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Prospective study of sensorineural hearing loss in patients of head and neck cancers after radiotherapy and chemotherapy

Abstract

Introduction: The multimodality approach in locally advanced squamous cell carcinoma of head and neck has been found to reduce the risk of local failure and improves survival. Radiation treatment strategies have not been adopted to protect the inner ear. Radiation damage can thus occur from the pharyngotympanic tube to the brain stem auditory pathway and therefore may cause hearing loss.

Materials and methods: Histopathologically proved 66 Head and Neck cancer patients were subjected to radiotherapy and 34 patients were subjected to concomitant chemoradiation to study the occurrence of SNHL from 1st September 2010 to 31st August 2012.

Results: The sensorineural hearing loss was more in higher frequencies. A paired sample t-test was conducted to compare the hearing losses before and 6, 12 months after therapy and were found to be significant ($p<0.05$). It was found that hearing loss was persistent. The difference of proportions of hearing loss after RT and RT+CT ($p<0.05$) after 1 month were found to be significant.

Conclusion: As the radiation field descends down from nasopharynx effect on otological structures decreases. Both incidence and severity of hearing loss increased with time especially at high frequencies. Patients who received concomitant chemoradiation experienced greater sensorineural hearing loss compared with patients treated with radiotherapy alone.

Keywords: sensorineural hearing loss, radiotherapy, chemotherapy, head and neck cancers.

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Introduction

Cancer has gained as an emerging major problem in India. 70% of the affected patients present with clinically advanced disease, either at the primary site or in the cervical lymph nodes.[1] The cure of cancer, with preservation of structure, function and aesthetics, has become more evident with advances in modern radiation oncology, based on technologic gains in radiation physics and insights to radiation biology and pathophysiology.[2] Surgery and radiation, used alone or in combination are the only curative treatments. Approximately, 80-90% of patients with stage I or II head and neck cancer are cured with surgery or radiotherapy alone. A combination of chemotherapy and radiation therapy is used in patients with inoperable or unresectable [stage III and IV] disease in an attempt to increase the cure rates over radiation alone. The advantages of the treatment combination are the preservation of cosmesis and function as compared to radical surgeries.

Locoregional control is critical in management of head and neck malignancies as salvage of locoregional disease is often difficult. The multimodality approach in locally advanced squamous cell carcinoma of head and neck has been found to reduce the risk of local failure and improves survival.

The head and neck is a fascinating area of the body with complex physiology and anatomy and where the basic function like vision, hearing, swallowing, smell depend on a symphony of parts working together. The goal of treatment in Head and Neck cancers is to maintain a strong emphasis on individual's quality of life. The ability to communicate is a crucial aspect of human life and the auditory sense is very important for communication of any kind. Hearing impairment constitutes an unseen misery and its problems are quiet deep and complex. In the current treatment of head and neck cancers especially squamous cell carcinoma strategies for organ preservation using radiation therapy for head and neck have been the main stay of treatment. In radiation therapy for head and neck cancers, certain strategies have been developed to minimize the effects of radiation exposure to sensitive structures like CNS, optic chiasma and pituitary gland. Additionally, in radiation treatment of paranasal sinus carcinoma shielding is adopted to minimize radiation exposure to the eyes.

Although radiotherapeutic instruments and techniques have greatly improved in recent years, the temporal bone and the brain stem still cannot be protected from the radiation field. Also radiation treatment strategies have not been adopted to protect the inner ear. Radiation damage can thus occur from the pharyngotympanic tube to the brain stem auditory pathway and therefore may cause hearing loss. Whenever radiation therapy or chemotherapy is given, it is difficult to avoid side effects to the normal surrounding structures including otological structures especially in head and neck cancers. Hearing loss is still given little recognition and little value, and, for this reason, it is not always treated as a health abnormality. However, it is one of the biggest chronic problems among elderly people and patients of cancer after radiotherapy and chemotherapy.

Aim and objectives

To investigate the incidence and severity of sensorineural hearing loss in patients of head and neck cancers receiving radiotherapy and chemotherapy.

