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Original Article

Ear, Nose and Throat Section

Evaluation of Sensorineural Hearing Loss as a Consequence of Conventional Radiotherapy in Head and Neck Cancer

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ABSTRACT

Introduction: Sensorineural Hearing Loss (SNHL) is potentially disabling and yet overlooked, while subjecting patients of head and neck cancer to conventional ionising radiation at most tertiary care centers. The demand for cancer care, along with the rising cost of therapy using newer treatment technologies such as intensity modulated radiotherapy is a concern to the health care system in India. Cochlea often remains in the field of radiation and hence need to be shielded to prevent development of SNHL.

Aim: To assess role of radiotherapy causing sensorineural hearing loss in patients of head and neck cancer.

Materials and Methods: A prospective study was initiated on 110 cases with normal hearing requiring Radiotherapy (RT), for biopsy proven tumours of head and neck in the Department of Otorhinolaryngology. All cases were treated with external beam conventional radiotherapy using telecobalt machine and a shielding collimator. Out of 110 cases treated by either curative or palliative dose of RT which was around 60 Gray (Gy) and 30 Gray (Gy) respectively, 16 did not come for follow-up. The study was concluded with remaining 94 cases who completed the follow-up. Hearing acuity was assessed using 500, 1000 and 2000 Hz frequency before start of radiotherapy, immediately following radiotherapy and at first follow-up after six months in all cases. Quantification of the degree of SNHL was done using one-way analysis of variance (ANOVA). During follow-up the hearing loss noted was graded into mild and moderate.

Results: The ototoxic effect after RT was found amongst the cases who received curative dose of 60 Gy, while none in cases who received palliative dose of 30 Gy. Out of 188 ears in 94 cases, 59 ears (31.38%) had SNHL, including newly developed SNHL in 44 ears during the 6 month post-RT follow-up period. The number of ears having SNHL was 18 at immediate post-RT which further increased to 59 at 6 month follow-up as compared to pre-RT normal hearing levels.

Conclusion: In cases of head and neck cancer treated by conventional radiotherapy using telecobalt machine and shielding, the risk of consequent sensorineural hearing loss -SNHL was about just less than one third (31.38%). The tolerance of cochlea to total dose of radiotherapy was less than 60 Gray in cases of head and neck cancer treated by conventional radiotherapy.

Keywords: Cochlea, Follow-up study, Ionising radiation, India, Tertiary care centers

INTRODUCTION

Sensorineural hearing loss is potentially more disabling to the patient, since it has a chronic and often progressive natural history [1]. Irradiation is commonly used either alone or in combination with surgery for the treatment of malignant tumours of head and neck. However, in the application of irradiation to any disease process, its effect on adjacent normal tissues must be considered as an integral part of the therapy from the view point of both morbidity and mortality. Certain strategies have been developed to minimise radiation exposure to vital structures including spinal cord, brainstem, optic chiasma, pituitary gland and eyes, but none of them has been adopted for effective shielding of the ear in order to prevent radiation induced sensorineural hearing loss. Thus, the hearing apparatus which is invariably included in the radiation field may get affected if the total dose of ionising radiation received exceeds its tolerance. Studies on ototoxic effects of radiation are less. Animal studies have demonstrated that SNHL with histopathological damage to the organ of corti and spiral ganglion is observed at 40 Gy of radiation [2].

In most of experimental animals studies (often dogs or guinea pigs) after the exposure to large single doses of ionising radiation animals were sacrificed shortly [1,3-5], the results of these studies provide little insight into the mechanisms responsible for the delayed development of SNHL observed in patients treated with fractionated radiotherapy.

The rising cost of cancer treatment has imposed a challenge to the health system in India [6]. Due to non-availability of such advanced radiotherapy technique at most of the tertiary care centres while treating head and neck cancer patients, it is important to evaluate the untoward effect of radiotherapy, such as affection of acuity of hearing in the patient. Because of this need, the present study was undertaken at tertiary care hospital to assess the role of radiotherapy as a cause of SNHL in patients with normal hearing, receiving radiotherapy for head and neck cancer, and to know the dose of radiation in such patients.

