International Journal of Otorhinolaryngology and Head and Neck Surgery
Feshan M et al. Int J Otorhinolaryngol Head Neck Surg. 2022 Jul;8(7):595-601
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20221651

Original Research Article

A prospective observational study of ototoxicity in head and neck cancers treated with chemoradiotherapy

Musarrat Feshan*, Preetham A. Puthukudy, Brema Devadass

Department of Otorhinolaryngology, Southern Railway Headquarters Hospital, Ayanavaram, Chennai, Tamil Nadu, India

Received: 31 May 2022
Accepted: 15 June 2022

***Correspondence:**
Dr. Musarrat Feshan,
E-mail: dr.feshan@gmail.com

ABSTRACT

Background: Head and neck cancer is a major global health problem. Cisplatin has been widely used in the treatment of head and neck malignancies. Ototoxicity is considered as the primary outcome of interest and the type of hearing loss is the secondary variable of interest. The Chi-square test/Fisher's exact test is used to test statistical significance. P value<0.05 is considered statistically significant. IBM statistical package for the social sciences (SPSS) version 22 is used for statistical analysis.
Methods: In this prospective observational study, 62 patients with head and neck cancers were evaluated for chemoradiotherapy-induced ototoxicity. The hearing assessment included air and bone conduction thresholds, frequency, and pattern of hearing loss. The assessment was done at baseline, at the end of treatment, and after 8 weeks of completion of chemoradiotherapy.
Results: Results showed the mean age group to be, between 61 to 70 years. Gender distribution showed that 80.65% are males and 19.35% are females. The most common site of malignancy is the larynx (20.97%). Cisplatin is used in 51 patients (82.26%) and carboplatin in 7 patients (11.29%). Radiotherapy was given to 82.26% of the patients. Results showed an increased incidence of sensorineural hearing loss (SNHL) after 8 weeks of treatment. There was a statistically significant difference between pure tone average (PTA) values before treatment, at the end of treatment, and after 8 weeks of chemoradiotherapy.
Conclusions: Pure-tone hearing threshold was most affected at 8 kHz and sensorineural hearing loss at higher frequencies is the most common finding.

Keywords: Ototoxicity, Head and neck cancer, Chemotherapy, Radiotherapy, Pure tone audiometry, High-frequency sensorineural hearing loss

INTRODUCTION

The term ototoxicity is used to refer to the process by which many therapeutically useful drugs, certain environmental agents and bacterial toxins cause damage to the peripheral end organs of hearing and balance. Head and neck cancer is a major health problem globally. Tobacco and alcohol play an important role in the aetiopathogenesis of head and neck cancers.[1,2] A German chemist Paul Ehrlich set about developing drugs to treat infectious diseases. He was the one who coined the term 'chemotherapy' and defined it as the use of chemicals to treat disease.[3] A commonly used group of alkylating agents is the platinum compound which includes cisplatin, oxaliplatin, and carboplatin. Cisplatin irreversibly binds to plasma proteins and can be detected up to 6 months after completion of therapy. Cisplatin causes bilateral high-frequency sensorineural hearing loss; it can also cause tinnitus and vertigo. Permanent hearing loss or balance disorders caused by ototoxic drugs may have serious educational, communication, and social consequences. Therefore, the benefits of drugs must be weighed against

the potential risks and alternative medications should be considered.

METHODS

Hearing loss due to ototoxicity is considered as the primary outcome of interest and the type of hearing loss is the secondary variable of interest. A prospective observational study is done in southern railways headquarters hospital, Chennai from October 2019 to June 2021. Ethical committee approval was obtained from hospital in house. Descriptive analysis is carried out by mean and standard deviation for quantitative variables, whereas frequency and proportion are used for categorical variables. Data is represented by using appropriate diagrams like bar diagrams, pie diagrams, and box plots. The mean values of the numeric variable are compared between people with and without ototoxicity using an independent sample t-test. Association between explanatory variables and ototoxicity are assessed by cross-tabulation and comparison of percentages. The Chi-square test/Fisher's exact test is used to test statistical significance. P value<0.05 was considered statistically significant. IBM statistical package for the social sciences (SPSS) version 22 is used for statistical analysis. The study aimed to assess the effect of chemoradiotherapy associated with ototoxicity in patients with head and neck cancers and to ascertain the pattern and type of hearing loss in different frequencies.

