

## Radiotherapy-enhanced ototoxicity in elderly

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## Abstract

**Introduction:** Most head and neck cancers occur in elderly age and there is a natural occurrence of sensorineural hearing loss (SNHL) due to age also. Despite the ages and the physiological changes inherent to ageing, their auditory systems when exposed to aggressive agents caused the hearing loss to be greater as a consequence of the treatment received. **Materials and Methods:** Histopathologically proved 66 head and neck cancer patients were subjected to radiotherapy (RT) and 34 patients were subjected to concomitant chemoradiation (RT + CT) to study the occurrence of SNHL from 1<sup>st</sup> September 2010 to 31<sup>st</sup> August 2012. **Result:** It was found that the percentage of significant SNHL was more in patients >50 years after RT and RT + CT. It was also found that the results were significant. **Conclusion:** The occurrence of SNHL is more in elderly and the concern for the quality of life of patients undergoing cancer treatment is necessarily growing. Hence, the determination of hearing loss should be a part of investigations to enable better rehabilitation in elderly.

**Key words:** Elderly, ototoxicity, radiotherapy

## Introduction

Most head and neck cancers occur in elderly age and there is a natural occurrence of sensorineural hearing loss (SNHL) due to age also. Hearing loss associated with ageing is highly prevalent phenomenon among elderly population. Despite the ages and the physiological changes inherent to ageing, their auditory systems when exposed to aggressive agents caused the hearing loss to be greater as a consequence of the treatment received.<sup>[1]</sup> Hearing loss affects individual's psychosocial situation. Social isolation can be attributed to the cancer or to the functional sequelae of the treatment. This study was performed to evaluate the adverse effects of radiation and concurrent chemoradiation (RT + CT) in elderly.

## Materials and Methods

A total 100 patients were studied in the Department of Ear, Nose, Throat and Head and Neck Surgery, Mahatma Gandhi Institute of Medical Sciences, Sevagram from 1<sup>st</sup> September 2010 to 31<sup>st</sup> 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 (RT) alone and or concurrent RT + CT. 3) Cases with Karnofsky's score  $\geq 80\%$ . Criteria for exclusion: 1) Cases having bilateral severe SNHL, that is, with bone conduction more than 60 dB, 2) Patients with retrocochlear pathology, and 3) Karnofsky score  $< 80\%$ .

Of the 100 patients, 66 were treated by definitive RT; whereas, 34 received concurrent RT + CT. All patients were evaluated before treatment with baseline audiogram. After completion of the full course of RT alone or with concurrent RT + CT, 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 World Health Organization (WHO) as normal  $< 15$  dB, slight: 16-25 dB, mild: 26-40 dB, moderate: 41-55 dB, mod severe: 56-70 dB, severe: 71-90 dB, and profound:  $> 91$  dB. 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.<sup>[2-4]</sup> 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 cisplatin-based weekly chemotherapy was administered in a dose of 30-35 mg/m<sup>2</sup> given over 2-3 h of infusion.

## Statistical analysis

To see for significant difference in hearing loss in patients  $< 50$  years and  $> 50$  years after treatment, *t*-test was applied; where  $P < 0.05$  indicated significant difference, whereas,  $P > 0.05$  indicated no significant difference in proportions. The limitation of the study is small numbers.

## Results

Out of the total 100 cases selected 72 were males and 28 were females. Out of the 100 patients, 66 cases (132 ears) received RT alone and 34 cases (68 ears) received concurrent RT + CT. The male:female ratio was 2:1 and 1.8:1 in patients who received RT alone and those who received concurrent RT + CT, respectively. Out of the 66 patients who received RT alone, 40 patients were aged  $> 50$  years. Amongst the 34 patients who received RT + CT, 17 patients were  $> 50$  years of age.

