RESEARCH ARTICLE

Effects of Radiotherapy on Auditory and Vestibular Function

Sachin Sharad Nilakhe

ABSTRACT

Introduction: Radiotherapy either primary or adjuvant, is a commonly used modality of treatment in head and neck malignancies. The audiovestibular apparatus is often within the fields of radiation treatment, and hearing loss is a possible complication. This study was undertaken to assess the audiovestibular functions in patients undergoing radiation therapy for head and neck malignancies to determine the type and severity of hearing loss and vestibular dysfunction following radiation therapy.

Materials and methods: Fifty patients with head and neck malignancies reported to the malignant disease treatment center of INHS Asvini and received radiotherapy as a primary modality of treatment or in combination with surgery during the period May 2003 to Sep 2004 were included in this study. None of these patients had prior treatment by chemotherapy.

Conclusion: A significant number of patients who were subjected to radiation therapy for head and neck malignancies develop conductive hearing loss is predominant in the immediate postradiation period. Conductive hearing loss is reversible and improves with the conservative line of treatment. Sensorineural hearing loss more commonly affects the higher frequencies and is more common in older patients. Sensorineural hearing loss is more common when radiation doses exceed 60 Gy. There is no conclusive evidence of vestibular dysfunction in patients undergoing radiotherapy for head and neck cancers.

Keywords: Auditory, Vestibular, Radiotherapy.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Radiotherapy either primary or adjuvant, is a commonly used modality of treatment in head and neck malignancies.

Associate Professor

Department of ENT, Bharati Medical College and Hospital, Sangli Maharashtra, India

Corresponding Author: Sachin Sharad Nilakhe, Associate Professor, Department of ENT, Bharati Medical College and Hospital, Sangli, Maharashtra, India, Phone: 2375598 e-mail: sachinsnilakhe@gmail.com

The audiovestibular apparatus including the temporal bone, which houses part of the external ear, the middle, and inner ear; the auditory nerve; and a portion of the brainstem is often within the fields of radiation treatment, and hearing loss is a possible complication.[1] Patients with large lymphadenopathy in zone 2 and upper zone 5 of the neck may experience up to 50% of the total radiation dose to their cochleas. Even patients with primary tumor sites anatomically far removed from the nasopharynx and hypopharynx may receive high doses of radiation in selected cases.[2] Radiation can cause two kinds of hearing impairment, conductive hearing loss originating in the outer and middle ear, and sensorineural hearing loss caused by damage to the cochlea and auditory nerve.[3] In the acute stage, patients often have signs and symptoms of otitis media or middle ear effusion due to Eustachian tube dysfunction giving rise to conductive hearing loss.[3] Radiation induced changes in the middle ear mucosa are delayed ultrastructural changes, undergoing various ciliary, connective and vascular changes during or soon after completion of radiotherapy.[3,4] The vestibular part of inner ear and the central vestibular pathway may also be within the radiation field when patients are treated for head and neck cancer. Experimental data have shown degeneration of the sensory cells and damaged vestibular function after radiation.[5] A possible relationship between radiation and vestibular disorders has been shown in patients treated for head and neck cancers.[6-8]

The inner ear is claimed to be most resistant to effects of ionizing radiation.[9] Early and temporary changes in inner ear are transient in nature.[10] Delayed vascular changes are related to changes in collagen content of the vascular framework that lead to a permanent hearing loss.[3] However, the degree to which an ear may be affected by radiation during treatment for malignancies of head and neck cannot be predicted, as is the time of onset. It is possible that the patient may suffer from hearing impairment years after therapy.[11] Various workers of audiovestibular dysfunction in patients undergoing radiation therapy have given conflicting reports. This study was undertaken to assess the audiovestibular functions in patients undergoing radiation therapy for head and neck malignancies to determine the type and severity of hearing loss and vestibular dysfunction following radiation therapy.