Inclusion criteria

Patients with age above 18 years, with head and neck cancer receiving chemotherapy; and head and neck cancer receiving concurrent chemoradiotherapy were included in the study.

Exclusion criteria

Patients with ear discharge or having a middle ear infection, who had undergone ear surgery, and congenital hearing loss were excluded from the study.

Methodology

The present study evaluated the head and neck cancer patients coming to the ear, nose and throat (ENT) department of our hospital. These patients were evaluated in detail and advised chemoradiation by a medical oncologist. A detailed otological examination was done for each patient before treatment. Patients with a history of congenital hearing loss or middle ear diseases were excluded from the study. The patients received chemotherapy with either cisplatin or carboplatin once weekly for 6 weeks. They were also treated with image-guided radiation therapy (IGRT) and received doses between 60-75 Gy in 30-35 fractions over 6-6.5 weeks. The study compared the hearing assessment in the patients before and after receiving chemotherapy or chemoradiotherapy. Pure tone audiometry (PTA) tests were done before treatment to assess the individual baseline hearing thresholds. The hearing assessment included audiological history, air and bone conduction thresholds, frequency, and pattern of hearing loss. PTA was done in a sound-treated audiometric testing suite and masking was used whenever necessary. Bone and air conduction thresholds were obtained at 250 kHz, 500 kHz, 1000 kHz, 2000 kHz and 8000 kHz by using an audiometer (diagnostic diameter 2001, Arphi model). The assessment was done at baseline, at the end of treatment, and after 8 weeks of completion of chemoradiotherapy. At each visit, hearing loss due to ototoxicity was assessed.

RESULTS

Age and gender distribution

The total number of 62 patients were included in the study, 50 (80.65%) were males and 12 (19.35%) were females. The mean age of the study population was 60.87 with a SD of ±9.616. The majority of the 45.16% of the study population belonged to the age group of 61-70 years. Age and gender distribution is shown in Figure 1 and Table 1.

Table 1: Gender wise distribution of study population.

Sex distribution	Number	Percentage
Male	50	80.65
Female	12	19.35

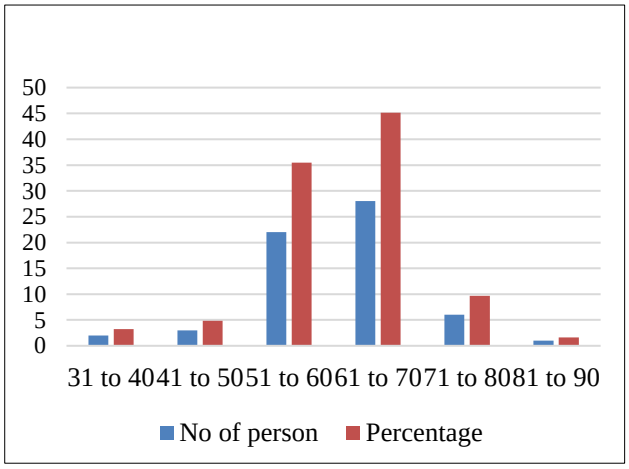

Figure 1: Age distribution.

Site of malignancy

Analysis based on the site of malignancy demonstrated that the most common site was the larynx (20.97%) followed by the hypopharynx (19.35%). The site-wise distribution is shown in Figure 2.

Chemotherapy

In this study population, the chemotherapy drug cisplatin was used in 82.26% of cases, carboplatin in 11.29%, and no chemotherapy was given for 6.45% of cases. This is shown in Table 2.