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Materials and methods

A total 100 patients were studied in the Department of ENT-HNS, MGIMS, Sewagram from 1st September 2010 to 31st August 2012. This study was approved by the institutional ethics committee. Criteria for inclusion: 1) histopathologically confirmed cases of head and neck malignancies. 2) Patients of head and neck cancers receiving radiotherapy alone and or concurrent chemoradiation. 3) Cases with Karnofsky's score ≥80%. Criteria for exclusion: 1) Cases having bilateral severe sensorineural hearing loss i.e. with bone conduction more than 60 dB.2) Patients with retrocochlear pathology. 3) Karnofsky's score < 80%.

Of the 100 patients, 66 were treated by definitive RT, whereas 34 received concurrent chemoradiation [RT+CT]. All patients were evaluated before treatment with baseline audiogram. After completion of the full course of RT alone or with concurrent chemoradiation, follow-up audiogram was performed after 1 month, 6 months and 1 year. Audiological evaluation was done using Arphi-700 Mk IV diagnostic- research audiometer calibrated to ANSI-69 specifications. Hearing loss was classified according to WHO as Normal <15dB, Slight: 16-25dB, mild: 26-40dB, Moderate: 41-55dB, mod severe: 56-70dB, severe: 71-90dB, Profound: >91dB. Hearing loss of more than 15 dB either in the speech frequency or in the high frequency or in both before and after therapy was considered significant [3-5]. To rule out retrocochlear pathology, Short Increment Sensitivity Index test was done. Treatment schedule: Site specific treatment planning with a curative dose of 60-70 Gy units in 30-35 fractions with 1.8-2 Gy per day five fractions per week over 6-7 weeks. Concurrent cisplatinum based weekly chemotherapy was administered in a dose of 30-35 mg/m² given over 2-3 hrs of infusion.

Statistical analysis

At the end of 1 month following treatment with radiotherapy alone out of the 66 patients 45.45% developed significant hearing loss. Whereas in RT+CT group 67.64% of the 34 patients had significant hearing loss. The hearing loss was persistent. Statistical analysis was done using Z-test and it was found that there was significant difference in proportions of hearing loss due to RT and RT+CT ($p<0.05$) after 1 month but no significant difference in proportions of hearing loss due to RT and RT+CT ($p>0.05$) after 6 months and 12 months.

Results

Of all the patients of Head and Neck malignancies attending the Department of Otorhinolaryngology and Head Neck Surgery; 100 cases who met the inclusion criteria were selected. Out of the 100 patients 66 (66 %) received radiotherapy alone and 34 (34 %) received concurrent chemoradiation with M:F of 2:1 in RT group and 1.8:1 in RT+CT group. Sociodemographic profile is given below in the Table 1 and Figure 1.

Among the100 cases of Head and Neck malignancies, oral lesions contributed the largest group [38%] followed by laryngeal [21%] and hypopharyngeal cancers [12%]. Next in order were oropharyngeal, nasopharyngeal, nose and PNS tumors. Smallest group was of occult primary with secondaries in neck with 2% of cases. Details are given in Table 2.

At the end of 1 month following treatment with radiotherapy alone out of the 66 patients 45.45% developed significant SNHL. 51.51% of patients in RT group developed SNHL after 6 & 12 months. A detail of significant hearing loss in various malignancies is shown in Table 3. It was also noticed as shown in Figure 2 that higher frequencies were more affected than lower frequencies. However some patients had hearing loss in both speech and high frequencies. The hearing loss was persistent. The percentage of hearing loss was maximum in patients treated for nasopharyngeal malignancy. A paired sample t-test was conducted to compare the hearing losses before and 6 months after therapy. It was found that hearing loss before and 6 months after RT were statistically significant ($p<0.05$). Also it is seen that as the radiation field descends down from nasopharynx, effect on otological structures decreases, which is evident from the percentages of significant hearing loss with descending sites.

