Evaluation of Inner Ear Damage by Using Otoacoustic Emissions in Patients Who Underwent Mastoidectomy and Tympanoplasty Operations in the Early Period

Original Investigation

Abstract ▶

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Objective: We aim to demonstrate inner ear damage caused by drilling in the early period. Healthy contralateral ears of patients who underwent mastoidectomy using drill or tympanoplasty without using drill were compared.

Methods: A total of 38 patients (mastoidectomy: 22, tympanoplasty: 16) who were diagnosed as chronic otitis media and were scheduled for surgery were included. Distortion product (dp) otoacoustic emissions measurements were performed on healthy contralateral ears of patients on pre- and post-operative 1. hour, 1. day, 2. day, 3. day, and 4. day.

Results: In mastoidectomy group, dp otoacoustic emission values on post-operative 1. hour, 1. day, 2. day, 3. day, and 4. day at a frequency of 4000 Hz were significantly lower than in tympanoplasty group (p<0.05). In mastoidectomy group, dp values on post-operative 1. hour,

Introduction

It is known that hearing loss can occur due to acoustic trauma. It has been suggested that an audiometry test is insufficient for the early detection of damaged cochlea associated with noise but that this damage can be found through otoacoustic emissions (1, 2). In addition, a damaged outer hair cell in the inner ear is one of the first findings of sensorineural hearing loss (3, 4). Therefore, otoacoustic emissions are used for the early detection of noise-induced damage in the inner ear (5-7).

Drilling the bone during mastoidectomy can also lead to sensorineural hearing loss in the healthy contralateral ear as well as in the operated ear because of undesired acoustic trauma (8). It has been found that the noise level is 100 decibels (dB) in the operated ear and 90–95 dB in the contralateral ear during the drilling procedure in mastoidectomy (9). In addition, in the study by Tos et al. (10), which was conducted on cadavers, they reported that a noise of 114–128 dB was produced in association with instruments used in middle ear surgery.

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 The aim of the a

The aim of the present study was to compare inner ear damage that developed in normal-hearing 1. day, 2. day, 3. day, and 4. day at 4000 Hz significantly decreased in comparison with pre-operative period, decrease in dp values on post-operative 1. hour, 1. day, and 2. day at 4000 Hz in mastoidectomy group is significantly higher than those in tympanoplasty group (p<0.05). In tympanoplasty group, dp values on post-operative 1. hour at 4000 Hz significantly decreased in comparison with pre-operative period (p<0.05).

Conclusion: Drilling used in mastoidectomy operation damage healthy contralateral ears by causing acoustic trauma. This damage can be determined by otoacoustic emissions in the early period. According to our study, hearing loss is temporary and more distinct at higher frequencies.

Keywords: Acoustic trauma, distortion product otoacoustic emissions, hearing loss, mastoidectomy

contralateral ears in mastoidectomy performed using a drill to that which developed in tympanoplasty performed without a drill.

Methods

This study was performed prospectively on patients who applied between December 2012 and May 2014 after receiving approval from the Ethics Committee of the Otorhinolaryngology Clinic in Bağcılar Training and Research Hospital (No: 2013/115). Thirty-eight patients diagnosed with chronic otitis media and who planned to undergo surgery were included. Written informed consent was received from the patients after interviewing them face-to-face. Sixteen of the patients underwent tympanoplasty and 22 underwent mastoidectomy. In the healthy contralateral ears of patients, pure tone thresholds were below 26 dB in the air conduction. Patients with a history of previous ear surgery, gaps of air-bone conduction above 10 dB, and myringosclerosis and retraction in contralateral ears were excluded. All patients were operated under general anesthesia by otorhinolaryngologists. Drilling was performed with a Bien Air drill (Bien Air Surgery SA, le Noirmont, Switzerland) at 20000 rpm in all patients undergoing mastoid-



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ectomy. During mastoidectomy, cutting and diamond drills of various sizes were used.

Irrigation was performed during drilling. Intervals during drilling and total drilling time were not calculated. Patients in the mastoidectomy group underwent radical or modified radical mastoidectomy with postauricular incision. For all patients in the tympanoplasty group, only myringoplasty (type 1 tympanoplasty) was performed without any intervention to the bony

chain or the use of a drill. Distortion product otoacoustic emission (DPOAE) values of healthy contralateral ears were measured preoperatively and in the postoperative 1st hour, 1st day, 2nd day, 3rd day, and 4th day, and the amplitudes were recorded in all patients.

