Original research article

ROLE OF AUDIOLOGICAL SCREENING (PURE TONE AUDIOMETRY AND DISTORTION PRODUCT OTOACOUSTIC EMISSIONS) IN PATIENTS UNDERGOING CONCURRENT CHEMORADIATION FOR HEAD AND NECK CANCERS

Anisha Kocchar[1#], Rohit Sharma[2], Piyush Kumar[2*], Vineet Sharma[3], Kumar Shubhanshu[1]

Publication Info

Paper Submission Date
22nd February 2016

Paper Acceptance Date
10th June 2016

Paper Publication Date
July 2016

DOI

Abstract

Introduction: Chemoradiation is an important component in the management of Head and Neck Cancers, which has hearing loss as a major adverse effect. This is due to the inclusion of ear structures in the radiation field and Cisplatin, an anti-neoplastic drug which can cause ototoxicity. The role of audiological screening in the form of Pure Tone Audiometry & Distortion Product Otoacoustic Emissions is hereby studied in these patients.

Material and Methods: The present study was undertaken to highlight the effects of concurrent chemoradiation on the audiological profile of Head and Neck Cancer patients. The patients underwent pre-treatment and post treatment Pure Tone Audiometry and Distortion Product Otoacoustic Emission. The results were statistically analysed.

Results: 36 patients who underwent concurrent chemoradiation for Head and Neck Cancers were enrolled. Post treatment PTA values were significantly different from Pre-treatment values especially at 500Hz. DPOAEs also indicated significant changes in cochleotoxicity grading after concurrent chemoradiation.

Conclusion: Concurrent Chemoradiation exerts a significant effect on hearing status of the patients. Simple screening tests like DPOAE can detect cochlear damage prior to detection with Pure Tone Audiometry. Addition of these tests is recommended as routine screening during Concurrent Chemoradiation.

Keywords: Chemoradiation, Ototoxicity, PTA, DPOAE, Screening

INTRODUCTION

Head and Neck Cancer (HNC) is a major form of cancer in India, accounting for 23% of all cancers in males and 6% in females.[1] The use of smokeless tobacco (Pan Masala, Zarda, gutka etc.) is highly prevalent in North India, especially in Uttar Pradesh, and is the causative factor for the large majority of these cancers.[2,3] Squamous cell carcinoma (SCC) is the commonest histological type in HNC comprising about 93.29 % cases.[4]

Surgery and Chemoradiotherapy form the mainstay of treatment for head and neck cancers, alone or in combination. During radiotherapy, the ear structures are often included in the radiation fields and it is generally accepted that radiation-induced sensorineural hearing loss can result along with other adverse effects.[5] Cisplatin, widely used as an effective antineoplastic drug for these cancers, is also known to cause ototoxicity. Ototoxicity resulting from cisplatin chemotherapy constitutes a significant clinical problem that may have serious vocational, educational and social consequences.[6] Cisplatin ototoxicity is well documented to cause initial damage in the basal turn of the cochlea, thus affecting high frequencies before progressing to affect lower frequencies. Consequently, audiometry is used in the early detection of ototoxicity, OAEs provide a non invasive objective measure of cochlear function. For the purpose of ototoxicity monitoring, DPOAEs have been found to be effective and articularly valuable for monitoring ototoxicity in patients who are unable to provide reliable behavioral thresholds.

Hearing loss from ototoxicity can be minimized or prevented if detection is timely and intervention appropriate, such as modifying the dose of the ototoxic drug or changing to an alternative, less ototoxic therapy. Thus, this study investigates the effects of chemoradiotherapy on the middle ear as well as the inner ear by audiological screening using Pure Tone Audiometry

Senior Resident[1], Professor[2], Associate Professor[3]
Department of ENT, *Department of Radiotherapy, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh
Corresponding E-mail : rohitsharma.dr@gmail.com
Department of ENT, Cantonment General Hospital, New Delhi (Present affiliation)

and Oto Acoustic Emmisions in patients suffering from Head and Neck Cancers.

MATERIAL AND METHODS

This study was undertaken to highlight the effects of concurrent chemoradiation on the audiological profile of Head and Neck Cancer patients and to predict the need for audiologic screening using tests such as PTA and Distortion Product Otoacoustic Emission (DPOAE). This was a tertiary care teaching hospital based, randomized, prospective, observational study done in Department of ENT, Head and Neck Surgery and the Department of Radiotherapy, Shri Ram Murti Smarak Institute of Medical Sciences. Bareilly, India between January 2012 and July 2013.