MATERIALS AND METHODS

Head and neck cancer accounts for 40 to 45% of all the malignancies in India. Majority of them are squamous cell carcinoma, which involves surgery and radiotherapy as a primary modality of treatment separately or in combination.

This study was taken up to evaluate the adverse effects of radiotherapy on audiovestibular functions in the treatment of head and neck malignancies. Fifty patients with head and neck malignancies reported to the Malignant Disease Treatment Center of INHS Asvini and received radiotherapy as a primary modality of treatment or in combination with surgery during the period May 2003 to Sep 2004 were included in this study. None of these patients had prior treatment by chemotherapy.

INCLUSION CRITERIA

a. Case of head and neck malignancy reported to the Malignant Disease Treatment Center of INHS Asvini and received radiotherapy as a primary modality of treatment or in combination with surgery.
b. Six months of audiological follow-up after completion of radiotherapy.
c. No pre-existing audiological disease other than serous otitis media (SOM) related to nasopharyngeal carcinoma.
d. No significant pre-irradiation sensorineural hearing deficit defined as bone conduction hearing threshold more than 50 db at any of the four frequencies (0.5, 1, 2 and 4 kHz) tested before irradiation. This is necessary to avoid error from thresholds, because the maximum level for the perception of sound through bone threshold is around 70 dB.

All selected patients subjected to pure tone audiometry in an acoustically treated room. Impedance audiometry was done in all patients to evaluate middle ear pathology. The Fitzgerald Hallpike bithermal caloric test was performed using hot (44ºC) and cold (30ºC) water irrigation to the external ear canal with electronystagmography (ENG) recordings. Maximum slow phase velocity (SPV) caloric nystagmus was measured for comparison. Canal paresis was defined as a greater than 25% difference between maximum SPV for each ear compared with the sum of SPVs.

Table 1: Primary site of lesions included in the study (n = 50)

Primary site	*Cases*	*Percentage*
Nasopharynx	6	12
Oral cavity	14	28
Hypopharynx	4	8
Larynx	12	24
Salivary glands tumors	6	12
Unknown primary with cervical Metastasis	8	16

The above pre-irradiation data were noted as base line data. The examination, audiovestibular evaluation like PTA, impedance audiometry and caloric tests were carried out in all cases before radiation, immediately on completion of radiation therapy, at 3 and 6 months after irradiation therapy.

OBSERVATION AND RESULTS

The head and neck comprise a large number of anatomical structures. A malignant tumor can involve any structure as a primary lesion. The distribution of primary site of lesion of 50 patients is shown in the Table 1.

It is observed that the majority of cases were encountered in stage III and IV disease.

The age distribution of patients in the present study is as Table 2.

The highest incidence was between the age group 61 and 70. The youngest patient in the study was 32 years old and the oldest one was 76 years old.

There was a very strong male preponderance in the study group.

AUDIOMETRIC EVALUATION

Every patient underwent audiometric evaluation before radiotherapy to get the baseline hearing threshold. After completion of radiotherapy, hearing assessment was done immediately and at 3 and 6 months intervals. The hearing thresholds obtained were compared with the baseline hearing threshold to assess hearing loss. The data collected are presented in tabular form in Table 3 and Graph 1.

During immediate post-radiation audiometric evaluation, 32% of patients showed conductive hearing loss that was related to Eustachian tube dysfunction due to the effect of radiation. This was temporary, improved partially in the next 6 months. At the end of 6 months, only 14% of patients showed conductive hearing loss.

During the early phase of evaluation 4% of patients showed increase in the bone conduction hearing threshold. At the end of 6 months follow-up a total 14 patients (28%) showed sensorineural hearing loss.

Most of the patients showing sensorineural hearing loss showed the mixed type of hearing loss, i.e. both conductive and sensorineural hearing loss. At 6 months follow-up 12% of patients showed mixed type of hearing loss.