DPOAE measurements were performed with a GSI Audera (Viasys Healthcare Group Inc, Berlin, Germany) otoacoustic emission device. In the DPOAE test, two tones, in which f1 showed a lower frequency and f2 showed a higher frequency, were used. Stimulation levels for f1 and f2 frequencies were L1 and L2, respectively. The DPOAE f2/f1 ratio was adjusted to 1.22, and the difference between the stimulation levels (L1>L2) was adjusted to 10 dB. The noise level was accepted as 6 dB and above. During measurement, two stimuli were given to the external auditory canal and two speakers were used for these stimuli. For sealing the external auditory canal, 10–14 mm probes were applied to the patients. The DPOAE results were recorded at 1000 Hertz (Hz), 1582 Hz, 2000 Hz, 3176 Hz, and 4000 Hz.

Statistical Analysis

In the presentation of the descriptive statics of the data, mean, standard deviation, median, minimum-maximum values, frequency, and ratios were used. The distribution of variables was controlled with the Kolmogorov-Smirnov test. Quantitative data were analyzed using the Mann-Whitney U test. The Wilcoxon test was employed in the analysis of repetitive measurements. For the analyses, SPSS 22.0 (IBM Corp; Armonk, New York, USA) was used.

Results

Seven patients undergoing tympanoplasty were females and nine were males. The mean age was 34.7±4.6 years (12–64 years). Twelve patients undergoing mastoidectomy were females and 10 were males. The mean age was 36.4±5.2 years (9–70 years).

The tympanoplasty group (Group I) and mastoidectomy group (Group II) did not display any statistically significant difference in terms of the preoperative and postoperative 1st hour, 1st day, 2nd day, 3rd day, and 4th day distortion product (dp) values at 1000 Hz, 1582 Hz, 2000 Hz, and 3176 Hz (p>0.05). In the tympanoplasty group, the postoperative 1st hour, 1st day, 2nd day, 3rd day, and 4th day dp values at 1000 Hz, 1582 Hz, 2000 Hz displayed no significant difference compared to the values in the preoperative period (p>0.05). Similarly, in the mastoidectomy group, the postoperative 1st hour, 1st day, 2nd day, 2nd day, 3rd day, and 4th day dp values at 1000 Hz, 1582 Hz, 2000 Hz, and 3176 Hz displayed no significant difference compared to the values in the preoperative period (p>0.05). Similarly, in the mastoidectomy group, the postoperative 1st hour, 1st day, 2nd day, 3rd day, and 4th day dp values at 1000 Hz, 1582 Hz, 2000 Hz, and 3176 Hz demonstrated no significant difference compared to the values in the values in the values in the significant difference compared to the values in the values in the values at 1000 Hz, 1582 Hz, 2000 Hz, and 3176 Hz demonstrated no significant difference compared to the values in the values in

Table 1. Comparison of t	wo groups at 1000	Hz (Group I:	tympanoplasty; Gro	oup II: mastoidector	my)			
		Group I			р			
	M±s.d.	Med (Min-Max)		M±s.d.		Med (Min–Max)		
1000 Hz dp								
Preop	-3.5±11.4	0.0	-23.9-12.4	1.4±7.7	0.8	-26.1	12.0	0.238
Postop 1st hour	-4.6±12.3	1.2	-24.9-11.8	0.1±5.6	-0.8	-10.1	13.1	0.585
Postop 1st day	-3.5±12.8	0.7	-26.3-13.5	-0.6±7.1	0.6	-18.2	10.6	0.714
Postop 2nd day	-3.7±12.0	0.3	-24.6-13.2	0.1±6.5	0.7	-13.4	11.5	0.448
Postop 3rd day	-4.7±12.0	-1.9	-24.2-12.0	0.1±6.6	0.2	-13.6	11.4	0.288
Postop 4th day	-11.6±14.1	-17.8	-23.2-12.0	-0.9±7.9	-0.1	-21.6	10.8	0.101
Change compared to the pr	reop values							
Postop 1st hour	-1.0±6.6	0.4	-12.6-12.9	-0.7±6.4	-2.2	-9.8	17.4	0.990
Postop 1st day	0.1±5.0	0.6	-12.5-7.9	-2.5±6.6	-2.7	-17.1	9.9	0.126
Postop 2nd day	0.0±5.0	-0.7	-7.7-13.9	-1.6±7.1	-1.3	-14.2	19.5	0.384
Postop 3rd day	-0.4±6.7	-1.2	-13.9-11.4	-1.1±6.3	-1.4	-15.4	12.5	0.642
Postop 4th day	1.7±5.5	3.1	-6.7-8.2	-2.5±5.3	-2.0	-11.0	5.3	0.089

