

Effect of Radiotherapy on Hearing Thresholds in Patients of Head and Neck Malignancies

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Abstract

Objective: To study the effect of radiotherapy on hearing in patients with head and neck cancer.

Methods: A prospective study was undertaken comprising of 30 patients (60 ears) with histopathologically proven head and neck cancer in the age group of 30-75 years. Hearing status was evaluated before and after one month of radiotherapy treatment by pure tone audiometry (PTA) and brainstem evoked response audiometry (BERA).

Results: Pre-radiation hearing assessment revealed normal hearing in 20% (12 ears), mild hearing loss in 33.3% (20 ears), moderate hearing loss in 28.3% (17 ears) and moderately severe hearing loss in 18.3% (11 ears). Post-radiation hearing remained same in 58.3% (35 ears), deteriorated in 33.3% (20 ears), and improved in 8.3% (5 ears). Post radiotherapy hearing loss was seen more common in patients older than 50 years of age and who had abnormal pre-radiation hearing status.

Conclusion: Hearing loss can occur in a significant number of patients undergoing radiotherapy for head and neck malignancies hence the patient must be counseled for any post-irradiation hearing loss.

INTRODUCTION

Cancer is a leading cause of death worldwide, it accounted for 7.6 million deaths (around 13% of all deaths) in 2008 and is projected to rise continuously, with an estimated 12 million deaths in 2030[1]. In India, head and neck cancers are the major cause of cancer morbidity and mortality. According to various studies, the prevalence of head and neck cancers with respect to total malignancies varies from 9.8% to 42.7% [2-4]. Partly due to life style changes and partly due to traditional acceptance of tobacco and smoking in the society, the prevalence of head and neck malignancies is on the rise in our country. Further, the lacks of awareness about cancer and nonexistent cancer prevention programs have made the scenario even worse. Unfortunately, these very factors result in late presentation and delayed diagnosis of these patients and many end up heading for just palliative radiotherapy. Among the single or combined treatment modalities of head and neck malignancies like radiotherapy, surgery and chemotherapy, the radiotherapy invariably is still the major treatment modality preferred by patients as well as surgeons.

The side effects of radiotherapy on normal tissues of head and neck are relatively common and unavoidable, which

depend on the site of radiation, total dose delivered and daily fraction of radiation used. High total dose and larger daily fractions cause more complications. Cutaneous erythema, mucositis and xerostomia have been extensively reported in the literature as acute side effects. Other side effects include alteration of taste, pain on swallowing and hair loss on head, neck and face. Fatigue or feeling tired is very common. The acute reactions are self-limited and usually do not affect the dose of radiation therapy. Long term sequel occurs many months or years after completion of therapy. Organ dysfunction often manifests by cell lines with slow turn over e.g. radio-necrosis of bone. In some tissues, such as inner ear hair cells, functional progenitor cells may be lacking, resulting in greater organ system dysfunction [5]. The total recommended dose limit for use in clinical practice with fractionated and single dose radiotherapy is < 60 grey (Gy) for brain and < 45 grey (Gy) for cochlea [6].

Since the radiotherapy used in management of head and neck tumors often includes the temporal bone and brain stem in the portals. So the middle ear, inner ear and brain stem may receive a significant radiation dose. Hearing loss is a common complication of radiation treatment, which may be conductive, sensorineural and mixed. Temporary hearing

impairment can result from Eustachian tube dysfunction, radiation induced otitis media and transient vasculitis of inner ear vessels, whereas the delayed radiation induced hearing loss has been attributed to the effects of radiation on inner ear with cellular changes, inflammatory reaction and hemorrhage involving the vessels [7-9].

With the development of advanced treatment options available for the management of head and neck malignancies the survival has improved, so the hearing disability owing to radiotherapy can significantly affect the quality of life (QOL). By reviewing the available literature on radiotherapy induced ear toxicity, radiotherapy induced ear injuries remain under- evaluated and under-reported, hence, it was planned to evaluate post radiotherapy hearing status in patients of head and neck malignancies.

MATERIAL AND METHODS

This prospective study was undertaken at Pt. B.D. Sharma PGIMS, Rohtak (India) to evaluate the effect of radiotherapy on hearing 30 patients of head and neck cancer.

Inclusion Criteria: Thirty consecutive patients (60 ears) of clinically diagnosed head and neck malignancies of either sex in age group of 30-75 years were taken. The clinical diagnosis was confirmed in all the cases by histopathological examination.

Exclusion Criteria: Patients having past history of hearing disability and chronic suppurative otitis media were excluded from the study. The patients already having severe to profound hearing loss were also not included in this study.

Hearing Assessment: Pure tone audiometry (PTA) and brain stem evoked response audiometry (BERA) were done in all the recruited cases before and after one month of the radiation treatment. PTA: Air conduction threshold level was measured at frequencies 0.25 to 4 kHz and bone conduction threshold level was measured at frequencies 0.5 to 4 kHz. BERA: Latency of wave I and inter peak latency interval (IPLI) of wave I-III, I-V and III-V were measured in all patients.