Patient Selection : All head and neck cancer patients scheduled for concurrent chemo radiation treatment were included in this study. Patients having pre-existing otological pathologies and/or abnormal pre-treatment audiological test reports and those who previously received chemo and/or radiotherapy were excluded from the study.

The patients were randomly selected with regards to diagnosis from both sexes in the age range of 31 to 70 years. The malignancies were staged according to the tumor-node-metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC).

Treatment Protocol : Radiotherapy was given to all patients to a cumulative dose in the range of 60-70 Gy in 30 - 35 fractions over a period of 6-7 weeks at 200 cGy per fraction using 6 MV photon energy by High Energy Linear Accelerator along with concurrent chemotherapy drug cisplatin given as intravenous infusion in 150 ml or 0.9% normal saline in a dose of 35 mg/m^2 at weekly intervals. The patients were adequately hydrated with 2-2.5 litres of i.v. fluids and supplemented with Inj. KCI, Inj. $MgSO_4$.

Patient Assessment : A detailed history was recorded especially pertaining to audiological and oncological profile of all the patients. Detailed ENT and oncological examination was carried out and recorded along with records of various investigations**.**

The patients recruited underwent pre treatment and post treatment audiological tests comprising Tuning fork tests (Rinne's, Weber's and Absolute bone conduction), Pure Tone Audiometry (PTA) by air and bone conduction and Distortion Product Otoacoustic Emissions (DPOAE) after obtaining a written informed consent for participation.

The audiological tests were carried out in the audiometry lab as well as the neuro-otology lab in the department of ENT and Head and Neck Surgery, SRMS IMS, Bareilly. Pure Tone Audiometry was carried out with ELKON eda 3 N 3 diagnostic audiometer. DPOAE was carried out with Neurosoft Neuro-audio electrophysiological equipment. The pre-treatment and post-treatment observations of the subjects were documented and analysed statistically.

Statistical Methods : The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean ± SD. The primary methods of analysis used were measures of central tendencies (mean and median), standard deviation, chi square test, student t test and calculation of level of significance (p value).

Level of hearing was calculated as the PTA of 0.5, 1, 2, 4, 6 and 8 kHz for standard audiometry for right and left ears separately. The classification used when describing degree of hearing loss was that of Jerger and Jerger (1980) which states the following:

- 10 to 20 dB HL Normal hearing
- 21to 40 dB HL Mild hearing loss
- 41 to 55 dB HL Moderate hearing loss
- 56 to 70 dB HL Moderately-severe hearing loss
- 71 to 90 dB HL Severe hearing loss
- 91+ dB HL Profound hearing loss

A cochleotoxic threshold shift was assessed during the post treatment phase by the ASHA criteria on the basis of the DPOAE data for right and left ears of all patients.

- ASHA CC1 e"20 dB decrease at any one test frequency.
- ASHA CC2 e"10 dB decrease at any two adjacent test frequencies:or
- ASHA CC3: loss of response at three consecutive test frequencies where responses were previously obtained.

RESULTS

A total of 36 patients who were treated for the diagnosis of head and neck cancers were enrolled for the study. The age of the patients ranged from 31-70 years with a mean age of 55.86 ± 10.26 years and included 32 males and 4 females. Of the 36 patients, 15 had been diagnosed with SCC of the oropharynx, 12 of the larynx, 6 of the oral cavity, 2 of the nasopharynx and 1 of the nose. All of the 36 patients

Table-1: Treatment dosage and cycle values

N=36	AGE	TOTAL IRRADIATION FRACTIONS	TOTAL RADIATION DOSAGE	CUMULATED CISPLATIN DOSAGE
Mean	55.86	30.28	64.3	228.3
Median	55	30	66	300
Std. Deviation	10.26	2.87	6.48	89.1
Minimum	31	25	45	140
Maximium	0	35	70	350

underwent concurrent chemo radiation. The mean total radiotherapy fractions were calculated as 30.28±2.87 mean total radiation dosage 64.30±6.48 Gy and cumulated cisplatin dosage 228.30±89.10 mg. It was observed that 50% of the patients received 70 Gy and 44.4% patients underwent 35 fractions of radiotherapy. The cisplatin dose received by the patients was as follows – 18(50%) patients received a cumulative dose of 300 mg of cisplatin, 7 (19.4%) received 250 mg, 4 (11.1%) received a high dose of 350 mg, 3 (8.3%) received 240 mg, 2 (5.6%) received low dose cisplatin at 200 mg, I (2.8%) received 150mg and 1 (2.8%) received 140 mg (Table 1).