MATERIALS AND METHODS

A prospective study was conducted between October, 2017 and August, 2018 in the department of Otorhinolaryngology of tertiary care teaching hospital affiliated to KIMS, deemed to be University, Karad. The Institutional Ethics committee permission for the study was obtained with reference No. KIMSDU/IEC/03/ 2017. Cases with normal hearing on pure tone audiometry requiring radiotherapy for biopsy proven tumours of laryngopharynx, oropharnyx, oral cavity, parotid and paranasal sinuses were included. However, children less than six years of age and patients receiving drugs known to cause ototoxicity, and with abnormal middle ear status like otitis media, effusion, tympanic membrane perforation or conductive hearing loss, and on chemotherapy were excluded from the study. All cases were enrolled in the study as per inclusion and exclusion criterions and Informed consent was obtained from these cases.

All cases were evaluated by history, clinical examination and pure tone audiometry. To determine effects of varying dosages of ionising radiation on hearing, the patients were classified into two groups, curative and palliative, depending on the spread of the disease. Cases were subjected to total dose of ionising radiation of 60 Gray and 30 Gray in curative and palliative groups respectively. All cases were treated using conventional external beam telecobalt radiation machine and lead shielding collimator.

The baseline Pure Tone Audiometry (PTA) was recorded before radiotherapy and subsequently repeated at completion of treatment and after a period of 6 months. Mean hearing thresholds were obtained using pure tones of 500, 1000 and 2000 Hz frequencies, in each case at different times. Hearing loss observed was staged as per classification of hearing loss by American Speech Language Association specification into Mild (26-40 dB) and Moderate (41-55 dB) [4]. The pure tone averages at three different times (pre-RT, immediate post-RT and after six months of completion of RT), was compared applying one-way analysis of variance (ANOVA) using SPSS Version 20.

RESULTS

Of 110 cases enrolled, 94 cases attended the audiometric evaluation at six months follow-up whereas 16 cases were lost to follow-up. Amongst 94 cases, the majority were of age group between 51 to 60 years, of which 19 were males and 6 were females. The primary site of malignancy noted in majority of cases was laryngopharynx i.e., 40.90% (45 cases) and the least common site was parotids i.e., 4.55% (5 cases) [Table/Fig-1].

At immediate post radiotherapy follow-up of 94 cases presenting symptoms were more than one, the most common being decrease hearing in 30 (27.27%) followed by heaviness of ear in 26 (23.63%), tinnitus in 18 (16.36%), earache in 6 (5.45%) and dizziness in 4 (3.63%). After 6 months follow-up post radiotherapy in 94 cases the above symptoms persisted except ear ache and dizziness, the most common symptom being decrease hearing in 31 (32.98%) followed by tinnitus in 22 (23.40%) and ear heaviness in 2 (2.12%). The fields and type of RT used in both curative and palliative groups were the same. Amongst 94, 81 cases were treated by curative radiotherapy using a total dose of 60 Gy-2 Gy per fraction and 5 fractions per week over 6 weeks; 13 cases were treated with palliative radiotherapy using a total dose 30 Gy-3 Gy per fraction and 5 fractions per week over 2 weeks. The ototoxic effect after irradiation was found amongst the cases who received curative RT (60 Gy), while none in cases who received palliative RT (30 Gy).

Further, the observations in this study were noted for the analysis as below:

➢ Assessments of degree of conductive hearing loss (CD) immediately post radiotherapy

Amongst 94 cases (110-16=94) with 188 ears (is only being discussed), which were finally taken for analysis during immediate post-radiotherapy period, 34 cases developed CD. The CD was of mild degree in 37 ears and moderate in 11 respectively. Out of 34 cases and 68 ears, 48 ears (25.53%) had CD which was bilateral in 18 and unilateral in 12. After 6 month post-radiotherapy period amongst 94 cases and 188 ears, the unilateral mild CD was noted in 8 (4.25%) ears. Out of these 8, it was persistent in 6 while in 2 it developed newly during the follow-up period.

