Evaluation of the Early Radioprotective Effect of Curcumin on the Rat Larynx

Original Investigation

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Abstract

Objective: The aim of this study was to investigate whether the side effects of radiotherapy (RT) could be reduced by curcumin administered to rats receiving RT to the larynx.

Methods: Forty male Wistar Albino rats were randomly and equally divided into four groups: RT only (Group I), RT+curcumin+dimethyl sulfoxide (Group II), RT+dimethyl sulfoxide (Group III), and curcumin+dimethyl sulfoxide (Group IV). Curcumin was administered intraperitoneally, dissolved in dimethyl sulfoxide, starting five days before RT. A single 16 Gy dose of X-ray was applied to the neck region in groups receiving RT. All groups were sacrificed on the third day after RT. Laryngeal tissues were excised and analyzed histopathologically (for edema, hyperemia, pseudostratification, necrosis, cilia loss, and inflammation) and immunohistochemically [Tumor Necrosis Factor-alpha (TNF-α) expression]. Histopathological parameters were graded as none, mild, moderate, and severe (0, 1+, 2+, 3+). The severity of TNF-α expression was scored between 0 and 3.

Results: The formation of edema, hyperemia, necrosis, and pseudostratification in Group II rats was statistically significantly reduced (p=0.001, 0.003, 0.004, and 0.005, respectively). Similarly, TNF-α expression was also significantly decreased in Group II rats (p=0.009). However, no statistically significant differences were observed for cilia loss and inflammation (p=0.055 and 0.091, respectively).

Conclusion: Our findings suggest that curcumin may reduce the development of edema, hyperemia, necrosis, and pseudostratification in laryngeal tissue due to RT. While further research is needed to determine whether curcumin confers protection against RT-induced damage in tumor tissues, the results of this study suggest that curcumin, a natural, non-toxic, and cost-effective dietary compound, has the potential to be used as a radioprotective agent.

Keywords: Larynx, curcumin, radiotherapy, radiation protection, antioxidants, tumor necrosis factor-alpha, inflammation

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Introduction

Laryngeal cancers (LCs) rank second among head and neck malignancies after oral cavity cancers, excluding skin cancer (1). Radiotherapy (RT) for LCs is used for primary (definitive), adjuvant, palliative, and salvage purposes. Primary RT is particularly beneficial for patients with early-stage LC, those who do not accept surgical treatment, and inoperable cases (2). Adjuvant RT is administered to all T3-T4 stage laryngeal tumors, as well as to those with neck lymph node involvement, extracapsular extension, or histopathologically positive surgical margins (2,3). Clinical side effects of RT in patients with LC include laryngeal edema, impairment of vocal function, dysphonia, dysphagia, aspiration, and chondronecrosis (4,5).

To reduce the secondary morbidity of RT, healthy non-cancerous cells in laryngeal tissue should be preserved as much as possible. Various methods have been developed to reduce or eliminate the adverse effects of RT on laryngeal tissue and its associated pathologies. One of the most used methods is the systemic administration of radioprotective agents. Amifostine, a widely used radioprotective agent, has been approved for clinical use by the U.S. Food and Drug Administration. However, due to adverse effects such as hypotension and allergic reactions, the use of amifostine is limited (6). Therefore, natural, non-toxic radioprotective substances with a long half-life and minimal side effects are being investigated. The radioprotective activity of curcumin (CUR) has been widely studied, and its protective effects have been reported in numerous rat studies (7,8).

CUR (diferuloylmethane) is a bioactive compound with the chemical formula $C_{21}H_{20}O_6$, which gives turmeric its characteristic yellow color. It is extracted from the rhizomes of the Curcuma longa plant. CUR exhibits various biological effects, including antioxidant, anti-inflammatory, anti-angiogenic, chemoprotective, chemosensitizing, radioprotective, and radiosensitizing properties (9-11). Regarding the underlying mechanisms of CUR's potential therapeutic effects, it inhibits cell membrane lipid peroxidation, thereby reducing the formation of free radicals. Moreover, it has been shown to interact with several signal transduction molecules, including mitogen-activated protein kinases, Janus kinase/signal transducer and activator of transcription, and nuclear factor-kappa B (NF-κB). As a result of these interactions, CUR can reduce pro-inflammatory cytokines, such as interleukin-1 (IL-1), IL-8, Tumor Necrosis Factor-alpha (TNF-α), and interferon-gamma (12).