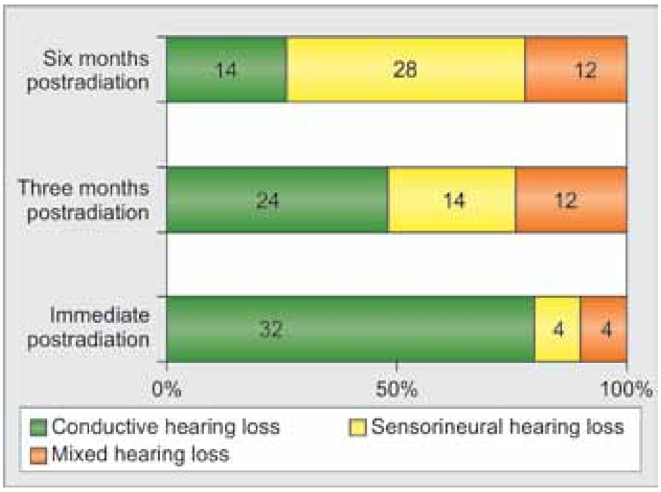
Table 2: Age distribution in the study (n = 50)

Age group	*Total*	*Percentage (%)*
31-40	4	8
41-50	10	20
51-60	14	28
61-70	16	32
71-80	6	12

Table 3: Types of hearing loss (n = 50)

Type of hearing loss	*Immediate postradiation*	*Three months postradiation*	*Six months postradiation*
Conductive loss	*16 (32%)	*12 (24%)	*7 (14%)
Sensorineural loss	2 (4%)	7 (14%)	*14 (28%)
Mixed loss	2 (4%)	6 (12%)	6 (12%)

*on applying chi-square test $p < 0.05$, significant



Graph 1: Number of patients showing different types of hearing loss in relation to duration after radiation (n = 50)

Eleven patients out of 14 having sensorineural hearing loss were in the age group >50 years.

As this is a male predominant study, 12 out of 14 were males showing sensorineural hearing loss.

DEGREE OF HEARING LOSS

The post-radiation at 6 months, the status of sensorineural hearing loss at low (0.5, 1 and 2 kHz) and high (4 kHz) frequencies were as shown in Table 4 and Graph 2.

Sensorineural hearing loss at high frequencies was more common compared to that at low frequencies. For low frequencies, six patients had an increase in bone conduction hearing threshold 6 months after radiotherapy while the high frequencies were affected in all patients.

RELATION OF HEARING LOSS TO DOSE OF RADIATION

At 6 months post-treatment, the status of sensorineural hearing loss at low (0.5, 1 and 2 kHz) and high (4 kHz) frequencies and their relation to the dose of radiation received is as Table 5 and Graph 3.

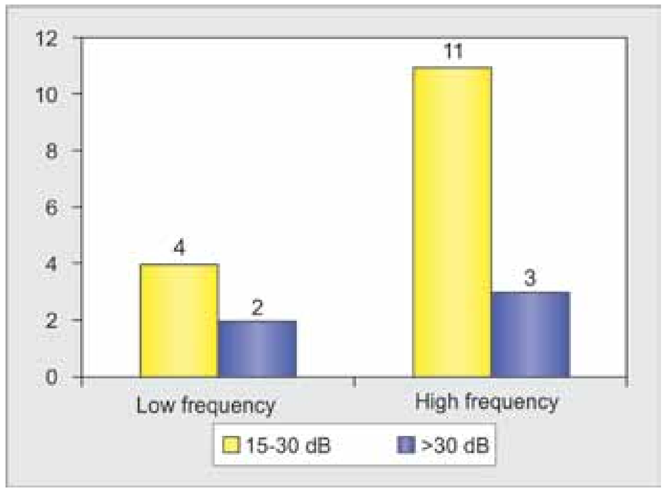
Sensorineural hearing loss was seen in the majority of patients who had received radiation doses more than 6000 cGy.