Table 2: Distribution of study population according to chemotherapy and radiotherapy received.

Parameters	Number	Percentage
RT- yes	51	82.26
RT- no	11	17.74
Cisplatin	51	82.26
Carboplatin	7	11.29
Nil	4	6.45

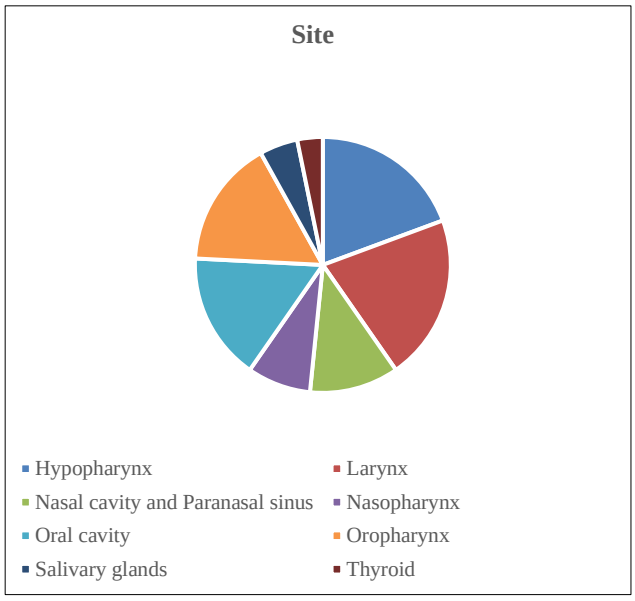

Figure 2: Pie chart of site wise distribution of tumour.

Radiotherapy

In this study, radiotherapy was given for 82.26% of cases and this is shown in Table 2.

Type of hearing loss

Right ear

Analysis based on the type of hearing loss was done in the right ear before starting treatment. 59.68% had normal hearing and 33.87% had SNHL. At the end of treatment, 46.77% had normal hearing and 51.61% had SNHL. After 8 weeks post-treatment, 33.87% had normal hearing and 66.13% had developed SNHL. This is shown in Table 3 and Figure 3.

Table 3: Type of hearing loss in right ear.

Type of hearing loss	NH (%)	MHL (%)	SNHL (%)
Baseline	37 (59.68)	4 (6.45)	21 (33.87)
At the end of treatment	29 (46.77)	1 (1.61)	32 (51.61)
After 8 weeks of treatment	21 (33.87)	0	41 (66.13)

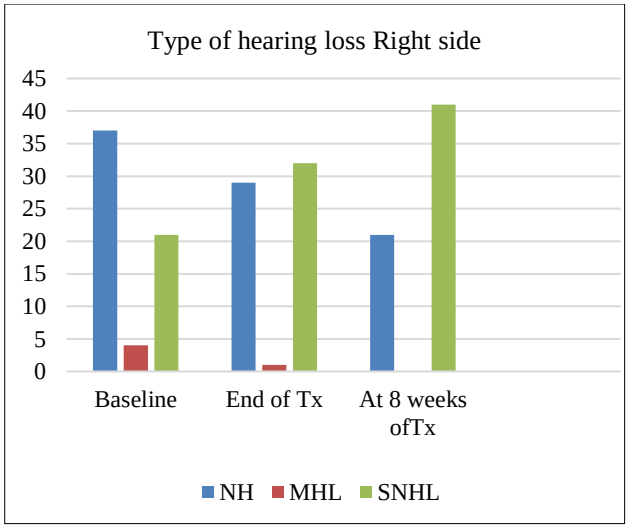

Figure 3: Bar chart of type of hearing loss in the right ear.

Left ear

Analysis based on the type of hearing loss was done in the left ear before starting treatment. 58.06% had normal hearing and 32.26% had SNHL. At the end of treatment, 46.77% had normal hearing and 50.00% had SNHL. After 8 weeks post-treatment, 30.65% had normal hearing and 69.35% had developed SNHL. This is shown in Table 4 and Figure 4.