Dimethyl sulfoxide (DMSO) is a widely used chemical solvent and a free radical scavenger. It has been observed to exhibit analgesic, anti-inflammatory, radioprotective, and chemoprotective properties (13). In laboratory settings, water-insoluble therapeutic and toxic substances are commonly dissolved in DMSO (14). According to the manufacturer's specifications, the CUR powder used in this study is soluble in DMSO (15).

The objective of this study was to determine whether the adverse side effects of RT could be mitigated by administering CUR to rats receiving RT to the larynx.

Methods

Ethical Approval and Experimental Groups

Ethical approval for this study was obtained from the Burdur Mehmet Akif Ersoy University (MAKU) Animal Experiments Local Ethics Committee (date: 20.05.2021, number: 773). A total of 40 male Wistar Albino rats (250±20 g) were procured from the Burdur MAKU Laboratory Animals Production and Experimental Research Center. After a one-week acclimatization period, the rats were randomly assigned to four equal groups:

- Group I: Received only RT
- Group II: Received RT+CUR+DMSO
- Group III: Received RT+DMSO
- Group IV: Received CUR+DMSO

All animals were housed under standard environmental conditions (24 °C, with a 12-hour light-dark cycle) and provided ad libitum access to standard food and fresh water.

Curcumin-Dimethyl Sulfoxide Application

The solubility of CUR powder (C1386, Sigma-Aldrich, Schnelldorf, Germany) in DMSO (Isolab Chemicals, Eschau, Germany) was determined to be 25 mg/mL, as stated in the product catalog. CUR was administered at a dose of 100 mg/kg, with the corresponding DMSO dose calculated as 4 mL/kg based on solubility and the required CUR amount. CUR and DMSO administration in Groups II, III, and IV commenced five days before RT and was continued once daily via intraperitoneal (IP) injection (16).

Radiotherapy Application

For RT application, all rats in Groups I, II, and III were first sedated with xylazine (10 mg/kg, Rompun 2%, Bayer, Leverkusen, Germany) and ketamine (90 mg/kg, Ketasol 10%, Richter Pharma, Wels, Austria) via IP injection. The rats were then immobilized in the supine position, and three-dimensional conformal RT was planned based on computed tomography images of the rat's neck region.

A single dose of 16 Gy RT was administered using 6 MV photon energy, maintaining a source-to-skin distance of 100 cm at a depth of 3 cm, utilizing the Varian DBX (Varian Medical Systems, Palo Alto, CA, USA) device (17,18). Following RT, one rat in Group I died in the second hour, while two rats in Group II died in the fourth and fifth hours, respectively. On the third day after RT, all remaining rats were sacrificed via IP administration of a ketamine (270 mg/kg) and xylazine (30 mg/kg) mixture.

A necropsy procedure was performed to obtain laryngeal tissue samples, which were immediately fixed in formaldehyde and labeled according to their respective groups (Figure 1).

Histopathological and Immunohistochemical Examinations

Laryngeal samples obtained during necropsy were fixed in 10% neutral formaldehyde solution. After two days of fixation, the samples were longitudinally sectioned and placed into cassettes for routine tissue processing using a fully automated tissue processor (Leica ASP300S; Leica Microsystem, Nussloch, Germany). The processed samples were embedded in paraffin wax, cooled for 4-5 hours, and then serial sections (5 μm thick) were obtained using a Leica 2155 fully automatic rotary microtome (Leica Microsystem, Nussloch, Germany).

The sections were stained with hematoxylin-eosin and cover-slipped for examination under an Olympus CX21 light microscope. Microscopic digital images were captured using an Olympus DP26 camera and transferred to a computer for analysis via the Database Manual Cell Sens Life Science Imaging Software System (Olympus Corporation, Tokyo, Japan).