TYMPANOMETRIC EVALUATION

Tympanometry was carried out in all 50 patients pre-irradiation and immediate post-irradiation, at 3 and

Table 4: Degree of hearing loss (n = 50)

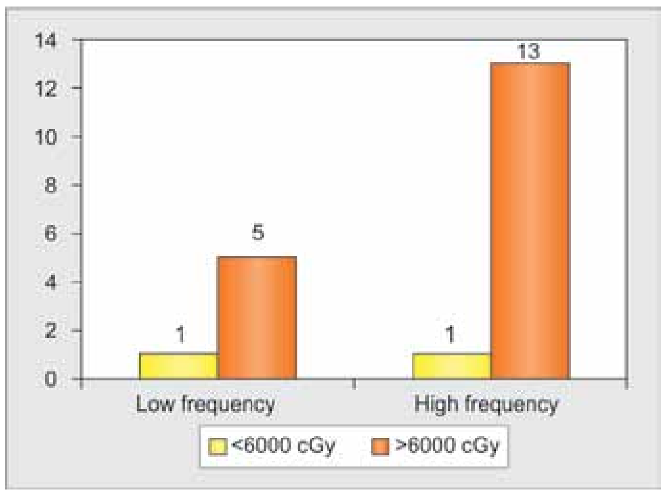
Degree of SNHL (dB)	*At low frequencies (mean of 0.5, 1 and 2 kHz)*	*At high frequency (4 kHz)*
15-30	4 (8%)	11 (22%)
≥30	2 (4%)	3 (6%)



Graph 2: Number of patients having various degree of hearing loss affecting lower or higher frequencies (n = 50)

Table 5: Relation of hearing loss to dose of radiation (n = 50)

Dose of radiation (cGy)	*No. of cases*	*At low frequencies (mean of 0.5, 1 and 2 kHz)*	*At high frequency (4 kHz)*
<6000	7 (14%)	1 (2%)	1 (2%)
≥6000	43 (86%)	5 (10%)	13 (26%)



Graph 3: Number of patients with hearing loss related to dose of radiation (n = 50)

6 months postradiation. The results of the tympanometry were classified into types A, B and C as proposed by Hayes and Jerger as shown in Table 6.

In the pretreatment evaluation, five patients showed type B curve due to middle ear effusion related to nasopharyngeal carcinoma. Incidence of Secretory otitis media (SOM) is higher (24%) immediate postradiation and related to Eustachian tube dysfunction due to the effects of radiation.

Table 6: Types of tympanogram (n = 50)

Tympanogram (n = 50)	*Pre-irradiation*	*Immediate post-radiation*	*Three months post-radiation*	*Three months post-radiation*
Type A	42 (84%)	28 (56%)	31 (62%)	39 (78%)
Tybe B	5 (10%)	12 (24%)	11 (22%)	8 (16%)
Type C	3 (6%)	10 (20%)	8 (16%)	3 (6%)

VESTIBULAR EVALUATION

Two (4%) patients showed vestibular disturbance in the form of episodes of rotatory vertigo immediate postradiation but the ENG studies were normal. The symptoms improved in one patient with medication while it was persistent in one patient for 3 months. No patient had shown canal paresis or directional preponderance during the 6 months follow-up period.

DISCUSSION

In the 1920s, the effects of small doses of ionizing radiation on the human ear was investigated for its therapeutic value in treating chronic otitis media, otosclerosis, perceptive deafness and tinnitus. The nasopharynx used to be irradiated in the treatment of conductive deafness due to lymphoid tissue around the Eustachian tube.[12] Later radiation was used for treating malignancies of the head and neck and despite refinements in radiation therapy, treatment of tumors in areas, such as the parotid gland, the nasopharynx and the tonsils do not allow the exclusion of the temporal bone from the irradiation field.