➢ Assessment of degree of SNHL immediately post-RT

Out of 94 cases, 13 cases developed only mild degree of SNHL immediate post-RT. Of which 5 were bilateral and 8 were unilateral. Five cases were right sided and 3 cases were left sided [Table/Fig-2].

➢ Assessment of degree of SNHL after 6 months post radiotherapy

Out of 94 cases, in 36 SNHL was noted after 6 months post-RT. The SNHL was of mild (26-40 dB) in 30 and moderate (41-55 dB) in 6 cases. Amongst cases with mild SNHL it was bilateral in 18; right sided in 6 and left sided in 6. Amongst cases with moderate SNHL it was bilateral in 5 and left sided in 1. Out of 18 ears which had mild SNHL immediately post radiotherapy, 11 ears remained static [Table/Fig-2]. This also means that out of 188 ears in 94 cases, 59 ears (31.38%) had SNHL including 44 newly developed ears during the 6 month post-RT period.

➢ Quantification of the degree (severity) of SNHL

The mean and SD of hearing threshold before start of RT amongst 188 ears was 21.3 dB and 1.9 dB respectively. [Table/Fig-3] depicts details of SNHL found immediately after RT and after 6 months of RT. Quantification of the degree (severity) of SNHL was done using one way Analysis of variance (ANOVA). The mean difference was compared between Pre-RT, Post-RT and after 6 months post-RT groups [Table/Fig-3,4].

During first and second follow-up it revealed that there was significant rise in hearing threshold.

Also it was observed that in 170 ears (188-18=170) there was no significant change in hearing threshold immediately after RT. However, this number of normal ears reduced to 129 ears (188-59=129) at 6 month post-RT follow-up.

Primary site of malignancy	No. (%) of cases Enrolled	Gender No. (%)		Curative Group 60 Gy RT No. (%)		Palliative Group 30 Gy RT No. (%)		Lost during study follow-up period No. (%)	
		Male	Female	Male	Female	Male	Female	Male	Female
Laryngopharynx	45 (40.90%)	36 (32.73)	9 (8.18)	30 (27.27)	7 (6.36)	6 (5.46)	2 (18.18)	5 (4.55)	2 (18.18)
Oral cavity	28 (25.45%)	25 (22.73)	3 (2.73))	17 (15.46)	0	8 (7.27)	3 (2.73)	4 (3.64)	0
Oropharynx	17 (15.45%)	12 (10.91)	5 (4.55)	12 (10.91)	5 (4.55)	0	0	1 (0.91)	1 (0.91)
Para nasal sinuses	8 (7.28%)	7 (6.36)	1 (0.91)	7 (6.36)	1 (0.91)	0	0	2 (18.18)	0
Neck nodes with Occult primary	7 (6.36%)	5 (4.55)	2 (18.18)	5 (4.55)	2 (18.18)	0	0	1 (0.91)	0
Parotids	5 (4.55%)	1 (0.91)	4 (3.64)	1 (0.91)	2 (18.18)	0	2 (18.18)	0	0
Total	110 (100%)	86 (78.18)	24 (21.82)	72 (65.46)	17 (15.46)	14 (12.73)	7 (6.36)	13 (11.82)	3 (2.73)

[Table/Fig-1]: Distribution of primary site of malignancy.

Degree of SNHL	Pre radiotherapy		Immediate post radiotherapy follow-up		6 months post radiotherapy follow-up	
	Cases	No of ears	Cases	No of ears	Cases	No of ears
Normal	94	188	81	162	58	116
Mild (26-40 dB)	Nil	Nil	13	18	30	48
Moderate (41-55 dB)	Nil	Nil	Nil	Nil	6	11

[Table/Fig-2]: Assessment of degree of senorineural hearing loss after immediate post radiotherapy and at 6 month follow-up.