Histopathological parameters for evaluation included: Edema, hyperemia, pseudostratification, necrosis, ciliary loss, inflammation.These parameters were graded as follows:

None (0)

Mild (1 positive)

Moderate (2 positive)

Severe (3 positive) (Table 1).

Histopathological evaluations were performed by a single pathologist who was blinded to the study groups to eliminate bias. For immunohistochemical analysis, additional sections were mounted on Poly-L-lysine-coated slides and stained for TNF-α expression using the streptavidin-biotin complex peroxidase method. Primary and secondary antibodies from Abcam (UK) were used for this procedure. Immunohistochemical staining for TNF-α [Anti-TNF alpha antibody (EPR21753-109) (ab205587), diluted 1:100] was conducted using the UltraVision Detection System Anti-Polyvalent HRP kit (TP-060-HL) (Thermo Shandon Limited, Cheshire, England).

The reaction was visualized using 3,3'-diaminobenzidine chromogen, and negative controls were obtained by incubating sections with antibody dilution solution instead of primary antibodies. Finally, counterstaining was

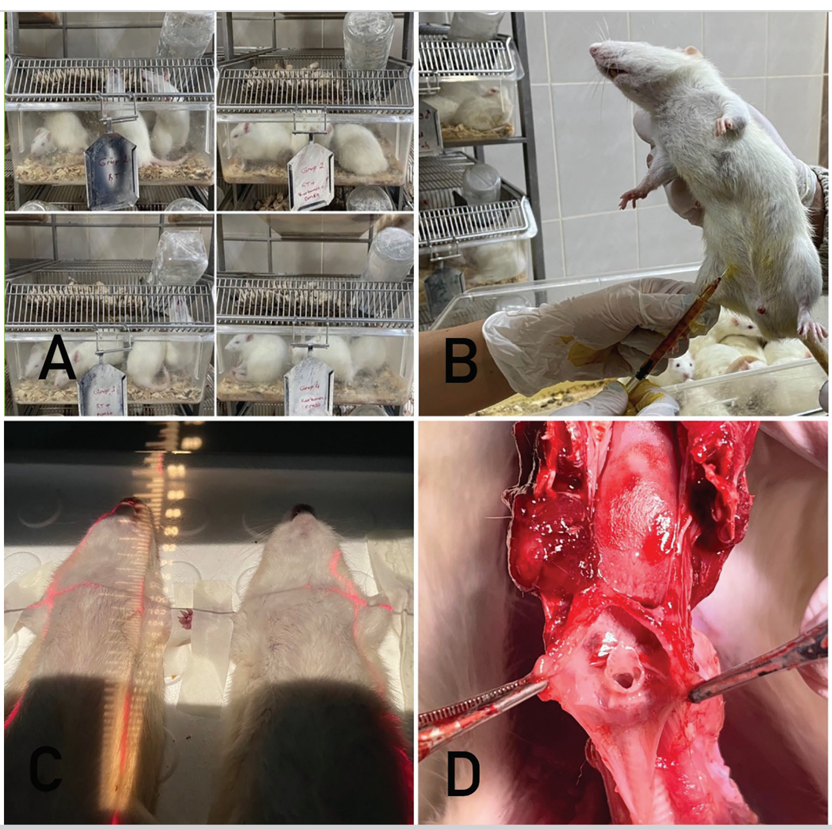

Figure 1. Experimental setup demonstrating the establishment of study groups (A), administration of **curcumin and/or dimethyl sulfoxide (B), irradiation of the neck region (C), and excised laryngeal tissue (D).

