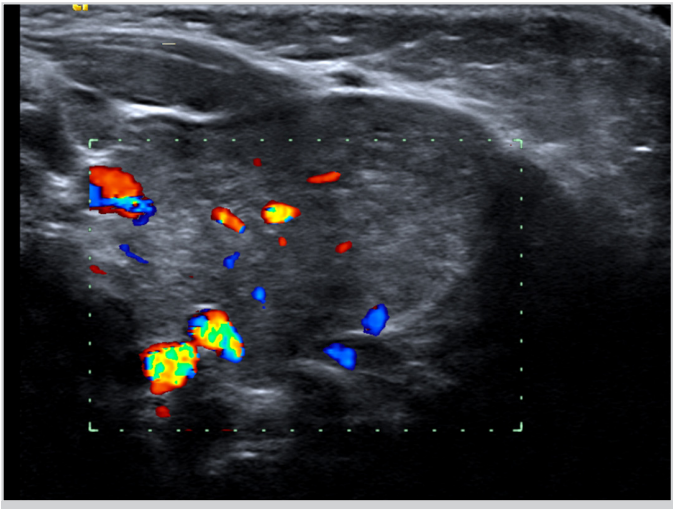

Figure 1. Doppler ultrasonography image of ECT showing the vascularization of the tissue
ECT: Ectopic cervical thymus

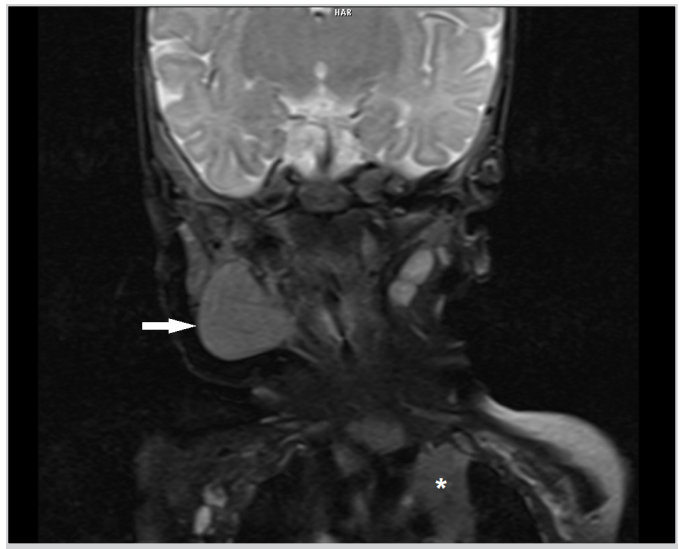

Figure 2. MRI of the neck showing ECT (arrow) is in the same intensity as the normal thymus tissue (asterisk)
MRI: Magnetic resonance imaging ECT: Ectopic cervical thymus

Figure 3. Excision of the solid mass; view highlighting its vicinity to major vasculature. a. solid mass, b. carotid artery, c. internal jugular vein

larger in size, typically diagnosed at a young age (4). In most cases, ECT is asymptomatic with only 10% presenting with compressive symptoms including dyspnea, hoarseness, stridor, dysphagia, and pain (5). It is important to differentiate symptomatic ectopic thymus cases from other neck masses to prevent serious consequences.

USG is the most practical and easy method for the diagnosis of ECT. Doppler USG is the most preferred technique for detailed visualization of thymic tissue. In Doppler USG ectopic thymus shows vascular structures corresponding to the echogenic septae with a linear structure (5). As in our patient, USG features revealed blood vessels within the lesion and were more homogenous in structure than the salivary glands.

MRI is another tool to use in diagnosing soft tissue lesions of the neck. MRI of ECT is homogeneous, has similar features with normal thymus tissue and is hyperintense in T2-weighted sequence. Visualization of normal thymic tissue is important before surgical intervention; hence, excision of thymic tissue can lead to immunologic consequences (6). We pre-operatively confirmed the existence of normal thymus in the mediastinum in our patient and identified the similarity of the images of the lesion with normal thymic tissue.

In rare cases, cytopathological examination with FNAB can lead to a certain diagnosis. Some authors refuse to perform FNAB in children because of its controversial diagnostic benefits and general anesthetic requirements (4, 7). As the lesion was large, FNAB was performed without general anesthesia in our case. Considering its possible contribution to a differential diagnosis we did perform FNAB. The ectopic thymus can be cystic or solid. Most of the cases are cystic ECT, only 10% present in solid form (8).

In the recent years, the conservative approach is more accepted in asymptomatic ECT regardless of its location. Purcell et al. (4) proposed a classification based on its location in the neck and claimed that most ectopic thymus are intrathyroidal or in the central neck. In the referred study, only 9% of the cases were in the submandibular region. Furthermore, lesions located in the submandibular region were larger in size, mostly solid and did not show significant change in size over time (4). If ECT is incidental or there are no symptoms at the time of examination, it is reasonable to follow-up the patient without any surgical intervention.