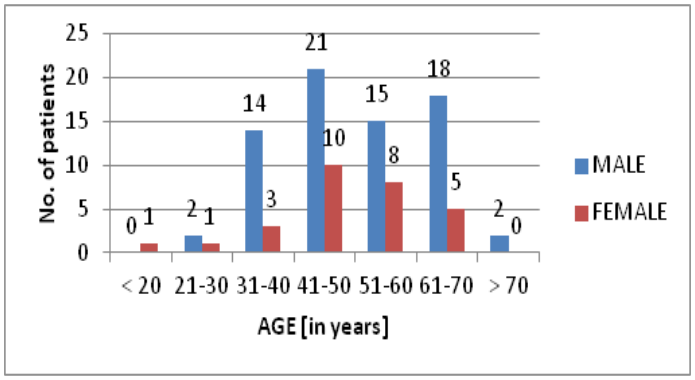

Figure 1 Distribution of patients according to their age and sex.

Table 1 Distribution of patients

Sr.no.	Case distribution	RT	RT + CT
1.	N	66	34
2.	M:F	2:1	1.8:1
3.	Age range and Mean in years	21-79 [52 years]	18-70 [50 years]

Whereas in RT+CT group out of the 34 patients 67.64% had significant hearing loss after 1 month and 70.58% after 6 & 12 months. Higher frequencies were more affected than lower frequencies as shown in Figure 2. A detail of significant hearing loss in various malignancies is shown in table no.4. However some patients had significant hearing loss in both speech and high frequencies. The hearing loss was persistent. Hearing losses in the second group who received concurrent RT+CT were more as compared to those who received RT alone. Statistical analysis was done using Z-test and it was found that there was significant difference in proportions of hearing loss due to RT and RT+CT ($p<0.05$) after 1 month but no significant difference in proportions of hearing loss due to RT and RT+CT ($p>0.05$) after 6 months and 12 months . The distribution of significant hearing losses after RT and RT+CT after 1, 6 and 12 months is shown in Figure 3.

Discussion

Largest group of cases [n= 66; 66%] received radiotherapy alone, ranged in the age from a minimum of 21 years to a maximum of 79 years. While number of cases [n=34; 34%] who received concurrent chemoradiation ranged from a minimum of 18 years to a maximum of 70 years. As expected and as per concept, malignant disease process in Head and Neck is generally noted beyond 40 years of age

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and the same has been found to be true in approximately 78% of our patients. Male female ratio of 2:1 is seen in RT group whereas 1.8:1 in RT+CT group. A high male predominance has also been seen by Sankaranarayanan et al.[6] Maximum numbers of studies have been done on malignancy nasopharynx and parotid because otological structures are mainly involved in field of radiation of malignancies of these sites. We have also included laryngeal and hypopharyngeal malignancies to see for effects if any, on otological structures with descending sites involvement in Head and Neck malignancies. Today, only one thirds of affected patients present with early disease stage. Most of the oral cavity/pharynx patients present with locally advanced disease hence, combination of chemotherapy and radiation therapy is used in patients with inoperable or unresectable [stage III and IV] disease in an attempt to increase the cure rates over radiation alone. Hence, such cases who received concomitant chemoradiation were also included in the study to see for any synergistic effects if any.

Table 2 Site wise distribution of cases

Sr. No.	SITE	N (%)	RT Cases				RT + CT Cases			
			Total	Right	Left	Midline	Total	Right	Left	Midline
1	Nasopharynx	9	7	3	1	3	2	-	-	2
2	Nose & PNS	7	5	2	3	-	2	-	2	-
3	Oral cavity	38	30	13	14	3	8	5	2	1
4	Oropharynx	11	-	-	-	-	11	1	7	3
5	Larynx	21	17	5	6	6	4	-	2	2
6	Hypopharynx	12	7	2	3	2	5	3	-	2
7	Occult primary with secondaries in neck.	2	-	-	-	-	2	2	-	-
TOTAL (%)		100	66	25	27	14	34	11	13	10