Mann-Whitney U test/Wilcoxon test

Preop: preoperative; Postop: postoperative; Hz: Hertz; Dp: distortion product; Med: median, min: minimum; Max: maximum; M.s.d: mean standard deviation; p: confidence interval

	Group I							
	M±s.d.	Med (Min–Max)		M±s.d.	Med (Min–Max)			р
1582 Hz dp								
Preop	2.2±11.1	2.2	-18.4-17.6	2.1±8.2	2.5	-10.4	18.5	0.782
Postop 1st hour	1.9±10.3	-0.7	-18.5-19.6	-0.2±7.4	-0.5	-10.6	17.6	0.467
Postop 1st day	2.0±11.4	1.1	-21.0-18.5	1.8±7.5	3.1	-11.0	18.2	0.713
Postop 2nd day	2.6±11.1	4.7	-13.2-17.2	3.1±8.4	5.2	-13.4	17.3	0.932
Postop 3rd day	0.8±14.0	1.7	-20.6-19.7	0.9±9.3	1.1	-18.0	18.0	0.962
Postop 4th day	-5.0±14.3	-8.4	-19.4-20.7	2.6±6.0	5.1	-9.6	7.8	0.133
Change compared to the pr	reop values							
Postop 1st hour	-0.3±6.3	0.5	-16.6-10.4	-1.2±6.7	-0.6	-15.9	8.7	0.504
Postop 1st day	0.5±7.0	-0.8	-10.0-14.0	-0.2±6.8	-1.0	-16.9	12.2	0.883
Postop 2nd day	1.2±5.2	0.9	-7.5-16.2	0.6±6.4	0.6	-8.8	16.8	0.686
Postop 3rd day	-1.5±7.9	-1.2	-14.6-14.8	-0.7±7.8	-0.1	-22.6	13.5	0.680
Postop 4th day	-0.6±8.1	-0.1	-14.1-10.6	0.7±5.9	0.3	-7.6	12.5	0.717

Table 2.	Comparison of	of two groups	at 1582 Hz	(Group I:	tympanoplast	y; Group	II: mastoidectomy)
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Mann-Whitney U test/Wilcoxon test

Preop: preoperative; Postop: postoperative; Hz: Hertz; Dp: distortion product; Med: median, Min: minimum; Max: maximum; M.s.d: mean standard deviation; p: confidence interval

	Group I			Group II					
	M±s.d.	Med (Min-Max)		M±s.d.	Med (Min–Max)			р	
2000 Hz dp									
Preop	7.1±8.1	8.0	-7.9-18.7	5.1±8.0	4.6	-8.0	22.5	0.310	
Postop 1st hour	5.9±8.4	6.1	-10.6-19.6	0.7±10.2	1.1	-18.4	23.2	0.067	
Postop 1st day	7.8±7.1	7.8	-10.5-19.0	4.1±8.7	5.3	-13.8	23.0	0.145	
Postop 2nd day	8.9±5.9	7.4	0.0-18.6	3.9±8.4	6.5	-15.0	15.5	0.106	
Postop 3rd day	8.4±7.4	7.8	-6.7-19.4	3.7±8.5	8.2	-11.6	13.2	0.235	
Postop 4th day	6.0±6.5	4.8	-3.8-17.1	5.1±5.7	6.9	-3.5	12.1	0.838	
Change compared to the pr	reop values								
Postop 1st hour	-1.5±5.6	-1.0	-11.3-14.2	-2.1±5.8	-2.2	-13.5	10.0	0.696	
Postop 1st day	1.4±5.5	0.4	-11.4-11.9	-0.9±7.3	0.2	-13.3	15.5	0.315	
Postop 2nd day	1.6±4.4	1.0	-4.4-11.1	-2.0±7.1	-1.6	-13.2	15.1	0.042	
Postop 3rd day	-0.1±6.8	0.7	-10.4-16.1	-2.4±7.6	-2.0	-18.3	16.2	0.285	
Postop 4th day	-4.8±8.8	-4.0	-19.4-8.4	-0.8±6.5	-0.3	-13.0	10.6	0.247	