Assessment of SNHL At Three different times	No. of ears with SNHL	Hearing Threshold in dB Mean±SD	95% confidence interval	
			From	To
Pre-RT	188*	21.3±1.9	20.83	21.85
Post-RT	18	27.97±1.31	27.33	28.27
At 6 months	59	35.4±5.6	33.90	36.84

[Table/Fig-3]: Quantification of the degree (severity) of sensorineural hearing loss. *188 ears of 94 cases having normal thresholds of hearing at start of RT

Comparison Between Groups (A, B and C)	Mean difference	p-value
A) Pre-RT and post-RT	6.47	p<0.001
B) Post-RT and at 6 months	7.57	p<0.001
C) Pre-RT and at 6 months	14.02	p<0.001

[Table/Fig-4]: Quantification of the mean difference and p-value of sensorineural hearing-Comparison between three groups of a) Group A-Pre-RT and post-RT, b) Group B-Post-RT and at 6 months, c) Group C-Pre-RT and at 6 months.

On comparing the mean difference amongst 3 groups namely A, B and C which were 6.47, 7.57 and 14.02 respectively we found that changes in PTA thresholds were statistically significant at all points of time with p<0.001 [Table/Fig-4] i.e., variation among column means are significantly greater than expected by chance.

DISCUSSION

Although it is true that the cochlea is not intentionally included in the clinical target volumes during RT for most head and neck cancer, these structures do get clinically measurable doses from primary beam-(entrance, exit, and scatter radiation). Because this is an epidemiologic type of study, the primary factors of interest were the exposure and consequent radiation to cochlea causing SNHL.

In this study, there were more males compared to females in ratio of 7.8:2.2. The reason for this may be more prevalence of consumption of tobacco and alcohol amongst males as these are also the most common aetiologic agents in head and neck cancer. The present study was conducted in head and neck cancer patients receiving RT. The mean age of the cases in the study was 50.7 years (Mean±SD: 50.7±11.09) which was less than 57.9 and 54 years as stated in studies by Pan CC et al., and Herrmann F et al., respectively [5,6]. This could be due to the difference in exclusion criterions between the studies, as cases having affected hearing as well as normal hearing are included in above mentioned studies unlike only the cases having hearing sensitivity within normal limits were included in our study. (a factual observation during the study and is mentioned).

In this study ototoxic effects were noted in cases who received curative RT (60 Gy), while not in cases who received palliative RT (30 Gy), indicating that minimum 60 Gy of total radiation dose was required for noticeable ototoxicity and it is in accordance with study done by Thibadoux GM et al. [7] where no statistically significant hearing loss is noted amongst 61 cases after receiving 24 Gy of total radiation and concluding that more than 30 Gy of radiation is minimum requirement for affection of hearing. Similarly, Hua C et al. reported that the probability of ototoxicity is very low for mean radiation dose of 30 Gy or less and increases at 40-45 Gy [8].

The present study is based on 6 month follow-up after completion of RT. Amongst 188 ears, 18 ears (9.57%) developed SNHL immediate post-RT. At 6 months after completion of RT, 32 ears (16 cases) did not come for follow-up and SNHL was noted in 59 ears (31.38%) amongst remaining 188. The reported incidence of post-RT sensorineural deficit is very variable ranging from of 0% to 50 %. [5] Anteunis LJ et al., have concluded that 50% of patients developed a clinically relevant hearing loss at the end of 2 years [9]. Bhandare N et al., reported a SNHL in 15.1% patients [10]. Merchant TE et al., found the rate of permanent hearing loss ranged from 24.2% to 36% for doses approaching 60 Gy [11]. Chan SH et al., in a study on SNHL with a median follow-up of 2 years after treatment of nasopharyngeal carcinoma found persistent SNHL in patients receiving either RT alone or in combination with chemotherapy in 40% and 56.4%, respectively [12].

In present study on comparing the mean difference between the 3 groups (A, B & C), 6.47 dB loss was found in group A- (Pre-RT to immediate post-RT group), 7.57 dB loss was found in group B (Immediate post-RT to 6 months), 14.02 dB loss was found in group C- (Pre-RT to 6 months post-RT). A hearing decrement of ≥10 dB was considered clinically significant in the present study as reported by Pan CC et al., [5].