Table 3 Audiological changes after RT

Sr.no.	Site	No. (n=66)	1 Months		6 Months		12 Months	
			speech freq (Sf)	High freq (Hf)	speech freq (Sf)	High freq (Hf)	speech freq (Sf)	High freq (Hf)
1	Nasopharynx	7	4 (57.14%)	7 (100%)	6(85.71%)	7 (100%)	7 (100%)	7 (100%)
2	Nose & PNS	5	4 (80%)	5 (100%)	4 (80%)	5 (100%)	4 (80%)	5 (100%)
3	Oral cavity	30	-	15(50%)	-	17(56.6%)	-	17(56.6%)
4	Oropharynx	-	-	-	-	-	-	-
5	Larynx	17	-	1(58.8%)	-	7(41.17%)	-	3(17.64%)
6	Hypopharynx	7	-	2(28.5%)	1(14.28%)	2(28.5%)	1(14.28%)	2(28.5%)
7	Occult primary with secondaries in neck	-	-	-			-	-
Total		66	8 (12.12%)	30 (45.45%)	11 (16.66%)	34 (51.51%)	12 (18.18%)	34 (51.51%)
Total number of patients having significant hearing loss (Sf+Hf)			30(45.45%)		34 (51.51%)		34 (51.51%)	

Table 4 Audiological changes after RT+CT

Sr.no.	Site	No. (n=66)	1 Months		6 Months		12 Months	
			speech freq (Sf)	High freq (Hf)	speech freq (Sf)	High freq (Hf)	speech freq (Sf)	High freq (Hf)
1	Nasopharynx	2	2(100%)	1(50%)	2(100%)	1(50%)	2(100%)	1(50%)
2	Nose & PNS	2	1(50%)	2(100%)	1(50%)	2(100%)	1(50%)	2(100%)
3	Oral cavity	8	-	6(75%)	-	6(75%)	-	6(75%)
4	Oropharynx	11	-	8(72.7%)	1 (9.09%)	8(72.7%)	1 (9.09%)	8(72.7%)
5	Larynx	4	-	-	-	1(25%)	-	1(25%)

Table Continued

Sr.no.	Site	No. (n=66)	1 Months		6 Months		12 Months	
			speech freq (Sf)	High freq (Hf)	speech freq (Sf)	High freq (Hf)	speech freq (Sf)	High freq (Hf)
6	Hypopharynx	5	-	3(60%)	-	3(60%)	-	3(60%)
7	Occult primary with secondaries in neck	2	-	2 (100%)	-	2 (100%)	1(50%)	2 (100%)
Total		34	3 (88.23%)	22(64.70%)	4(11.76%)	23(67.64%)	5(14.70%)	23(67.64%)
Total number of patients having significant hearing loss (Sf+Hf)			23 (67.64%)		24 (70.58%)		24 (70.58%)	

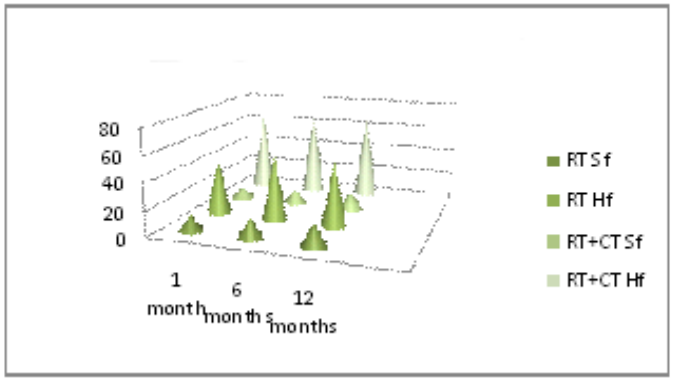

Figure 2 Audiological changes.

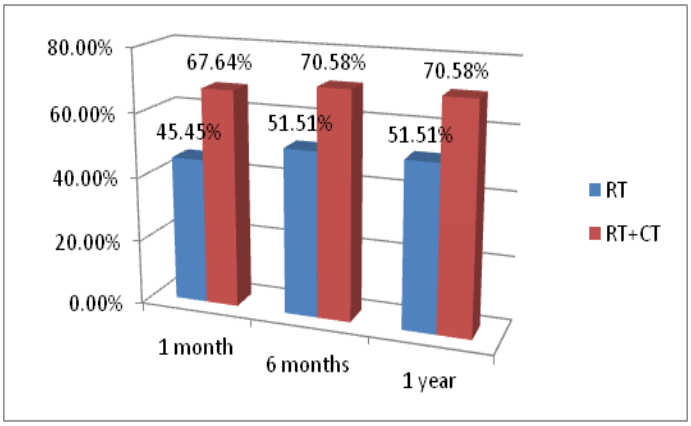

Figure 3 significant hearing losses after RT and RT+CT.