Table 3. Comparison of two groups at 2000 Hz (Group I: tympanoplasty; Group II: mastoidectomy)

Mann-Whitney U test/Wilcoxon test

Preop: preoperative; Postop: postoperative; Hz: Hertz; Dp: distortion product; Med: median, Min: minimum; Max: maximum; M.s.d: mean standard deviation; p: confidence interval

preoperative period (p>0.05). Compared to the preoperative period, no significant difference was observed between the two groups in terms of the dp values of the postoperative 1st hour, 1st day, 2nd day, 3rd day, and 4th day at 1000 Hz, 1582 Hz, 2000 Hz, and 3176 Hz (p>0.05). With regard to

the preoperative period, there was no statistically significant difference between the two groups in terms of the 1st hour, 1st day, 2nd day, 3rd day, and 4th day dp values at 1000 Hz, 1582 Hz, 2000 Hz, and 3176 Hz (p>0.05). Compared to the preoperative period, there was a significant difference be-

	Group I			1				
	M±s.d.	Med (Min–Max)		M±s.d.	Med (Min–Max)			р
3176 Hz dp								
Preop	1.8±12.2	5.6	-18.3-17.3	-0.6±9.7	-0.4	-18.2	15.1	0.332
Postop 1st hour	1.1±9.6	1.3	-18.3-13.3	-3.5±9.0	-3.5	-19.3	13.9	0.116
Postop 1st day	4.7±9.4	5.6	-13.3-18.4	-1.7±11.2	-0.8	-18.7	18.5	0.077
Postop 2nd day	4.7±10.3	8.8	-18.4-16.2	1.4±10.9	4.2	-18.0	16.9	0.340
Postop 3rd day	5.6±9.7	8.6	-18.6-18.0	-1.4±11.6	-5.1	-18.3	17.4	0.055
Postop 4th day	7.7±6.5	7.7	0.3-19.6	2.1±11.4	2.5	-14.8	18.5	0.232
Change compared to the p	reop values							
Postop 1st hour	-0.8±8.2	-1.9	-12.6-15.2	-2.0±10.4	-1.5	-23.8	19.7	0.715
Postop 1st day	2.4±8.0	1.3	-18.1-22.3	-1.8±12.4	-2.0	-25.6	23.9	0.124
Postop 2nd day	2.4±10.2	1.8	-23.2-29.2	1.5±12.3	0.8	-19.5	32.5	0.771
Postop 3rd day	1.9±10.0	0.3	-11.4-26.2	-3.2±9.7	-2.0	-19.6	19.4	0.166
Postop 4th day	0.3±6.6	-1.8	-7.3-13.0	0.0±10.7	-1.3	-17.8	23.5	0.828

Table 4.	Comparison of	f two groups a	t 3176 Hz (Group	I: tympanoplasty	; Group I	I: mastoidectomy)
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Mann-Whitney U test/Wilcoxon test

Preop: preoperative; Postop: postoperative; Hz: Hertz; Dp: distortion product; Med: median, Min: minimum; Max: maximum; M.s.d: mean standard deviation; p: confidence interval

	Group I							
	M±s.d.	Med (M	Med (Min–Max)		Med (Min–Max)			р
4000 Hz dp								
reop	1.0±12.9	5.4	-26.1-16.7	-1.0±7.4	-2.2	-15.2	- 14.0	0.212
Postop 1st hour	-2.4±13.9'	1.5	-28.7-19.1	-11.0±8.6*	-12.2	-25.7	- 7.4	0.027
Postop 1st day	1.0±11.0	3.3	-18.5-19.4	-9.3±9.7*	-7.9	-30.4	- 10.2	0.004
Postop 2nd day	1.5±10.0	1.9	-15.3-18.2	-7.3±9.8*	-10.8	-21.7	- 10.5	0.010
Postop 3rd day	2.4±10.1	3.9	-24.5-17.4	-7.3±111*	-7.2	-24.9	- 16.5	0.007
Postop 4th day	3.3±7.7	5.1	-9.9-12.6	-6.1±10.7*	-7.0	-20.5	- 13.8	0.048
Change compared to the p	reop values							
Postop 1st hour	-3.4±8.5	-2.5	-29.0-17.1	-9.6±9.1	-10.2	-30.1	- 13.9	0.002
Postop 1st day	0.0±8.5	0.1	-23.9-15.5	-9.1±7.8	-9.7	-21.4	- 4.3	0.002
Postop 2nd day	0.5±7.9	-0.1	-18.0-16.9	-5.2±9.4	-7.3	-19.8	- 13.9	0.045
Postop 3rd day	-0.5±9.3	1.0	-17.9-17.8	-6.9±6.8	-8.3	-16.4	- 3.0	0.086
Postop 4th day	-2.1±7.3	-1.3	-14.7-10.1	-6.5±9.6	-10.5	-16.4	- 17.4	0.205