The pre-treatment and post treatment percentages of hearing loss in the left and right ears separately as well as overall percentage for both ears were compared as shown in Table 2.

The pre and post treatment values for pure tone audiometry at different frequencies for both the ears were compared. We found that the variations were maximum for 500 HZ (correlation 0.557) in the both ears showing its effect on smaller frequencies. The difference in the mean of pre-treatment and post-treatment PTA values at different pair frequencies was statistically significant. Figure 1 & 2 shows a representation of the obtained mean values that were obtained for both, left and right ears during pre and post treatment testing using audiometry.

The patients in our study were categorized on the basis of the ASHA criteria into cochleotoxicity grades during testing for DPOAEs for both pre and post treatment tests. Figure 3 & 4, depicts the change seen in cochleotoxicity grading in the patients after concurrent chemo radiation.

Figure-1: Mean Values of PTA At Different Frequencies For Right Ear Pre And Post Treatment

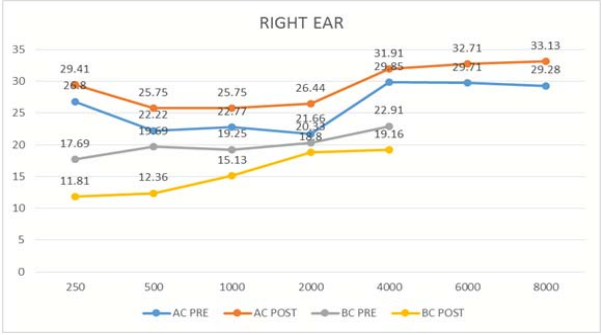


Figure-2: Mean values of PTA at different frequencies for left ear pre and post treatment

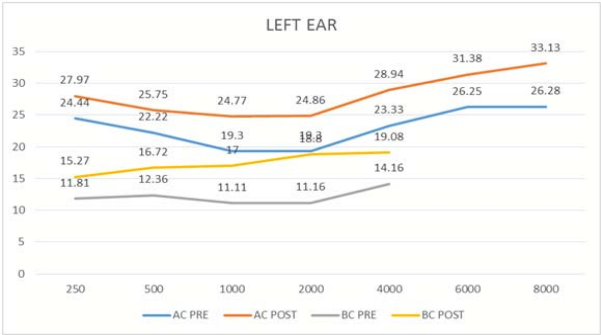


Figure-3: Cochleotoxicity grading as per ASHA criteria for right ear pre and post treatment

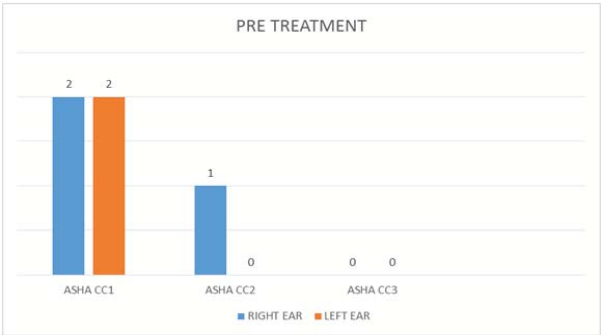
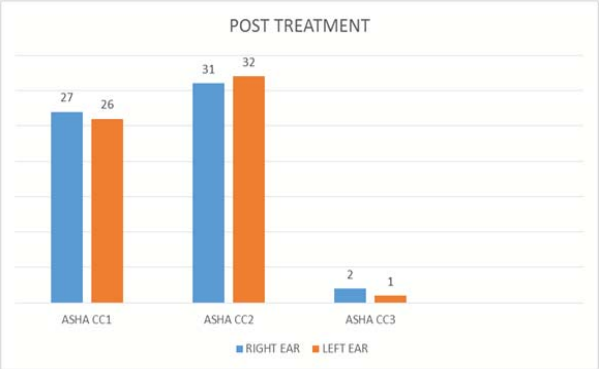


Table-2: Distribution of Pre and Post treatment patients according to severity of hearing loss on PTA

HEARING LOSS (in dB)	PRE TREATMENT PTA LEFT (%)	POST TREATMENT PTA LEFT (%)	PRE TREATMENT PTA RIGHT (%)	POST TREATMENT PTA RIGHT (%)	PRE TREATMENT PTA OVERALL (%)	POST TREATMENT PTA OVERALL (%)
Normal	19(52.8)	17(47.2)	10(27.8)	5(13.9)	15(41.7)	15(41.7)
Mild	17(47.2)	16(44.4)	26(72.2)	29(80.6)	21(58.3)	19(52.8)
Moderate	0(0)	2(5.6)	0(0)	1(2.8)	0(0)	1(2.8)
Moderately Severe	0(0)	0(0)	0(0)	1(2.8)	0(0)	1(2.8)
Severe	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
Profound	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
Total	36(100)	36(100)	36(100)	36(100)	36(100)	36(100)