Although ECT is asymptomatic in most cases, some cases in the literature led to a catastrophic result and patient's death. Ishida et al. (2) reported two infant deaths due to compression of the solid ectopic thymus to the cervical trachea, causing sudden infant death syndrome. Modabber et al. (3) reported a congenital case of Horner's syndrome associated with ECT in a 19-month-old patient. Considering all these symptoms of ECT, even if they are not prevalent, we recommend the total excision of the lesion to avoid an unwanted outcome.

Conclusion

Although rare, ECT should be considered in the differential diagnosis of mass lesions of the neck region in pediatric patients. In imaging modalities, the normal location of the thymus should also be scanned along with the region of the mass. The surgical treatment should be planned only if the thymus gland is observed in the normal location. Even they are mostly asymptomatic, a solid variant of ECT in the submandibular location should be excised given the risk of airway compression.

Informed Consent: A written informed consent was obtained from the patient's parents.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.C.E., N.A., Design: F.C.E., N.A., Supervision: G.D.E., Materials: F.C.E., N.A., G.D.E., Data Collection and/or Processing: N.A., G.D.E., Analysis and/or Interpretation: F.C.E., G.D.E., Literature Search: N.A., Writing: F.C.E., Critical Reviews: F.C.E., G.D.E.

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Giant Epignathus (Teratoma of Palatine Tonsil): A Case Report

Case Report

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Abstract

Teratomas are benign tumours containing tissues derived from ectoderm, endoderm and mesoderm Epignathus is a rare congenital teratoma and originates from oropharyngeal region. We present a case of giant epignathus arising from tonsillar region in a neonate. A male neonate that was born with a 38-week cesarean section presented with a pedunculated mass from left tonsilla palatina and protruding outside the mouth. The patient did not have any airway problem. Magnetic resonance imaging and computed tomography scan showed no intracranial extension. The patient was operated on the postpartum 3rd day and the mass was excised successfully. After histopathological examination, mature teratoma was diagnosed. During post-operative 6 months control visit, there was no recurrence. Epignathus is a rare congenital oropharyngeal teratoma, it should be diagnosed in the fetus as early as possible. Teratomas of the tonsilla palatina are extremely rare. In such cases, the mass may cause airway obstruction and feeding difficulties so complete resection is curative in most cases during the early neonatal period.

Keywords: Epignathus, teratoma, fetal anomaly, palatine tonsil, pediatric otorhinolaryngology, case report

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Introduction

Teratoma is composed by multiple tissues derived from the three germ cell layers (ectoderm, endoderm and mesoderm). The incidence of teratomas is 1:4,000 live births. (1). Teratoma can be seen almost anywhere in the body. The clinical presentation varies depending on the size and location of the lesion. Epignathus is a term commonly used for teratomas originating from the oropharyngeal region such as jaw, palate or pharynx (2). The incidence of epignathus is 1:35,000 to 1:200,000 in live births. Epignathus that arise from tonsillar region is very rare (1).

In this case report, we present a rare case of giant epignathus with different localization in a male neonate. The clinical characteristics, diagnosis and treatment of this rare disease are also reviewed.

Case Presentation

A male neonate with a birth weigth of 3.8 kg was born by elective caesarean section

delivery at the 38 weeks of gestation. He was presented with a giant mass protruding from the oral cavity. Apgar score of the newborn at the first and fifth minutes of birth was eight. The history of the mother did not reveal polyhydroamniosis although she had no regular prenatal follow-up. Prenatal ultrasonography showed that the fetus had a large mass protruding from its mouth. A caesarean section delivery was preferred because of fetal anomaly. After delivery, the patient did not have any airway problem and did not require oxygen support because the mass did not totally obstruct the baby's oral cavity. The patient was evaluated in the neonatal intensive care unit. Otolaryngological examination revealed a mass covered by skin and hair, attached to left palatine tonsil with a peduncle, extending the buccal mucosa and protruding from oral cavity. In radiological evaluation with magnetic resonance imaging (MRI) and computed tomography, it was observed that the mass did not compress the trachea and had no intracranial extension (Figure 1). The patient was operated under general anesthesia on postpartum 3rd day. Double excisions were performed for complete resection. First, the extraoral part of the mass was excised with double ligation using cautery and suture. Thus, access to the pedicle was provided. The mass removed from floor of the mouth and buccal mucosa, then excised totally with left palatine tonsil (Figure 2). Size of the mass was approximately 18x12x7cm and it weighed 950 g. The histopathological examination revealed mature teratoma. In the sections, adnexal structures, glandular formations, common neuroglial elements, choroid plexus formations, adipose tissue, mature structures consisting of muscular tissues and cystic structures lined with multilayered squamous epithelium containing keratin were observed. The routine blood tests and chromosomal analysis were normal.

Figure 1. The preoperative T2 weighted MRI coronal section of the mass. Heterogeneous mass with cystic and solid components that associated with tonsillar and buccal region, protruding from oral cavity

MRI: Magnetic resonance imaging

The patient was followed up for approximately one week in the intensive care unit. He was fed through a nasogastric tube for a while. He was discharged on the seventh postoperative day and oral feeding began on the postoperative second mounth. On a follow-up period of 6-months, there was no reccurence of the epignathus. The patient was examined by pediatricians and his growth and development was normal (Figure 3).