Table 1. Histopathological parameters and scoring for laryngeal tissue

Parameters	0 None	1+ Mild	2+ Moderate	3+ Severe
Edema	<25%	26-50%	51-75%	>76%
Hyperemia	<25%	26-50%	51-75%	>76%
Necrosis	None	Single cell necrosis	Necrosis in local area	Diffuse necrosis
Pseudostratification	Normal	Low and mild	Local and moderate	Diffuse and marked
Loss of cilia	None	Mild	Moderate	Severe
Inflammation	1-20 lymphocytes no neutrophils	21-50 lymphocytes 1-2 neutrophils	51-80 lymphocytes 3-10 neutrophils	81-120 lymphocytes >10 neutrophils

performed with Harris hematoxylin, followed by coverslipping in preparation for light microscopy examination. For immunohistochemical evaluations, 100 cells were counted in five fields under a 40× objective lens per section. Based on the percentage of positively stained cells, the scoring system was as follows:

<25% positive cells (0)

26-50% (1)

51-75% (2)

>76% (3)

Histopathological evaluations were conducted under a 20× objective lens, and scores were calculated based on the parameters in Table 1 using ImageJ 1.46r software (National Institutes of Health, Bethesda, MD).

Statistical Analysis

Data analysis was performed using SPSS 24.0 software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY, USA). Descriptive findings are presented as frequency (n) and percentage (%) distributions for categorical variables and as median, minimum, and maximum values for continuous variables. Since each group contained fewer than 30 samples, non-parametric statistical methods were applied. The Kruskal-Wallis test was used to compare histopathological and immunohistochemical scores across groups. If a significant difference was found, pairwise comparisons were conducted using the Bonferroni-corrected Mann-Whitney U test. The accepted level of statistical significance was $p<0.05$. Effect size was set at $f=0.75$, with a significance level (α) of 0.05 and statistical power ($1-\beta$) of 0.95. A total sample size of 36 animals was determined to achieve a power of 95.79%, as calculated using the G*Power 3.1.9.4 program (Heinrich-Heine-Universität Düsseldorf, Nordrhein-Westfalen, Germany).

Results

Widespread epithelial shedding and epithelial cell necrosis were observed in the rats in Group I. Epithelial proliferation was noted in various areas, along with the presence of intraepithelial neutrophils and leukocytes in multiple regions. Additionally, marked hyperemia and inflammatory cell infiltration were detected in the lamina propria. Mild cilia loss was observed in some cells.

A marked improvement in all pathological findings was noted in the laryngeal tissues of rats in Group II. Epithelial shedding was significantly reduced, and no proliferative changes were detected in any of the rats in this group. Additionally, cilia structures were significantly preserved. Similarly, a notable reduction in inflammatory cell infiltration was observed in the lamina propria.

A mild reduction in pathological findings was observed in Group III rats. Compared to Group III, rats in Group II exhibited greater protection and preservation, as reflected in their pathological scores. Laryngeal histology appeared normal in Group IV (Figure 2). A comparative analysis of histopathological parameters across all groups is presented in Table 2.

In immunohistochemical examinations, a significant increase in immunoreactivity was observed in all cell types, particularly in epithelial cells of Group I. However, a decrease in expression was noted in Groups II and III, with a more pronounced reduction in Group II. In Group IV, while no expression was detected in most rats, sporadic mild expression was observed in a few cells in some rats (Figure 3). A comparative analysis of immunohistochemical parameters across groups is provided in Table 3.

Discussion

Although RT is a successful treatment for LC, it also has adverse effects on the larynx. These may include alterations in taste perception, mucositis, pain, hyperemia, and tenderness in the irradiated skin area, as well as dysphonia, xerostomia (dry mouth), swallowing and chewing difficulties, nausea, and deterioration in hematological parameters (5,19). In a study examining RT-induced histopathological changes in the larynx, an acute inflammatory reaction characterized by leukocyte infiltration, necrosis, and hemorrhage was observed in the deep connective tissues within 2 to 12 days post-RT, leading to damage in the respiratory epithelium.