Figure-4: Cochleotoxicity grading as per asha criteria for left ear pre and post treatment



DISCUSSION

Cisplatin and radiation induced ototoxicity is a significant clinical problem that can result in vocational, educational and social consequences. Currently there is no clinically proven method to reduce or prevent this from occurring. In the present study, detailed pre and post-treatment audiological assessment was performed in 36 patients who had previously received concurrent cisplatin and cranial irradiation therapy for the treatment of head and neck cancer. We hope that this study will increase awareness of the impact of ototoxicity and the importance of comprehensive audiological monitoring with the potential of improving quality of life for oncology patients.

The maximum number of patients suffering from head and neck carcinoma in our study were in the age group of 51-70 years indicating that head and neck carcinomas mostly occur in 5th and 6th decade of life. This was in accordance with other studies such as that by Shinde et al who observed during a four year period with 1291 cases of head and neck malignancies that the commonest age group is the 6th decade comprising of 511 cases (39.58 %), 19.20% cases were from the age group 61-70 years and 15.41% in 41-50 years.[1] However, reports from other Indian authors suggest that the recent nationally representative mortality survey in India has confirmed that more than 70% of fatal cancers occur during the productive ages of 30-69 years.[7,8] The male : female ratio that we observed was 8: 2. Our results were very similar to those obtained by Neizekhotuo et al, who in their study reported a male : female ratio of 7.9:1.[9] The majority of HNC are epithelial in origin and histopathologically, about 90% of head and neck cancer are Squamous Cell Carcinoma.[10,11] All the 36 patients (100%) in our study were diagnosed as Squamous cell carcinomas with varied grades.

Radiation induced SNHL has been recognized as an important adverse effect which may develop immediately post treatment or 6 to 24 months after radiation treatment and may progress to complete deafness.[6,12] The inner ear is the most susceptible organ for a durable long term SNHL. Significant changes in hearing resulting from exposure to cisplatin and cranial irradiation therapy, as defined by the ASHA criteria, were observed in our patients. Out of the total 36 patients evaluated, 34 (94.4%) patients were reported to have hearing loss due to cochleotoxicity. This high incidence of the hearing loss due to cochleotoxicity is comparable to incidence reported by Mc Kcage et al (75 - 100%) and may be attributed to high cumulative cisplatin (288.33 ± 89.1 mg/m^2) and cranial irradiation therapy (71.80 ± 6.4 Gy) doses and the fact that most of the patients were of old age. The changes in the pre-treatment and post-treatment PTA values in our study indicated a significant increase in the bone conduction hearing losses after treatment with concurrent chemo radiation. Changes were also seen in the air conduction at certain frequencies but no statistical significance was proven. We observed that 2 patients acquired moderately severe hearing losses after the treatment. Most of the patients in our study showed losses in higher frequencies of PTA, similar to the reported findings in other series, as the high frequency (> 4 khz) would be the earliest sign for damage at the outer hair cells in the basal turn of the cochlea.[13]

Otoacoustic emissions (OAE) yield a promising instrument in the monitoring of ototoxicity since the emissions are generated by the outer hair cells (OHC) in the cochlea, which are assumed to be the most vulnerable site of ototoxicity due to cisplat in and radiotherapy. Recording of OAE does not require the cooperation of the patient and does not necessarily require a soundproof room. In our study we have demonstrated that a significant cochleotoxic change occurred in a majority of our patients with regards to DPOAE studies. Grading as per the ASHA criteria revealed 83.3% patients had cochlear damage to both ears, 5.6% patients had damage to one or the other ear and 5.6% patients showed no significant cochleotoxic change in either ear. Our findings were found to be in accordance with various other studies which in the past have established DPOAE as a non invasive and sensitive measure of cochlear function. Loss of DPOAE response indicates damage to

OHCs before it is able to be detected with standard pure-tone audiometry. Unlike pure-tone audiometry, however, there is no universally accepted criterion that indicates a significant decline in OHC function. Although not originally included in the ASHA cochleotoxicity criteria, investigations since have found that DPOAEs are particularly valuable for monitoring ototoxicity in patients who are unable to provide reliable behavioural thresholds due to age or illness. There is a high inter individual variability in response to treatment with cisplatin, it is difficult to identify which patients will be more susceptible after treatment. A screening protocol which includes the cost effective audiological tests may be useful in helping us determine individual susceptibility. In accordance with the screening protocol and various risk factors that have been studied in patients who develop hearing loss, dose reduction or alterations may be possible with the help of simple audiometric assessment. This study found that despite the high proportion of patients experiencing ototoxicity, not all are receiving appropriate assessment and follow-up. Fluent communication is vital, particularly for a group of patients for whom quality of life is already compromised due to illness and fatigue. Consideration must be given, however, to the emphasis placed on carrying out a vigorous monitoring protocol for patients whom are already facing significant physical and emotional challenges.