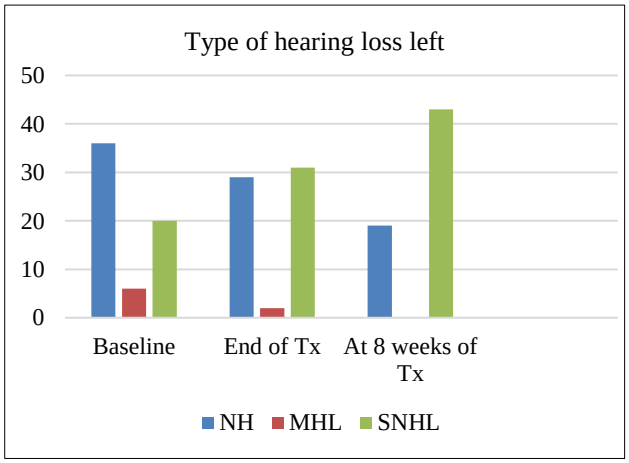

Figure 4: Bar chart of type of hearing loss in the left ear.

Table 4: Type of hearing loss in left ear.

Type of hearing loss	NH (%)	MHL (%)	SNHL (%)
Baseline	36 (58.06)	6 (9.68)	20 (32.26)
At the end of treatment	29 (46.77)	2 (3.23)	31 (50.00)
After 8 weeks of treatment	19 (30.65)	0	43 (69.35)

On applying Fischer's exact test, there is a significant difference (with p value<0.05) in the type of hearing loss between baseline, at the end of treatment, and after 8 weeks of treatment both on the right and left side. There is an increase in SNHL after 8 weeks of treatment.

Comparison of PTA values at various visits of treatment

In our study, the mean value for difference in PTA values between the baseline and at the end of treatment is 3.16 and 4.03 in right and left ear respectively.

The mean value for the difference in PTA values between baseline and at 8 weeks post-treatment is 8.63 and 9.89, in right and left ear respectively. In the right and left ear, the mean value for the difference in PTA values between the end of treatment and at 8 weeks post-treatment is 5.44 and 5.85 respectively. This is shown in Table 5.

Comparison of PTA values at 8 kHz during various visits of treatment

The comparison shows the mean value for difference in PTA values at 8 kHz between baseline and at the end of treatment is 4.00 and 4.11 in right and left ears respectively. The mean value for the difference in PTA values between baseline and at 8 weeks post-treatment is 10.82 and 10.68, in right and left ear respectively. In the right and left ears, the mean value for the difference in PTA values between the end of treatment and at 8 weeks post-treatment is 6.82 and 6.56 respectively. This is shown in Table 6.

Table 5: Difference in PTA values in normal frequency.

Parameters	Right ear			Left ear		
	Baseline and end of treatment	Baseline and after 8 weeks of treatment	At end of treatment and after 8 weeks	Baseline and end of treatment	Baseline and after 8 weeks of treatment	At end of treatment and after 8 weeks
Mean	3.16	8.63	5.44	4.03	9.89	5.85
SD	2.800	6.905	4.964	3.473	7.547	5.401
Median	2.00	7.00	4.50	3.50	8.00	5.00

Table 6: Difference in PTA values at 8 kHz frequency.

Parameters	Base and end of Tx 8 kHz right	Base and 8 weeks 8 kHz right	End of Tx and 8 weeks 8 kHz right	Base and end of Tx 8 kHz left	Base and 8 weeks 8 kHz left	End of Tx and 8 weeks 8 kHz left
Mean	4.00	10.82	6.82	4.11	10.68	6.56
SD	5.096	8.554	5.327	4.926	9.183	6.264
Median	5.00	10.00	5.00	5.00	10.00	5.00

DISCUSSION

Cisplatin induces a progressive loss of hair cells, the extent of which correlates with the dose of the drug administered.[4] The pattern of hair cell damage in the cochlea resembles that of the aminoglycosides; hair cells in the basal turn of the cochlea are preferentially affected with the damage spreading progressively to apical turns.[5] Initially cisplatin causes high-frequency irreversible hearing loss. It has been estimated that the current clinical protocol for its use results in, at least 60% of patients suffering some degree of hearing impairment. Hearing loss often progresses after the completion of drug therapy, which may in part be related to prolonged retention of platinum in the body.