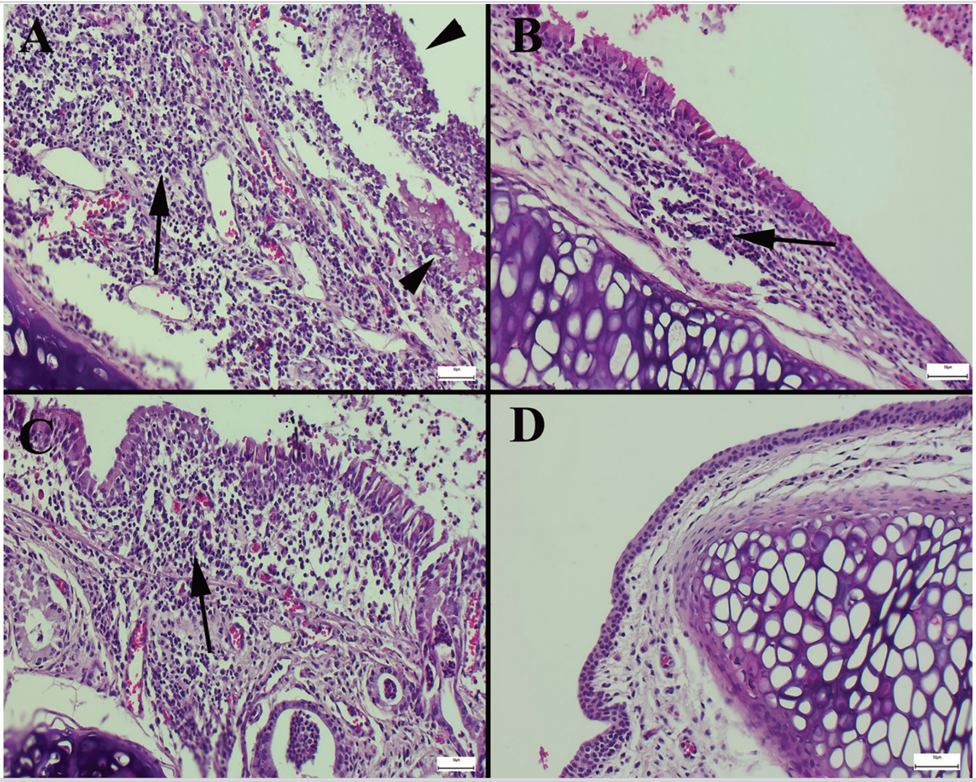

Figure 2. Histopathological comparison of laryngeal tissues across groups. (A) Severe epithelial loss, necrosis (arrowhead), and inflammatory reaction (arrow) in Group I. (B) Marked improvement in the pseudostratified epithelial layer with only mild inflammatory reaction (arrow) in the propria mucosa in Group II. (C) Slight healing of the pseudostratified epithelial layer with a mildly reduced inflammatory reaction (arrow) in Group III. (D) Normal laryngeal epithelial structure in Group IV. Hematoxylin & eosin (HE) staining; scale bar = 50 μm.