There have been no reports in the western literature of radiation induced changes in the human ear undergoing treatment for head and neck tumors until Borsanyi, Blanchard and Thorn in 1961 studied 100 patients undergoing radiation for the treatment of head and neck tumors.[10] Most of them were retrospective studies and pretreatment audiological evaluation was not always available. Some studies also used large radiation doses, up to 24000 rads[22] that would have little relevance to modern clinical practice. The reported incidence of post-irradiation sensorineural hearing loss varies, from no sensorineural hearing loss observed to 54% involvement.[10,13-16] Histological examination of temporal bones after irradiation had demonstrated damage to the organ of Corti, with atrophy of the basilar membrane, spiral ligaments, and stria vascularis. Hair cell atrophy was also noted.[17,19] In the present prospective study, the baseline audiogram and clinical assessment of every patient formed the basis for evaluation of the subsequent course of hearing change after irradiation. All patients were serially followed up with audiometry, tympanometry and clinical examination after irradiation for 6 months.

In the present study, as shown in Table 3 during audiometric evaluation immediate postradiation 16 (32%) patients showed conductive hearing loss. During subsequent follow-up at 3 and 6 months this number decreased to 12 (24%) and 7 (14%), respectively. On applying Chi-square test $p < 0.05$, a significant number of patients showed conductive hearing loss. This was related to Eustachian tube dysfunction or middle ear effusion due to the effect of radiation.[3,4,10,14] These findings were supported by clinical and tympanometric evaluation. As shown in Table 6, 12 (24%) and 10 (20%) patients showed type 'B' and 'C' curves, respectively in the immediate postradiation tympanometric evaluation. This suggests middle ear effusion and Eustachian tube dysfunction. At the end of 6 months, only 8 (16%) patients showed persistent middle ear effusion. Rest of the patients improved with conservative management. Thus, this study confirms the observations of Dias[14] and Elwany.[4] As stated by Young YH,[18] conductive hearing loss due to radiation otitis media is reversible if middle ear inflammation is controlled as confirmed in this study. At the end of 6 months, six (12%) patients showed mixed hearing loss. Postradiation SOM would account for conductive hearing loss. Other studies have reported transient increase in bone conduction hearing threshold in association with conductive hearing loss after radiotherapy.[14,19] These findings were consistent with the study by Antenius et al[19] and Dias.[14] The presence of middle ear effusion would thus, be an evidence of complications due to radiation and point to an increased risk of damage to the inner ear and development of persistent sensorineural hearing loss.[20]

In the present study, sensorineural hearing loss was seen in 14 (28%) patients at the end of 6 months follow-up. Low frequency sensorineural hearing loss occurred in six (12%) patients and the high frequencies were affected in all 14 patients. These findings are consistent with previous studies.[10,13,14,16,19] Sensorineural hearing loss at high frequencies was more commonly affected than at the low frequencies.[10,16,19,21] The outer hair cells in the basal coil of the cochlea are responsible for transduction of higher frequency sounds while lower frequency sounds are transduced by the inner hair cells situated in the apex. In animal and human pathological studies, more pronounced damage was found among outer hair cells after radiotherapy.[16,20]

As shown in the Table 5, 13 patients who had sensorineural hearing loss received a total radiation dose of more than 60Gy. This finding was consistent with studies by Grau et al[16] and Ho WK et al.[1] Grau et al reported no significant correlation between preirradiation hearing levels or patients age with postradiation sensorineural hearing loss.[16] In the present study, sensorineural hearing loss is more common in patients of more than 50 years of age. This was consistent with the study conducted by Kwong DL et al.[20]

None of the patients in the present study showed canal paresis or directional preponderance as an effect of radiation on the vestibular function during the 6 months follow-up period. Only two (4%) patients showed episodes of vertigo which were transient and improved after medication. These findings did not compare with the reported study by Singh IP[6] and Chow WY[8] who reported that a significant number of patients receiving radiotherapy for parotid and nasopharyngeal tumors respectively, showed canal paresis.