Table 5. Comparison of two groups at 4000 Hz (Group I: tympanoplasty; Group II: mastoidectomy)

Mann-Whitney U test/Wilcoxon test I change compared to Pre op period

Preop: preoperative; Postop: postoperative; Hz: Hertz; Dp: distortion product; Med: median, Min: minimum; Max: maximum; M.s.d: mean standard deviation; p: confidence interval

tween the two groups on the postoperative 2nd day at 2000 Hz (p<0.05) (Tables 1-4).

The preoperative 4000 Hz dp value did not display a significant difference in both the tympanoplasty and mastoidectomy groups (p>0.05). The postoperative 1st hour, 1st day, 2nd day, 3rd day, and 4th day dp values at 4000 Hz were significantly lower in the mastoidectomy group than in the tympanoplasty group (p<0.05). In the tympanoplasty group, the postoperative 1st hour 4000 Hz dp value was significantly lower than in the preoperative period (p<0.05).

In the tympanoplasty group, the postoperative 1st day, 2nd day, 3rd day, and 4th day dp values at 4000 Hz demonstrated no significant difference compared to the preoperative period (p>0.05). In the mastoidectomy group, the postoperative 1st



hour, 1st day, 2nd day, 3rd day, and 4th day dp values at 4000 Hz demonstrated a statistically significant decrease compared to the preoperative period (p<0.05) (Table 5, Figure 1).

Discussion

Acoustic trauma is one of the most common causes of hearing loss. Since drilling has begun to be used in mastoid surgery, sensorineural hearing loss due to drilling has been controversial. In mastoidectomy, sensorineural hearing loss can develop due to acoustic trauma associated with drilling (11- 13).

Many researchers have measured the levels of the noise that occur due to drilling in temporal bone surgery (8, 9, 12, 14). Kylen et al. (9) found noise levels associated with drilling in mastoid surgery as 100 dB in the operated ear and below 5–10 dB in the contralateral ear. It has been reported in many studies that noise occurs in the operated ear at rates varying from 88 dB to 121 dB due to drilling (8, 12, 14). However, in the present study, noise-induced sensorineural hearing loss was not evaluated.

There are some studies specifying that the incidence of sensorineural hearing loss varies between 1.2% and 4.5% in the ears applied drilling (10, 15). Besides these studies, another study revealed that although minimal changes associated with drilling were seen in the operated ear, no statistically significant change was observed in the hearing level of the contralateral ear (16). It has been reported that sensorineural hearing loss associated with drilling does not develop even in the operated ear after tympanomastoid surgery and that further causes of possible postoperative sensorineural hearing loss should be investigated (17, 18). Tos et al. (19) performed translabyrinthine acoustic neuroma surgery in 50 patients and they stated that these patients did not have hearing loss in their healthy contralateral ears after the drilling process. In our study, DPOAE was used to investigate outer hair cell damage, which can develop in healthy contralateral ears due to acoustic trauma, and accordingly, the occurrence of sensorineural hearing loss could be evaluated through otoacoustic emission more safely at an early period. Contrary to our study, the studies mentioned above revealed that drilling did not cause hearing loss, which might have resulted from the fact that the evaluation was not performed with acoustic emissions but with pure tone audiometry. Moreover, these evaluations were performed at a late period. Therefore, temporary sensorineural hearing loss, which develops at an early period, might have been overlooked.