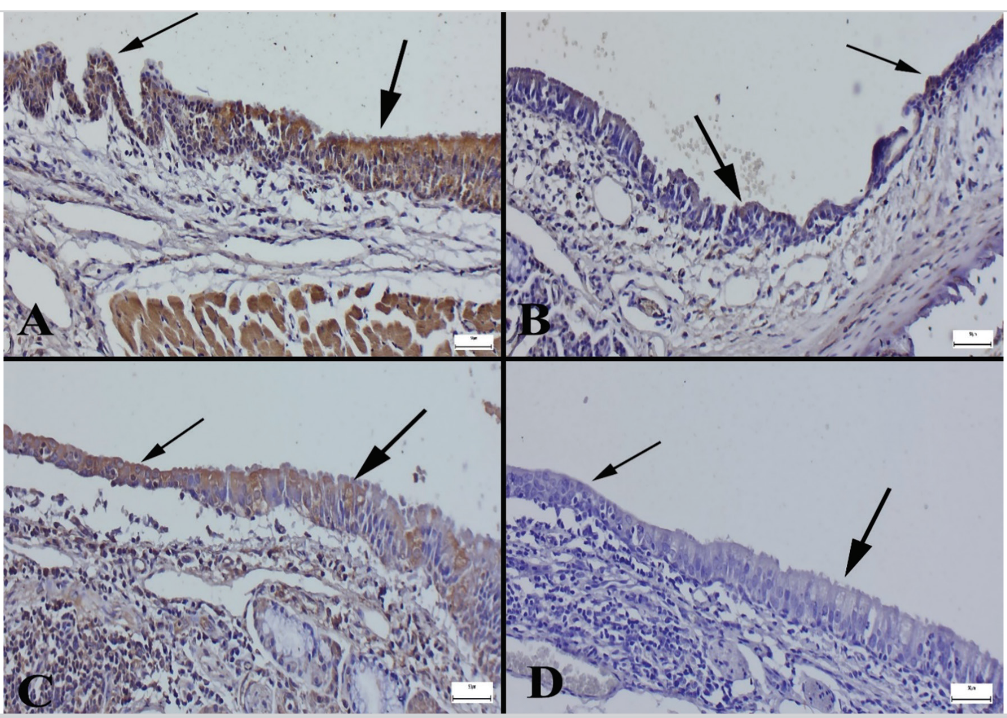

Figure 3. Immunohistochemical analysis of TNF-α expression across groups. (A) Strong TNF-α expression in Group I. (B) Decreased expression in Group II. (C) Slightly reduced expression in Group III. (D) Negative expression in Group IV. Thick arrows indicate the pseudostratified epithelium, while thin arrows denote the stratified squamous epithelium. Streptavidin-biotin peroxidase method; scale bar = 50 μm.

Table 2. Comparison of histopathological values in the groups

		n	Min.	Max.	Median	p-value*	p-value+	
Edema	**Group I**	9	2.00	3.00	3.00	<0.001	G1-G2	0.001
							G1-G3	0.091
	Group II	8	0.00	1.00	0.50		**G1-G4**	**<0.001**
							G2-G3	0.695
	Group III	10	1.00	2.00	1.00		**G2-G4**	1.000
							G3-G4	**0.027**
	Group IV	10	0.00	1.00	0.00		-	-
Hyperemia	**Group I**	9	2.00	3.00	3.00	<0.001	**G1-G2**	**0.003**
							G1-G3	0.143
	Group II	8	0.00	1.00	1.00		**G1-G4**	**<0.001**
							G2-G3	1.000
	Group III	10	0.00	2.00	1.50		**G2-G4**	1.000
							G3-G4	**0.031**
	Group IV	10	0.00	1.00	0.00		-	-
Necrosis	**Group I**	9	1.00	2.00	2.00	<0.001	G1-G2	0.004
							G1-G3	0.001
	Group II	8	0.00	1.00	0.00		**G1-G4**	**<0.001**
							G2-G3	1.000
	Group III	10	0.00	1.00	0.00		**G2-G4**	1.000
							G3-G4	1.000
	Group IV	10	0.00	0.00	0.00		-	-
Pseudo stratification	**Group I**	9	1.00	2.00	1.00	<0.001	**G1-G2**	**0.005**
							G1-G3	0.164
	Group II	8	0.00	1.00	0.00		**G1-G4**	**<0.001**
							G2-G3	1.000
	Group III	10	0.00	1.00	1.00		**G2-G4**	1.000
							G3-G4	0.296
	Group IV	10	0.00	1.00	0.00		-	-
Loss of cilia	**Group I**	9	1.00	2.00	1.00	<0.001	**G1-G2**	0.055
							G1-G3	1.000
	Group II	8	0.00	1.00	0.50		**G1-G4**	**<0.001**
							G2-G3	0.455
	Group III	10	0.00	2.00	1.00		**G2-G4**	0.608
							G3-G4	**0.002**
	Group IV	10	0.00	0.00	0.00		-	-
Inflammation	**Group I**	9	1.00	2.00	2.00	0.001	**G1-G2**	0.091
							G1-G3	0.130
	Group II	8	0.00	2.00	0.50		**G1-G4**	**<0.001**
							G2-G3	1.000
	Group III	10	0.00	2.00	1.00		**G2-G4**	0.758
							G3-G4	0.344
	Group IV	10	0.00	1.00	0.00		-	-

The significance value was calculated with Bonferroni correction for multiple comparisons. The significance value was determined as $p<0.05$.