The obtained data from pre and post radiotherapy audiograms were analyzed statistically by using paired students t-test.

RESULTS

The mean age of the patients was 51 years (range 30- 75). Most of the patients 63.34% (19/30) were above the age of 50 years. The Male: female ratio was 4.3:1 (Table-1).

TABLE 1

AGE/SEX DISTRIBUTION OF PATIENTS

Age Group	Male Patients	Female Patients	Total
21-30 yrs.	0	3	3
31-40 yrs.	3	1	4
41-50 yrs.	6	0	5
51-60 yrs.	7	3	10
61-70 yrs.	6	0	6
71-80 yrs.	1	0	1
Total	23 (76.7%)	7 (23.3%)	30

Maximum (46.7%) patients had carcinoma of oral cavity, 10% had of oropharynx, 20% of hypopharynx, 20% of larynx and 3.3% of paranasal sinuses (maxillary sinus). Histopathologically, all the cases had squamous cell carcinoma (Table-2).

TABLE 2

SITewise DISTRIBUTION OF HEAD AND NECK CARCINOMA

Site of Head and Neck Carcinoma		No. of Patients	Percentage
Oral Cavity	Carcinoma Tongue	6	20%
	Carcinoma Tonsil	4	13.3%
	Carcinoma Palate	2	6.7%
	Carcinoma Floor of Mouth	2	6.7%
Pharynx	Carcinoma Oropharynx	3	10%
	Carcinoma Hypopharynx	6	20%
Larynx	Carcinoma Larynx	6	20%
Nose/PNS	Carcinoma Maxillary Sinus	1	3.3%
Total		30	100%

Hearing status of patients: Pre-radiation and Post-radiation

Pure tone Audiometry

Out of 60 evaluated ears, post radiation hearing remained same in 35 (58.3%) ears, deteriorated in 20 (33.3%) ears, and improved in 5 (8.3%) ears (Table-3).

TABLE 3

CHANGE IN HEARING STATUS POST RADIATION
BASED ON PTA

Degree of Hearing loss Pre radiation		Unchanged		Deterioration		Improvement		Total
		No. of Ears	%	No. of Ears	%	No. of Ears	%	
Normal		4	6.7%	8	13.3%	0	0	12
Mild 26-40db	Cond.	7	11.7%	1	1.7%	0	0	8
	SNHL	7	11.7%	4	6.7%	0	0	11
	Mixed	0	0	1	1.7%	0	0	1
Mod 41-55 db	Cond.	0	0	3	5%	2	3.3%	5
	SNHL	7	11.7%	1	1.7%	1	1.7%	9
	Mixed	2	3.3%	1	1.7%	0	0	3
Mod Severe 56-70 db	Cond.	1	1.7%	0	0	1	1.7%	2
	SNHL	2	3.3%	1	1.7%	0	0	3
	Mixed	3	5%	0	0	1	1.7%	4
Severe 71-91 db	Cond.	0	0	0	0	0	0	0
	SNHL	0	0	0	0	0	0	0
	Mixed	2	3.3%	0	0	0	0	2
Total		35	58.3%	20	33.3%	5	8.3%	60

Of those 20 ears, hearing loss observed was conductive in 45% ears (9/20), sensorineural in 25% ears (5/20) and mixed in 30% ears (6/20).

The means of air conduction (AC) hearing threshold level was 40.22 db and 44.32 db pre and post radiation respectively. The two tailed p value was equal to 0.0007. By conventional criteria, this difference is considered to be statistically significant. The means of bone conduction (BC) hearing threshold level were 23.82 db and 25.95 db pre and post radiation respectively. The two- tailed p = 0.0030, which is also statistically significant.

BERA

The Mean latency of wave I were 2.000 m sec and 2.055 m sec pre and post radiation respectively. The two-tailed P value equals to 0.0308. By conventional criteria; this difference is considered to be statistically significant. Whereas, the differences of means of Inter Peak Latency Interval between wave I and III (IPLI I-III), I and V (IPLI I-V) and wave III and V (IPLI III-V) were not statistically significant as the P values were 0.3667, 0.0590 and 0.4537 respectively (Table-4).