## Age and hearing loss after RT alone

15.38% of patients below the age of 50 years had significant SNHL after 1 month; whereas, for those above the age of 50 it was 65%. The percentage of SNHL increased from 19.23% in patients below 50 years to 72.5% in patients above 50 years after 6 and 12 months. It was found that the percentage of significant hearing loss in patients  $> 50$  years was more as compared with patients  $< 50$  years and was statistically significant ( $P < 0.05$ ) [Table 1].

## Age and hearing loss after RT + CT

47.05% of patients below the age of 50 years had significant SNHL after 1 month, whereas, for those above the age of 50 it was 88.23%. The hearing loss was persistent after 6 months and 1 year. It was found that the percentage of significant hearing loss in patients  $> 50$  years was more as compared with patients  $< 50$  years and was statistically significant ( $P < 0.05$ ) [Table 2].

A total of 132 ears of the 66 patients in RT group were examined. The mean baseline threshold was 26.94 dB in patients less than 50 years of age; whereas, 22.71 dB in those who were more than 50 years of age. In the RT + CT group, 68 ears of 34 patients were examined where the mean baseline

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**Table 1: Percentages of hearing loss in age group <50 and >50 years after RT**

Duration in months	Hearing loss (%)		P value
	<50 years (n=26)	>50 years (n=40)	
1 month	4 (15.38)	26 (65)	<0.001
6 months	5 (19.23)	29 (72.5)	<0.001
12 months	5 (19.23)	29 (72.5)	<0.001

RT=Radiation therapy

**Table 2: Percentages of hearing loss in age group <50 and >50 years after RT+CT**

Duration in months	Hearing loss (%) (n=17)		P value
	<50 years	>50 years	
1 month	8 (47.05)	15 (88.23)	<0.001
6 months	7 (41.17)	16 (94.11)	<0.001
1 year	7 (41.17)	16 (94.11)	<0.001

RT+CT=Chemoradiation

threshold of patients was 30.5 dB in patients less than 50 years of age and 27.94 dB in those who were more than 50 years of age. The mean increase in threshold in dB was 11.6 dB in patients who received RT alone; whereas, 18.24 dB who received concurrent RT + CT after 1 month of treatment. The mean increase in threshold in dB after concurrent RT + CT was found to be more than after RT alone.

## Discussion

The cytotoxic effects of radiation therapy are mediated primarily through increased formation of hydroxyl radicals and reactive oxygen species, which can damage cells, proteins, and DNA. In the inner ear causes for SNHL after radiation are vascular insufficiency, reduced number of capillaries, degeneration of endotheliocytes in vessels, loss of cells in the organ of Corti, atrophy and degeneration of the stria vascularis, and atrophy of the spiral ganglion cells and the cochlear nerve.<sup>[5,6]</sup> Ageing is associated with physiological changes and comorbid illnesses, which may affect an individual's tolerance to radiation. Older patients are at greater risk, as preexisting degenerative changes make them more vulnerable to radiation injury. Kwong *et al.*, reported that older patients were more prone to develop SNHL.<sup>[2]</sup> Bhandare *et al.*, also found a significant correlation between high patient age and increased risk of developing hearing impairment.<sup>[7]</sup> Herrmann *et al.*, found that age and prior disease significantly decreased the hearing ability.<sup>[8]</sup> In our study, we have excluded patients with bilateral

severe SNHL and retrocochlear pathology and an increase in the hearing threshold of more than 15 dB from the baseline after treatment was considered significant. We found an increase in the percentage of hearing loss in patients >50 years of age as compared to that observed in patients <50 years of age. Walker *et al.*, suggested that postirradiation hyperemia could be the cause of increased sensitivity of cochlear to Cisplatin damage.<sup>[9]</sup> Kwong *et al.*, performed a multivariate analyses to identify the predicting factors for persistent SNHL and confirmed that age, sex, and postirradiation Serous otitis media as significant prognostic factors for persistent SNHL.<sup>[2]</sup> In our present study, CDDP was administered during (concomitant chemotherapy) RT, which was consistent with the belief that enhanced ototoxicity would occur.

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