Age distribution

The study showed that chemoradiotherapy-induced ototoxicity was most common in the age group 61 to 70 years with a standard deviation of ±9.62. Schuette et al also reported the most common age group as 60 years with a standard deviation of 10.[6] In the study by Dass et al, the mean age affected by chemoradiotherapy-induced ototoxicity was 55 years.[7]

Sex distribution

Gender distribution in our study showed that 80.65% were males and 19.35% were females. In the study conducted by Hitchcock et al, 90.3% of the study population were males and 9.7% were females.[8] Similarly, in the study by Mahler et al, the study population consisted of 79% of males and 21% of females.[9] The male preponderance seen in our study could be due to a higher incidence of head and neck cancer in the male population.

Site of lesion

Analysis based on the site of malignancy demonstrated that the most common site was the larynx (20.97%) followed by the hypopharynx (19.35%). Mahler et al reported oropharynx (76%) as the most common site of involvement followed by oral cavity cancers (11%) and laryngeal cancers (8%).[9] Analysis based on the subsite of malignancy showed the most commonly involved subsites

were, vocal cords and pyriform sinus, each accounting for 14.52%.

Risk factors

The commonest risk factors for head and neck cancers were observed to be smoking (66.13%), tobacco chewing (38.71%), and alcohol consumption (66.13%). This can be compared with the retrospective study by Singh et al including 45 patients with head and neck cancer treated with definitive concurrent chemoradiation among which 91.1% were smokers.[10]

Percentage distribution of symptoms

During analysis of symptoms, a history of hard of hearing, giddiness, and tinnitus was not reported by any of the study subjects before treatment. At the end of treatment, 5 patients (8.06%) presented with all the symptoms of hard of hearing, giddiness, and tinnitus. Whereas at 8 weeks after completion of treatment, hard of hearing was reported by 31 patients (50%), giddiness by 22 patients (35.48%), right ear tinnitus by 28 patients (45.16%), and left ear tinnitus by 29 patients (46.77%) respectively. There was a statistically significant difference in the symptoms reported at the end of treatment and 8 weeks after treatment. In the study by Trendowski et al, hard of hearing was reported by 24.7% and tinnitus by 14.8% of the patients respectively.[11] Zocoli et al conducted a study where 46% of the patients presented with tinnitus, and 31% of the patients presented with hard of hearing.[12]

Mode of treatment

Chemotherapy was the most commonly used mode of treatment. It was used in 58 patients (93.54%) cisplatin was used in 51 patients (82.26%) and carboplatin was used in 7 patients (11.29%). Chemotherapy as the only mode of treatment was given in 11 patients of which 10 patients (91%) developed SNHL. In the study by Green et al, cisplatin-induced hearing loss was seen in 63% of patients who received radiotherapy and cisplatin.[13] Mahler et al conducted a study to analyze the possible synergistic toxicity of chemotherapy combined with RT.[9] Cisplatin is known to cause hearing loss. Increased toxicity has been observed in patients treated with both adjuvant and concurrent chemoradiotherapy.[14] The study by Bapat et al, showed that 22-58% of patients developed ototoxicity after cisplatin with or without radiotherapy.[15]