*According to Kruskal-Wallis test, +According to Mann-Whitney U test, n: Number of rats in group, Min.: Minimum, Max.: Maximum

Table 3. Comparison of immunohistochemical values in the groups

TNF-α expression	n	Min.	Max.	Median	p-value*	p-value+	
Group I	9	2.00	3.00	3.00	<0.001	G1-G2	**0.009**
						G1-G3	0.407
						G1-G4	**<0.001**
Group II	8	1.00	2.00	1.00		G2-G3	0.845
						G2-G4	0.564
Group III	10	1.00	3.00	2.00		G3-G4	**0.005**
Group IV	10	0.00	1.00	0.00		-	-

The significance value was calculated with Bonferroni correction for multiple comparisons. The significance value was determined as p<0.05

*According to Kruskal-Wallis test, +According to Mann-Whitney U test, n: Number of rats in group, Min.: Minimum, Max.: Maximum

Additionally, thinning of small blood vessels and lymphatics resulted in increased endothelial permeability and interstitial edema (20,21).

Radioprotective agents are used to mitigate these complications. Hosseinimehr (22) suggested that an ideal radioprotective agent should effectively shield healthy tissues from RT-induced damage, be easy to administer, exhibit low toxicity, and be compatible with other medications taken by the patient. CUR, whose radioprotective properties have been widely reported, is a phytochemical with anticancer, anti-inflammatory, and antioxidant activities, historically used in traditional medicine (23,24).

In a study conducted by Lopez-Jornet et al. (25) in rats, a single dose of lycopene (20 mg/kg) and CUR (50 mg/kg) was dissolved in DMSO and administered IP'ly 24 hours before RT. Histopathological examination revealed that rats receiving lycopene and CUR exhibited reduced cell necrosis, structural damage, vacuolization, and acinar duct loss in the parotid glands following 20 Gy RT to the neck region.

While numerous studies have investigated the radioprotective efficacy of CUR in RT-treated rats, none have examined its effectiveness in laryngeal tissues. Therefore, our study aimed to evaluate the potential radioprotective effects of CUR on the rat larynx. In a study by Jagetia and Rajanikant (26), CUR doses of 25, 50, 100, 150, and 200 mg/kg were tested, and the maximum recovery rate was observed in rats receiving 100 mg/kg. Based on these findings, we selected a 100 mg/kg dose of CUR for our study. Additionally, due to CUR's low oral bioavailability, IP administration was preferred to standardize the delivered dose (10). Considering previous studies, sacrifice was scheduled for the third day after RT (25,27,28). A longer observation period could have allowed for compensatory antioxidant mechanisms, potentially masking the effects of CUR. Thus, sacrifice on day 3 was deemed appropriate.

In a study conducted by Chen et al. (29), IP'ly administered CUR significantly reduced brain edema in rats subjected to traumatic brain injury. Similarly, in our study, RT-induced edema in the larynx was significantly reduced in rats receiving CUR+DMSO, with a statistically significant difference between Groups I and II (p=0.001). Memis et al. (30) reported that CUR administration in rats with experimental sepsis reduced edema, inflammation, and hyperemia, as observed in histopathological examinations. Consistently, in our study, hyperemia was significantly reduced in Group II (p=0.003). Conversely, in an *in vitro* study by Ghoneim (31), CUR was not found to protect against ethanol-induced cell necrosis in rat hepatocytes. In contrast, in our study, RT-induced necrosis was significantly less common in the laryngeal tissues of Groups II and III, with statistically significant differences between Groups I-II and I-III (p=0.004 and p=0.001, respectively). RT-induced necrosis was observed at a moderate level in Group I, while CUR appeared to mitigate laryngeal necrosis, suggesting a protective effect. This result differs from some reports in the literature, possibly due to the increased epithelial damage associated with administering RT as a single dose rather than fractionally.

Pseudostratification due to RT was mild in our study. Comparisons of the pseudostratification parameter revealed that CUR+DMSO administration reduced this feature, with a statistically significant difference between Groups I and II (p=0.005).