In our study we found that out of the 66 cases after 1 month, significant hearing loss were seen in 8 [12.12%] cases in speech frequencies [500 Hz, 1 kHz and 2 kHz] whereas 30[45.45%] cases showed significant changes in higher frequencies. The observation that higher frequency hearing was generally more affected than lower frequency hearing is consistent with findings from other studies.[7-10] Although the mechanism of SNHL has not been entirely elucidated, there is evidence of hair cell loss on Organ of Corti.[11] Both the incidence and severity increased with time, especially at high frequencies which was also reported in other studies.[4,12] Lau et al.,[13] in their study reported that persistent impairment of auditory brain stem evoked response was detected immediately after completion of radiotherapy. The waves I-III and I-V interpeak latency intervals were significantly prolonged one year after radiotherapy.[13] The reported incidence of post RT sensorineural hearing loss in our study is 45.45% at 1 months and increased to 51.51% after 6 and 12 months. The significant variation in SNHL after RT in different studies may be attributed to factors including the study design, patient selection, total dose, fraction, size, length of follow up and variation in evaluation and interpretation.[14]

The onset of hearing deterioration may begin as early as 3 months after completion of radiotherapy.[15] Some reported that patients developed SNHL either immediately or upto 48 months after RT [mean 4 months] which usually progressed to severe SNHL and plateaued within 2 years of treatment.[3,16,17]

Significantly higher incidence of sensorineural hearing loss was for the development of post irradiation cochlear damage and appeared to be at least 12 month.[16] Deterioration of median hearing thresholds, occurred in the immediate post-treatment period.[18] In the present study we observed that hearing loss can be noticed by 1 month following treatment.

In the second group where patients were treated with concurrent chemoradiation the incidence of significant hearing loss was 67.64% after 1 month and increased to 70.58% after 6 and 12 months. In the present study it was found that patients who received concomitant chemoradiation experienced greater sensorineural hearing loss compared with patients treated with radiotherapy alone and the results are statistically significant. Similar results were reported by Low WK, Bhandare & Schell et al.[8,14,18] In a prospective study on 32 patients with NPC who were treated with concurrent chemoradiation the incidence of sensorineural hearing loss was found to be similar to the incidence of patients treated with radiotherapy alone.[11] Two other studies on patients with NPC treated with chemoradiotherapy also showed that CDDP did not have an additional adverse effect on sensorineural hearing.[3,19]

Walker et al.,[20] suggested that postirradiation hyperemia could be the cause of increased sensitivity of cochlear to CDDP damage. Mencher et al.,[21] proposed that due to radiation providing a predisposition to damage, synergistic ototoxic effect results whereas Miettinen et al.,[22] proposed that radiation caused changes in permeability of the inner ear leading to enhanced effect of CDDP in inner tissues. In our present study, CDDP was administered during [concomitant

chemotherapy] radiotherapy, and we found that enhanced ototoxicity occurred. Liberman reported higher prevalence of hearing loss after radiochemotherapy owing to the patients being more susceptible to hearing loss or having weaker health or more aggressive cancer, which might influence the results.[23]

Conclusion

1. As the radiation field descends down from nasopharynx effect on otological structures decreases.
2. Both the incidence and severity of hearing loss increases with time especially at high frequencies.
3. Hearing loss can be evident after 1month of therapy and is persistent.
4. Patients who received concomitant chemoradiation experienced greater sensorineural hearing loss compared with patients treated with radiotherapy alone.
5. Hearing losses are predominately of sensorineural type and mild.
6. Concern for the quality of life of patients undergoing cancer treatment is necessarily growing, and determination of hearing loss should be a part of investigations to enable better rehabilitation.

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None.

Conflict of interest

The author declares there is no conflict of interest.

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