According to this criterion, significant hearing loss occurred only at 6 months post radiotherapy. Kwong DL et al., reported the median time to documentation of SNHL was 4 months post-RT, ranging from immediate post irradiation to 48 months [13]. Grau C et al., and Chan SH et al., reported that most cases of SNHL was first noted 12 months after completion of RT [1,12]. Pan CC et al., and Johannesen TB et al., did not find any time association between hearing loss and RT [5,14]. The 6 months follow-up of present study may require longer follow-up to detect significant SNHL following incidental radiation to cochlea.

CONCLUSION

The cochlear function was significantly affected in cases receiving conventional radiotherapy for cancer of the head and neck region. Incidence of radiation induced SNHL using conventional RT increases with higher radiation dose.

In cases of head and neck cancer treated by conventional radiotherapy using telecobalt machine and shielding the risk of consequent sensorineural hearing loss-SNHL was about just less than one third (31.38%). The tolerance of cochlea to total dose of radiotherapy was >30 Gray and <60 Gray in cases of head and neck cancer treated by conventional radiotherapy.

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REFERENCES

[1] Grau C, Overgaard J. Postirradiation sensorineural hearing loss: a common but Ignored late radiation complication. Int J Radiation Oncology Biol Phys.1996;36(2):515-17.
[2] Gamble JE, Peterson EA, Chandler JR. Radiation effects on the inner ear. Arch Otolaryngol. 1968;88(2):156-61.
[3] Chauhan AS, Prinja S, Ghoshal S, Verma R, Oinam AS. Cost of treatment for head and neck cancer in India. PLoS ONE. 2018;13(1):e0191132.
[4] Clark JG. Uses and abuses of hearing loss classification. Asha.1981;2(3):493-500.
[5] Pan CC, Avraham E, Julia SL, Rhonda MS, Ten Haken RK, Kileny PR. Prospective study of inner ear radiation dose and hearing loss in head-and-neck cancer patients. Int J Radiation Oncology Biol Phys. 2005;61(5):1393-402.
[6] Herrmann F, Dorr W, Muller R, Herrmann T. A prospective study on radiation-induced changes in hearing function. Int J Radiation Oncology Biol Phys. 2006;65(5):1338-344.
[7] Thibadoux GM, Pereira WV, Hodges JM, Aur RJ. Effects of cranial radiation on hearing in children with acute lymphocytic leukemia. J Pediatr.1980;96:403-06.
[8] Hua C, Bass JK, Khan R, Kun LE, Merchant TE. Hearing loss after radiotherapy for paediatric brain tumours: effect of cochlear dose. Int J Radiation Oncology Biol Phys. 2008;72(3):892-99.
[9] Anteunis LJ, Wanders SL, Hendriks JJ, Langendijk JA, Manni JJ, de Jong JM. A prospective longitudinal study on radiation-induced hearing loss. Am J Surg.1994;168(5):408-11.
[10] Bhandare N, Antonelli PJ, Morris CG, Malayapa RS, Mendenhall WM. Ototoxicity after radiotherapy for head and neck tumours. Int J Radiation Oncology Biol Phys. 2007;67(2):469-79.
[11] Merchant TE, Gould CJ, Xiong X, Robbins N, Pritchard DL, Khan R. Early neuro-otologic effects of three-dimensional irradiation in children with primary brain tumours. Int J Radiation Oncology Biol Phys. 2004;58(4):1194-207.

[12] Chan SH, Kam WT, Lee MCH, Choi CW, Choi CW, Yau TK, et al. Sensorineural hearing loss after treatment of nasopharyngeal Carcinoma: a longitudinal analysis. Int J Radiation Oncology Biol Phys. 2009;73(5):1335-342.
[13] Kwong DL, Wei WI, Sham JS, Ho WK, Chua DP, Yuen PW, et al. Sensorineural hearing loss in patients treated for nasopharyngeal carcinoma: A prospective study of the effect of radiation and cisplatin treatment. Int J Radiation Oncology Biol Phys. 1996;36:281-89.
[14] Johannesen TB, Rasmussen K, Winther FO, Halvorsen U, Lote K. Late radiation effects on hearing, vestibular function, and taste in brain tumour patients. Int J Radiation Oncology Biol Phys. 2002;53(1):86-90.

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