Radiotherapy was given in 51 patients (82.26%). Out of this, the majority of the patients (47) received radiotherapy along with chemotherapy. Only in 4 patients' radiotherapy was given as the only mode of treatment. Out of which 3 patients (75%) developed SNHL. It can be compared with a study by Espenel et al, where radiation therapy-induced ototoxicity was 30 to 40% including irreversible sensorineural hearing loss.[16] Similarly, in the study by Tacyildiz et al, the incidence of ototoxicity in patients who received cranial radiotherapy was found to be 40%.[17] Study by Zheng et al showed that among 29 patients with follow-up evaluations after radiotherapy, 65.5% had hearing impairment in both ears. SNHL is a late effect of radiotherapy that likely worsens over time.[18]

Concurrent chemo-radiotherapy was given in 47 patients (75.80%) of which 17 patients developed SNHL. Theunissen et al study showed that the incidence of ototoxicity was 0% to 43% after radiotherapy and 17% to 88% after chemoradiotherapy.[19]

Analysis of PTA values at normal frequencies

In the right ear, the mean PTA values were 28.27 dB, 31.47 dB, and 36.9 dB before treatment, at the end of treatment, and after 8 weeks post-treatment respectively. The mean difference in PTA values between baseline and at the end of treatment was 3.2 dB, between the end of treatment and after 8 weeks post-treatment was 5.44 dB and between baseline and 8 weeks, post-treatment was 8.63 dB. There was a statistically significant difference between PTA values before treatment, end of treatment and at 8 weeks of post chemoradiotherapy with a high threshold shift at 8 weeks of post chemoradiotherapy with a p value<0.0001.

The mean PTA values in the left ear were 29.97 dB, 34 dB, and 39.85 dB before treatment, at the end of treatment, and after 8 weeks post-treatment respectively. The mean difference in PTA values between baseline and at end of treatment was 4.03 dB, between the end of treatment and after 8 weeks of treatment was 5.85 dB and between baseline and after 8 weeks of treatment was 9.89 dB. There was a statistically significant difference between PTA values before treatment, end of treatment and at 8 weeks of post chemoradiotherapy with a high threshold shift at 8 weeks of post chemoradiotherapy with a p value<0.0001. In the study by Feldman et al, mean PTA values were 12 dB and 17.75 dB before and after chemoradiotherapy respectively, which was statistically significant with a p value<0.0001.[20] Caballero et al showed the mean hearing loss between initial and final audiometry to be significant in both ears with p=0.002 at 4 and 8 kHz.[21]

Analysis of PTA values at 8 kHz frequency

In the right ear, the mean PTA values at 8 kHz were 55.02 dB, 59.03 dB, and 65.85 dB before treatment, at the end of treatment, and after 8 weeks post-treatment respectively. There was a statistically significant difference between PTA values before treatment, at the end of treatment, and 8 weeks post chemoradiotherapy with a high threshold shift at 8 weeks of post chemoradiotherapy with a p value<0.0001.

The mean PTA values in the left ear were 56.97 dB, 61.08 dB, and 67.65 dB before treatment, at the end of treatment, and after 8 weeks post-treatment respectively. There was a statistically significant difference between PTA values before treatment, at the end of treatment, and at 8 weeks of post chemoradiotherapy with a high threshold shift at 8

weeks post chemoradiotherapy with a p value<0.0001. A study conducted by Feldman et al showed that the threshold at 8 kHz was 25 dB before, and 57 dB after chemoradiotherapy respectively, which was statistically significant with a p value<0.0001.[20] Comparing our study with the study by Niemensivu et al, ototoxicity was determined by >10 dB threshold shift at 4 and 8 kHz in PTA.[22]