CONCLUSION

This study concludes that a significant number of patients who were subjected to radiation therapy for head and neck malignancies develop conductive hearing loss is predominant in the immediate postradiation period. Conductive hearing loss is reversible and improves with the conservative line of treatment.

Sensorineural hearing loss more commonly affects the higher frequencies and is more common in older patients. Sensorineural hearing loss is more common when radiation doses exceed 60 Gy.

There is no conclusive evidence of vestibular dysfunction in patints undergoing radiotherapy for head and neck cancers.

REFERENCES

1. Ho WK, Kwong DL. Long-term sensorineural hearing loss following radiotherapy in patients suffering from nasopharyngeal carcinoma. Head and Neck 1999;21(6):547-553.
2. Ondrey FG, Greig JR. Radiation dose to otologic structures during head and neck cancer radiation therapy. Head and Neck Surgery 2000;110(3):217-221.
3. Varghese G, Sahota JS, Hazarika P, Rajashekhar B. Hearing anomalies following radiation therapy for head and neck cancers. Indian J Exp Biol 1996 Sep;34(9):878-879.
4. Elwany S. Radiation induced changes in the middle ear mucosa. J Otolaryngol 1985;99(4):343-353.
5. Winther FO. X-ray irradiation of inner ear of guinea pig. Early degenerative changes in the sensory epithelia. Acta Otolaryngol (Stockh) 1969;68(6):514-525.
6. Singh IP, Slevin NJ. Late audiovestibular consequences of radical radiotherapy to the parotid. Clin Oncol R Coll Radiol 1991;3(4):217-219.
7. Gabriele P, Orecchia R, Magnano M, et al. Vestibular apparatus disorders after external radiation thrapy for head and neck cancers. Radither Oncol 1992 Sept 25;23(1):25-30.
8. Chao WY, Tseng HZ, Tsai ST. Caloric response and postural control in patients with nasopharyngeal carcinoma after radiation therapy. Clin Otolaryngol 1998;23(5):439-441.
9. Yang X, Lu Y, Chen Z. Delayed damage of ionizing radiation on the inner ear. Zhonghua Er Bi Yan Hou Ke Za Zhi 1997 Aug; 32(4):222-225.
10. Boranyi S, Blanchard CL. The effects of ionizing radiation on the ear. Annal Otorhinolaryngol 1961;70:255-261.
11. Zenman W. Pathology of the nervous system: the effects of atomic radiation. Minchler J Ed 1968;76(2):892.
12. Cullen, Girden. Effects of ionizing radiation on hearing. JAMA 1935;20(4):263.
13. Leach W. Irradiation of the ear. J Laryngol Otol 1965;79(10):870-880.
14. Dias A. Effects of the hearing of the patients treated by irradiation in the head and neck area. J Laryngol and Otology 1966;80(3):276-287.
15. Moretti JA. Sensorineural hearing loss following radiotherapy to the nasopharynx. Laryngoscope 1976;86(4):598-602.
16. Grau C, Moller K, Overgrand M. Sensorineural hearing loss in patients treated with irradiation for nasopharyngeal carcinoma. Ind J Radiat Oncol Biol Phys 1995 Aug;21(3):723-728.
17. Schukneeth HF, Karmody CS. Radionecrosis of the temporal bone. Laryngoscope 1976;86(3):598-602.
18. Young YH, Lu YC. Mechanism of hearing loss in irradiated ears: a long-term longitudinal study. Ann Otol Rhinol Laryngol 2001 Oct;110(10):904-906.
19. Antenius LJ, Wanders SL. Radiation induced hearing loss. Am J Surg 1994;168(5):408-411.
20. Kwong DL, Wei WI. Sensorineural hearing loss in patients undergoing radiation and cisplatin treatment. Int J Radiat Oncol Biol Phys 1996;36(2):515-517.
21. Gyrokey J, Pollock FJ. Radiation necrosis of the ossicles. Arch Otolaryng 1960;71:793-796.