Noise-induced hearing loss mostly occurs at high frequencies. Sutinen et al. (20) conducted an experimental study on guinea pigs and found that temporal bone vibration led to more severe hearing loss at high frequencies than at low frequencies. Domenech et al. (12) reported that temporal bone drilling could cause hearing loss in the operated ear at high frequencies. Goyal et al. (21) investigated postoperative DPOAE values in the healthy contralateral ears of 30 patients who had undergone mastoidectomy at low and high frequencies. In this study, statistically significant changes were obtained at high frequencies, but the changes at low frequencies were not statistically significant. Similarly, although there were decreases in the postoperative low-frequency DPOAE values in the healthy contralateral ears of patients after drilling in our study, these changes were statistically insignificant. Postoperative emission values at 4000 Hz were significantly lower than the preoperative values.

In the study by Da Cruz et al. (22), it was stated that hearing loss developed in the non-operated ears of 2 of 12 patients undergoing a drilling process and that this hearing loss healed at a later period. Similarly, decreases that were statistically significant at 4000 Hz but insignificant at lower frequencies were observed in the healthy contralateral ears of patients in the postoperative early period in our study. However, these decreases tended to improve by the 3rd and 4th days. Parallel to our study, Karatas et al. (23) found that a decrease occurred in the DPOAE values of all patients' healthy contralateral ears at specific frequencies during the postoperative early period with drilling and that all changes returned at the postoperative 72nd-96th hours. Contrary to the above-mentioned studies and our study, Goyal et al. (21) reported that sensorineural hearing loss developed in the healthy contralateral ears of 15 patients. In 10 of these patients, hearing loss completely recovered but, in the other 5, the DPOAE values only partially improved after 72 h or they were permanent.

In the study conducted by Şekercan et al. (24), statistically significant decreases in the emission values of the healthy contralateral ears of patients in the tympanoplasty group were found at 1000 Hz, 1400 Hz, 2000 Hz, and 2800 Hz on the postoperative 1st day. An increase was detected in the level of these decreases on the 7th day. In our study, a statistically significant decrease was observed in the emission values of the tympanoplasty group at 4000 Hz in the postoperative 1st hour, and these decreases increased in the following days. These changes in the healthy contralateral ears of the patients undergoing tympanoplasty may be associated with the activation of the medial olivocochlear system as stated in the study by Sekercan et al. (24). When an ear is exposed to noise due to the activation of the medial olivocochlear system, otoacoustic emissions are suppressed not only in that ear but also in the contralateral ear (25, 26). In addition, intense aspirations performed during tympanoplasty can lead to acoustic trauma. Parkin et al. (27) revealed that noise at the level of 10-31

dB occurs in association with aspiration. Parallel to that, inappropriate manipulation and intense aspirations can be a cause of acoustic trauma during the control of ossicular chain (12).

Migirov and Wolf (28) compared the DPOAE values of healthy contralateral ears in patients undergoing mastoidectomy and tympanoplasty and found statistically significant postoperative decreases in the mastoidectomy group. On the other hand, Sekercan et al. (24) detected statistically insignificant decreases in the DPOAE values of patients' contralateral ears on the postoperative 1st day in the tympanoplasty group. In our study, statistically significant changes were observed in the postoperative 1st hour, 1st day, and 2nd day values of the healthy contralateral ears of the mastoidectomy group at 4000 Hz compared to those in the preoperative period. However, this difference was statistically insignificant on the postoperative 3rd and 4th days. The detection of a statistically significant difference in the postoperative early period in the mastoidectomy group and the absence of this difference on other days suggests that drilling-related noise causes hearing loss in the early period but that this loss improves in the following days.

One of the limitations in our study is that the drilling time and the shapes and sizes of the drills were not specified. In this study, we aimed to examine the early effects of drilling on hearing in tympanomastoid surgery. We plan to investigate the long-term effects of drilling on hearing in a further study that will be focused on the changing times of affected hearing.

Conclusion

Drilling in mastoidectomy causes damage in the inner ear due to acoustic trauma. This damage can be detected through otoacoustic emission in the early period following surgery. According to the results of our study, this loss, which is more apparent at high frequencies, is temporary.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Bağcılar Training and Research Hospital (2013-115).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - K.Ö., H.E.K.; Design - S.A.; Supervision - M.F.O., Ü.T.; Resources - K.Ö., K.Y.; Materials - H.E.K.; Data Collection and/or Processing - H.E.K., K.Y.; Analysis and/or Interpretation - K.Ö., S.A.; Literature Search - K.Ö., H.E.K.; Writing Manuscript - K.Ö.; Critical Review - Ü.T., M.F.O.

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