Type of hearing loss

Normal hearing was observed in 59.68% of patients before treatment, in 46.77% of patients at the end of the treatment, and in 33.87% of patients after 8 weeks of treatment respectively in the right ear. Sensorineural hearing loss was present in 33.87% of patients before treatment, 51.61% of patients at the end of the treatment, and 66.13% of patients after 8 weeks of treatment respectively. The left ear showed a normal hearing in 58.06% of patients before treatment, in 46.77% of patients at the end of the treatment, and in 30.65% of patients after 8 weeks of treatment respectively. Sensorineural hearing loss was present in 32.26% of patients before treatment, in 50.00% of patients at the end of the treatment, and in 69.35% of patients after 8 weeks post-treatment respectively. There was a statistically significant difference with a p value<0.05 in the type of hearing in both right and left ears. Mujica-Mota et al in their study demonstrated that the incidence of SNHL varied from 0% to 85% for the speech frequencies and from 27% to 95% for high frequencies.[23] In the study by Petsuksiri et al the incidence of SNHL at high frequency was 52.9%.[24]

CONCLUSION

The exposure of the cochlea to chemo-radiotherapy is associated with ototoxicity in patients with head and neck cancer. The pure tone hearing threshold levels were most affected at 8 khz frequency, though even the lower frequencies were also affected but were not statistically significant. The most common ototoxicity associated with chemo-radiotherapy is sensorineural hearing loss at higher frequencies in both ears.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Franceschi S, Talamini R, Barra S, Barón AE, Negri E, Bidoli E, Serraino D, La Vecchia C. Smoking and drinking in relation to cancers of the oral cavity, pharynx, larynx, and esophagus in northern Italy. Cancer Res. 1990;50(20):6502-7.
2. Blot WJ, McLaughlin JK, Winn DM, Austin DF, Greenberg RS, Preston-Martin S, et al. Smoking and drinking in relation to oral and pharyngeal cancer. Cancer Res. 1988;48(11):3282-7.
3. DeVita VT, Chu E. A history of cancer chemotherapy. Cancer Res. 2008;68(21):8643-53.
4. Hoeve LJ, Zur Borg IM, Rodenburg M, Brocaar MP, Groen BG. Correlations between cis-platinum dosage and toxicity in a guinea pig model. Arch Oto-rhino-laryngol. 1988;245(2):98-102.
5. Laurell G, Bagger-Sjöbäck D. Degeneration of the organ of Corti following intravenous administration of cisplatin. Acta Oto-laryngologica. 1991;111(5):891-8.
6. Schuette A, Lander DP, Kallogjeri D, Collopy C, Goddu S, Wildes TM, Daly M, Piccirillo JF. Predicting hearing loss after radiotherapy and cisplatin chemotherapy in patients with head and neck cancer. JAMA Otolaryngol–Head Neck Surg. 2020;146(2):106-12.
7. Das J, Custer A, Blakaj D, Old MO, Zhao S, Bhatt AD, Kang SY, Agrawal A, Ozer E, Wobb J, Rupert R. Incidence of ototoxicity in head and neck cancer (HNSCC) patients (pts) receiving concomitant chemoradiation (CRT) with weekly or triweekly cisplatin (Cis). J Clin Oncol. 2018;36(15):6046.
8. Hitchcock YJ, Tward JD, Szabo A, Bentz BG, Shrieve DC. Relative contributions of radiation and cisplatin-based chemotherapy to sensorineural hearing loss in head-and-neck cancer patients. Int J Rad Oncol Biol Physics. 2009;73(3):779-88.
9. Mahler M, Zhang Y, Hueniken K, Brown MC, Chen Z, Mirshams M, et al. Cisplatin-induced ototoxicity in head and neck squamous cell carcinoma (HNSCC) patients treated with chemoradiation: The role of WFS1 and ABCC2 heritable variants. J Clin Oncol. 2018;36(15):6048.
10. Singh SRK, Malapati SJ, Lu P, Rosen FR. Factors affecting adherence to standard cisplatin (CDDP)-based chemotherapy regimen for locally advanced squamous cell head and neck (H&N) cancer in an inner-city safety net hospital. J Clin Oncol. 2017;35(31):252.
11. Gersten BK, Fitzgerald TS, Fernandez KA, Cunningham LL. Ototoxicity and platinum uptake following cyclic administration of platinum-based chemotherapeutic agents. J Assoc Res Otolaryngol. 2020;21(4):303-21.
12. Zocoli R, Reichow SL, Zocoli AMF. Otoacoustic emissions X Cisplatin: precocious detection of ototoxicity in oncologic patients. Braz J Otorhinolaryngol. 2003;69:222-5.
13. Greene JB, Standring R, Siddiqui F, Ahsan SF. Incidence of cisplatin-induced ototoxicity in adults with head and neck cancer. Adv Otolaryngol. 2015;245613.
14. Combs SE, Volk S, Schulz-Ertner D, Huber PE, Thilmann C, Debus J. Management of acoustic neuromas with fractionated stereotactic radiotherapy (FSRT): long-term results in 106 patients treated in a single institution. Int J Rad Oncol Biol Physics. 2005;63(1):75-81.
15. Waissbluth S, Del Valle Á, Chuang A, Becker A. Incidence and associated risk factors for platinum-