Figure 2a. The giant mass protruding from oral cavity b. Surgical specimen (measuring 18x12x7 cm)

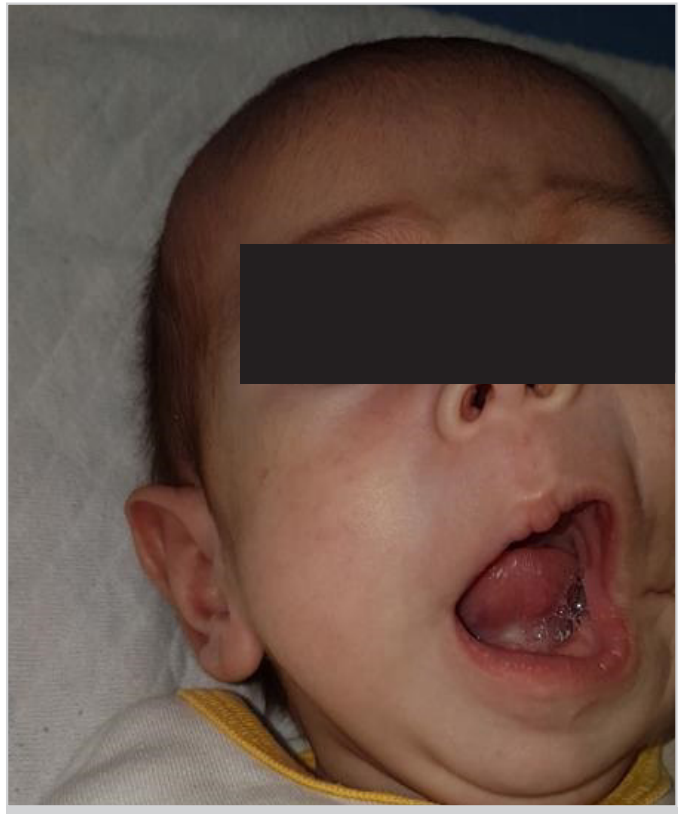

Figure 3. Patient at six months of age, with minimal facial deformity

Discussion

Teratomas are among the most common extragonadal germ cell tumors presenting in childhood and contain tissue from all three embryonic germ layers; ectoderm, endoderm and mesoderm. They are often located in the midline and paraaxial regions. They are most commonly seen in the sacrococcygeal region, anterior mediastinum, testis, ovary and retroperitoneum (2, 3).

Teratomas are classified into four types: Dermoid (hairy polyps), teratoid, true teratoma and epignathus. In terms of differential diagnosis, the hairy polyp presents at birth as pedinculated polypoid mass. It arises from naso-oropharynx mostly, and histologically composed of derivatives of ectoderm and mesoderm (4). However epignathus is a teratoma that arises from oropharyngeal region and includes tissues from ectoderm, mesoderm and endoderm.

The etiology of epignathus is still unclear. The most popular theory attributes its origin to disorganized growth of pleuripotential cells in the region of Rathke's pouch (5). There is no evidence suggesting that epignathus is caused by environmental agents, Mendelian or polygenic inheritance (6).

Teratomas contain ectoderm, endoderm and mesoderm layers. In addition, teratomas can be mature, immature or mixed tumors. In many cases, the presence of immature tissue indicates a diagnosis of malignancy (7). In our case, a mature teratoma was diagnosed. Mature teratomas are thought to have a benign character.

In recent years, the use of ultrasonography and MRI in prenatal follow-up for congenital anomalies has increased. MRI is a complementary diagnostic tool for epignathus to detect the relation of the tumor to the fetal airway and intracranial structures (8). There was no intracranial extention in our patient.

Epignathus may be a condition that can require tracheotomy in the neonate, leading to airway obstruction. In our case, the mass of the patient was derived from the tonsillar fossa and extending out of the oral cavity and did not cause respiratory problems, therefore no tracheostomy was needed. Postnatally, early surgical intervention is necessary. Early diagnosis, the establishment of a secure airway, complete excision of the tumor and timely follow-up should increase the survival of newborns with oral teratomas (9, 10).

Conclusion

Epignathus is a rare congenital oropharyngeal teratoma, it should be diagnosed in the fetus as early as possible. Teratomas of the tonsilla palatina are extremely rare. In this case report, we present a rare case of giant epignathus with different localization. Complete excision of the tumor is imperative to prevent relapse, maintain a secure airway and provide normal oral feeding of the patient.

Informed Consent: Consent was obtained from the patient's family.

Peer-review: Externally peer-reviewed

Authorship Contributions

Conception: F.A., Design: F.A., Analysis and/or Interpretation: M.M., M.A.E., Literature Review: M.M., Writing: F.A., Critical Review: M.A.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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Main Points

- Epignathus is a term commonly used for teratomas originating from the oropharyngeal region.
- Epignathus that arise from tonsillar region is very rare.
- Teratomas contain ectoderm, endoderm and mesoderm layers. In addition, teratomas can be mature, immature or mixed tumors.
- Epignathus may be a condition that can require tracheotomy in the neonate. MRI is an important imaging test in detecting airway obstruction.
- Epignathus should be diagnosed in the fetus as early as possible.

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