CONCLUSION

To conclude, we observed that on Pure Tone Audiometry there was a significant decrease in hearing thresholds after concurrent chemoradiation. Moreover, a high incidence of cisplatin induced ototoxicity with a predilection for involvement of the higher frequencies is seen.

DPOAE is a sensitive measure of hearing loss, as outer hair cell function may be affected much more before any clinical signs of hearing impairment are seen.

Thus on the basis of our observations, we recommend regular audiological screening of head and neck cancer patients undergoing chemoradiation using simple, cheap and non invasive tests such as PTA and DPOAEs. However, further studies may be required to formulate the screening protocols which may suggest dose reductions or alterations.

REFERENCES

1. Dr. K.J. Shinde, Dr. Syed Imdad Husain Hashmi**.** Retrospective Study Of Malignant Lesions Of Head & Neck In Rural Area Of Ahmednagar District. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)Volume 4, Issue 2 (Jan. - Feb. 2013), PP 12-19.
2. Mehrotra R, Singh M, Kumar D, Pandey AN, Gupta RK, SinhaUS. Age specific incidence rate and pathological spectrum of oral cancer in Allahabad. Indian J Med Sci 2003;57:400-4.
3. Imran Ali, Waseem A. Wani and Kishwar Saleem. Cancer Scenario in India with Future Perspectives. Cancer therapy Vol. 8 2011; 56-70.
4. Abhinandan Bhattacharjee, A. Chakraborty, P. Purkaystha. Prevalence of Head and Neck Cancers in the North East- an institutional study. Indian Journal of Otolaryngology and Head and Neck Surgery Vol. 58, No. 1, January-March 2006.
5. Wong-Kein Low, Sylvia WW Kong, Michelle GK Tan. Ototoxicity from combined cisplatin and radiation treatment: an in vitro study.
6. Low WK, Toh ST, Wee J, Fook-Chong SM, Wang DY.Sensorineural hearing loss after radiotherapy and chemoradiotherapy: a single, blinded, randomized study. J ClinOncol. 2006;24:1904-9.
7. Bhaven C, Kataria Dimple S, Mehta Sunita B, Chhaiya. Approval of antineoplastic agents in India: comparison with the US and EU regions.Int J Basic ClinPharmacol. 2012 Aug;1(1):13-21.
8. Rajesh Dikshit, Prakash C Gupta, Chinthanie Ramasundarahettige, Vendhan, Gajalakshmi, Lukasz Aleksandrowicz, Rajendra Badwe, Rajesh Kumar, Sandip Roy, Wilson Suraweera, Freddie Bray, Mohandas Mallath, Poonam K Singh, Dhirendra N Sinha, Arun S Shet, Hellen Gelband, Prabhat Jha. Cancer mortality in India: a nationally representative survey. Lancet 2012; 379: 1807–16.
9. Neizekhotuo Brian Shunyu Judita Syiemlieh. Prevalence of Head and Neck Canver in the State of Meghalaya: Hospital-based Study.Int J Head and Neck Surg 2013; 4(1): 1-5.

10. Tsukuda M. Recent treatment modality for advanced head and neck carcinomas. GanTo Kagaku Ryoho. 1998 Sep;25(11):1657-64.

11. Olli-Pekka Alho Heikki Teppo Pekka Mäntyselkä Saara Kantola.Head and neck cancer in primary care: presenting symptoms and the effect of delayed diagnosis of cancer cases. CMAJ • March 14, 2006 • 174(6).

12. Upadhya N. Jariwala J. DatarIndian. Ototoxic Effects of IrradiationJOtolaryngol Head Neck Surg (April–June 2011) 63(2):151–154; DOI 10.1007/s12070-011-0142-9.

13. Gerhard W Hill D. Kent Morest Kourosh Parham. Cisplatin-Induced Ototoxicity: Effect of Intratympanic Dexamethasone Injections. Otol Neurotol. 2008 October ; 29(7): 1005–1011.