induced ototoxicity in pediatric patients. Int J Pediatric Otorhinolaryngol. 2018;111:174-9.
16. Espenel S, Garcia MA, Guy JB, Vallard A, Mrad B, Langrand-Escure J, et al. Ototoxicity in head and neck cancers after radiotherapy and chemoradiotherapy: From primary prevention to tertiary prevention. Cancer Radiotherap J de la Societe francaise de radiotherapie oncologique. 2017;21(1):77-83.
17. Tacyildiz N, Cengiz H, Deda G, Ates C, Yilmaz S, Yavuz G, et al. Cisplatin-and carboplatin-related ototoxicity in children with cancer in a Turkish pediatric oncology center. J Clin Oncol. 2014;e21028.
18. Zheng Y, Han F, Xiao W, Xiang Y, Lu L, Deng X, Cui N, Zhao C. Analysis of late toxicity in nasopharyngeal carcinoma patients treated with intensity-modulated radiation therapy. Rad Oncol. 2015;10(1):1.
19. Theunissen EA, Bosma SC, Zuur CL, Spijker R, van der Baan S, Dreschler WA, de Boer JP, Balm AJ, Rasch CR. Sensorineural hearing loss in patients with head and neck cancer after chemoradiotherapy and radiotherapy: a systematic review of the literature. Head Neck. 2015;37(2):281-92.
20. Feldman DR, Knezevic A, Wilson K, Bromberg M, Budnick A, McHugh DJ, et al. Detailed evaluation of hearing loss (HL) associated with high-dose (HD) carboplatin for salvage treatment of germ cell tumors (GCT). J Clin Oncol. 2020;38(6):401.
21. Caballero M, Mackers P, Reig O, Buxo E, Navarrete P, Blanch JL, Grau JJ. The role of audiometry prior to high-dose cisplatin in patients with head and neck cancer. Oncology. 2017;93(2):75-82.
22. Niemensivu R, Saarilahti K, Ylikoski J, Aarnisalo A, Mäkitie AA. Hearing and tinnitus in head and neck cancer patients after chemoradiotherapy. Eur Archives of Oto-Rhino-Laryngol. 2016;273(9):25.
23. Mujica–Mota M, Waissbluth S, Daniel SJ. Characteristics of radiation-induced sensorineural hearing loss in head and neck cancer: A systematic review. Head Neck. 2013;35(11):1662-8.
24. Petsuksiri J, Sermsree A, Thephamongkhol K, Keskool P, Thongyai K, Chansilpa Y, Pattaranutaporn P. Sensorineural hearing loss after concurrent chemoradiotherapy in nasopharyngeal cancer patients. Radiation Oncol. 2011;6(1):1-8.

Cite this article as: Feshan M, Puthukudy PA, Devadass B. A prospective observational study of ototoxicity in head and neck cancers treated with chemoradiotherapy. Int J Otorhinolaryngol Head Neck Surg 2022;8:595-601.