TABLE 4

CHANGES OF BERA POST RADIATION

		Wave I	IPLI I-III	IPLI I-V	IPLI III-V
Pre RT	Mean (m sec)	2.000	2.102	4.142	2.040
	SD	0.157	0.213	0.193	0.189
	Range (m sec)	1.6-2.4	1.7-2.8	3.8-4.8	1.6-2.4
Post RT	Mean (m sec)	2.055	2.070	4.087	2.017
	SD	0.135	0.141	0.150	0.153
	Range (m sec)	1.8-2.3	1.8-2.4	3.6-4.3	1.7-2.4

DISCUSSION

The radiotherapy has been proved to be the most valuable modality in the cancer management, more so, in head and neck cancer patients. Due to the close proximity of the tumor, the normal neighboring organs also especially the ear receive a significant radiation dose, resulting in various toxic effects in a proportion of patients. The radiation induced hearing loss has long been recognized as an important side effect in the management of head and neck neoplasm, the earliest study reported in human beings is by Borsanyi et al in 1961, where, 14 patients out of 100 had pathological changes in hearing apparatus [10]. In the literature, is a wide range of incidence (0 to 65%) of post RT hearing impairment has been reported when the temporal bone was within the field of radiation in patients with neoplasm of head and neck [11-18].

In the present study we found most of the patients (63.34%) were above the age of 50 years, it is well known that head and neck cancers are encountered in this age group. Gender wise the male versus female ratio observed was 4.3:1, the probable explanation is that males are consuming more tobacco, smoking and alcohol than females, which are the main etiological factors of head and neck cancers. The similar findings are also noted by Upadhyaya et al [19].

In our study the hearing deterioration was observed in 33.3% ears (20/60). The documented hearing loss was conductive in 45% ears (9/60), sensorineural in 25% ears (5/60) and mixed in 30% ears (6/60). The observations are consistent with the studies by Jereczek et al in their review article on radiotherapy induced ear toxicity they commented that these reactions have acute or late character, may affect all structures of the hearing organ, and result in conductive, sensorineural or mixed hearing loss [14], by Bhandare et al observed that radiotherapy toxicity is observed in all parts of the auditory system with median doses varying between 60 to 66 Gy [20] and also by Anteunis et al who described that the changes found in middle and inner ear, auditory nerve

and brain stem at a dose of 50 Gy [21].

We found that conductive and mixed hearing loss was more common than sensorineural loss. The same is consistent with the studies in the literature during or immediately after radiotherapy [10,14,19]. Conversely, many other studies, which reported increased incidence of SNHL after radiotherapy [8,16,18,22-26]. They had long term follow up after radiation, which showed a high incidence of SNHL and we could not do the same because of time constraint of the study period.

The precise mechanism of post radiotherapy hearing loss from the previous studies in the literature on animals as well in human beings describe that at early stage therapeutic doses cause inflammatory reaction in endothelium of blood vessels leading first onto vasodilatation and later on narrowing and obliteration of vascular lumen [10,27-30]. At the later stages atrophy of mucous membrane and osteoradionecrosis occur, the atrophy of mucous membrane leading on to progressive hearing loss begins soon after treatment and often progress to profound deafness. The degenerative changes are particularly seen in the spiral and annular ligament, the earlier process may leads on to degeneration of organ of Corti at later stages [8,15,17,24]. Bhide et al [31] and Borsanyi et al [10] described the Eustachian tube edema and secretory otitis media are the main cause of conductive deafness in early stages and is mostly reversible. Whereas, external auditory canal stenosis, chronic otitis media, Eustachian tube pathology and the cochlear and/or retrocochlear damage are the causes of late conductive, sensorineural, or mixed hearing losses.

There is growing evidence that radiation induced electrophysiological changes in auditory system are of immediate onset and may effect on the ABR [32]. Lau et al found the prolongation of latencies of all ABR waves except wave IV immediately after RT [33]. Anteunis et al described that permanent hearing loss occurred in 6/18 patients, 3 of whom had an abnormal ABR suggestive of retrocochlear lesion [24]. In the present study we observed the prolongation of latency of wave I significantly after RT whereas, the Inter Peak Latency Intervals between wave I and III (IPLI I-III), I and V (IPLI I-V) and wave III and V (IPLI III-V) were not significantly changed. This indicates that the early changes are in the middle or inner ear (cochlear), rather than retro cochlear region. This is supported by Lau et al as they described that damage to cochlear hair cells may lead to prolongation of wave I and similar effects be produced by radiation induced middle ear

changes [33].

In our study we observed post radiation improvement in abnormal hearing in 8.3% patients. It could be attributed to the tumor regression following radiotherapy leading on to improvement in Eustachian tube functions. This finding has also been reported by other authors [22,32,34]. Somefun et al reported that abnormal hearing mainly conductive became normal post-radiation in 6 ears (7.5%) [34].

Our study showed that hearing loss was more common in patients older than 50 years of age, nineteen out of 30 (63.34%) showed post RT deterioration in hearing. In addition, hearing loss was more common in patients who had abnormal pre-radiation hearing status. This observation is consistent with other studies [16,17,35].

CONCLUSION

Hearing loss can occur in a significant proportion of patients undergoing radiotherapy for head and neck malignancies. The patient must be counseled to mentally prepare him for any post-irradiation hearing loss scenario.

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