In a study by Oyan et al. (27), pseudostratification following RT was found to be at a level comparable to the control group, while mild cilia loss was reported in laryngeal tissue. In our study, no statistically significant difference was observed between Groups I and II in cilia loss (p=0.055). Justo et al. (32) demonstrated that CUR suppressed TNF-α release and reduced inflammation in rats with apical periodontitis. However, in our study, comparisons between Groups I-II and Groups I-III for inflammation were not statistically significant (p=0.091, p=0.130, respectively). Although CUR+DMSO and DMSO-alone administration did not result in statistically significant reductions in RT-induced inflammation, the lower median values in Groups II and III compared to Group I suggest some degree of radioprotective efficacy.

TNF-α is a pro-inflammatory cytokine produced by lymphocytes, neutrophils, monocytes, and other immune cells during acute inflammation. It plays a key role in signaling pathways leading to necrosis and apoptosis (33). A significant increase in serum TNF-α levels was observed in patients receiving RT to the head and neck region, with X-rays inducing TNF-α release, leading to synergistic and distant cytotoxic effects (34). Another study reported elevated levels of NF-κB and growth factors, such as vascular endothelial growth factor, matrix metalloproteinases, IL-6, and IL-8, following RT and chemotherapy. It has been suggested that TNF-α plays a key role in the development of radioresistance and chemoresistance in oral cavity cancers (35). Therefore, inhibiting NF-κB may enhance the efficacy of RT and chemotherapy. In a study by Li et al. (36), CUR reduced TNF-α levels, alleviating diabetes-related allodynia and hyperalgesia in rats with experimental diabetes. In our study, TNF-α expression was significantly lower in Group II compared to Group I (p=0.009).

Yang et al. (37) demonstrated that DMSO reduced acute radiation-induced damage in the oral mucosa of rats. In our study, necrosis was significantly reduced in Group III compared to Group I (p=0.001). While partial improvements were observed in edema, hyperemia, cilia loss, inflammation, pseudostratification, and TNF-α expression, these differences were not statistically significant.

We acknowledge several limitations in our study. First, we only examined the acute effects of RT, excluding chronic period effects. Second, we did not measure oxidative and non-oxidative blood enzyme levels involved in pathological changes. Third, CUR and DMSO blood concentrations were not measured. Finally, the animal model used did not include laryngeal tumors, which may exhibit different responses to RT and CUR treatment.

Conclusion

Our findings suggest that CUR may reduce RT-induced edema, hyperemia, necrosis, and pseudostratification in laryngeal tissue, indicating potential radioprotective effects. Therefore, we conclude that CUR could serve as an effective radioprotective agent. Future studies should investigate CUR's protective effects on tumor tissues exposed to RT. We believe that our study is promising, as it highlights CUR-a food-derived, natural, non-toxic, and cost-effective compound-as a potential radioprotective agent.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Burdur Mehmet Akif Ersoy University (MAKU) Animal Experiments Local Ethics Committee (date: 20.05.2021, number: 773).

Informed Consent: Since this study was conducted on animals, patient consent was not required.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.C., Y.Ç.K., H.Y., E.O., Concept: F.C., Y.Ç.K., Ö.Ö., H.Y., E.O., M.E.S., Design: F.C., Y.Ç.K., H.Y., E.O., M.E.S., Data Collection and/or Processing: E.E.Ö., Analysis and/or Interpretation: F.C., Y.Ç.K., Ö.Ö., E.E.Ö., E.O., M.E.S., Literature Search: F.C., Y.Ç.K., Ö.Ö., E.E.Ö., M.E.S., Writing: F.C.

Conflict of Interest: The authors have no conflicts of interest to declare.

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Main Points

- Laryngeal cancers rank second among head and neck malignancies, following oral cavity cancers, excluding skin cancer.
- Radiotherapy (RT) for laryngeal cancer has been associated with clinical side effects, including laryngeal edema, vocal function impairment, dysphonia, dysphagia, aspiration, and chondronecrosis.
- Curcumin demonstrated radioprotective effects by preventing RT-induced edema, hyperemia, necrosis, and pseudostratification in laryngeal tissue, while also reducing TNF-α expression levels.
- This experimental study provides promising evidence that curcumin, a food-derived, natural, non-toxic, and cost-effective compound, may serve as a radioprotective agent. Our findings may contribute to guiding future research in this field.

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