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Changes in the hearing threshold using high frequency audiometry in medical personnel exposed to ionizing radiation

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ABSTRACT

Background: Effect on sensorineural hearing loss by low dose ionizing radiation exposure in radiation workers has been rarely evaluated. A case control study was done among the radiation associated workers and normal subjects.
Methods: The study was done among medical personnels exposed to low dose of ionizing radiation. Age and sex matched healthy control group of subjects were selected. Groups were evaluated by normal otoscopic evaluation; normal tuning fork test and normal standard pure tone audiogram at frequencies from 250 to 8000 Hz. They underwent impedance audiometry, transient evoked otoacoustic emissions, and high frequency audiometry (from frequencies 10000 to 20000 Hz).
Results: No statistically significant difference was found in the results of impedance audiometry, transient evoked otoacoustic emissions and standard pure tone audiogram from 250 to 8000 Hz between cases and controls. In high frequency range, statistically significant difference was obtained only at 12500Hz (p=0.001) and 16000 Hz (p=0.001). Mean thresholds were higher at all frequencies in cases compared to controls, except at 4000 Hz. A statistically significant correlation was found between duration of exposure and thresholds at 500 Hz (p=0.014) and 10000 Hz (p=0.048). Tinnitus, vertigo, ear block, hard of hearing and loss of appetite were seen more in cases, but was not significant.
Conclusions: Even though using standard pure tone audiometry or high frequency audiometry there was no statistically significant variation in frequencies between cases and controls except at 12500 and 16000 Hz, the mean thresholds were more at almost all frequencies in cases than in controls. Hence a pre placement and periodic high frequency audiometric evaluation in medical personnels with radiation exposure is indicated in future.

Keywords: High frequency audiometry, Ionising radiation, Sensorineural hearing loss, Ototoxicity

INTRODUCTION

Although hearing loss associated to radiation has been researched by many investigators, they all dealt with the hearing loss associated with high dose radiation therapy for head and neck especially in nasopharyngeal malignancies which is of the range 60-70 Gy. Most of these studies have proven that there is significant association between sensorineural hearing loss and high dose radiation.[1,2] Such hearing loss was found to be affecting the higher frequencies earliest which was similar to the effects of noise exposure and ototoxicity.[3-5] Common mechanisms like apoptotic pathways, p53 gene, reactive oxygen species etc. have been implicated in these injuries.[6-8] Such mechanisms have also been associated with ageing and autoimmune hearing loss which may be ascribed to the primary affliction of cochlea rather than the retrocochlear pathways by irradiation. [9,10]

The detrimental effects of radiation can be somatic or hereditary. Hereditary effects are due to damage to germ cells. Somatic effects can be early or late. Early effects are usually due to acute exposure of large doses over short period of time. All early effects show a threshold dose below which these do not occur. These are referred to as 'deterministic' effects. Those who recover from early effects may develop late effects. Similarly, exposure to low level radiation over long period of time can also produce late effects. It increases proportionately with dose without any threshold values. These are called 'stochastic' meaning of a random or statistical nature. Low dose radiation induced sensorineural hearing loss (SNHL) will belong to this category.[11]

Daily and monthly radiation exposures of radio diagnostic workers are monitored by the Indian Atomic Energy Research Board (AERB) according to ICRP recommendations. The annual dose limit should not exceed 50 milliSieverts (mSv) according to ICRP and 30 mSv according to AERB. At the end of five consecutive years, the average yearly exposure should be below 20 mSv. For the public, this limit is below 1 mSv per year. Pregnant workers limit is 2 mSv after declaration of pregnancy till term. [11] The literature regarding low dose ionising radiation and hearing loss is scant. Hence, this study was aimed to evaluate changes in hearing threshold in high frequency in medical personnel exposed to low dose radiation by high frequency pure tone audiometry and to compare it with a control group from general population. The result may help to prevent development of full blown SNHL in speech frequencies in those having occupational exposure to low dose radiation over long periods of time.

METHODS

Study design

A case control study was designed among 60 healthy radiology related medical personnel (17-40 years of age) with low dose radiation exposure (maximum of up to 30 mSv/year) from various departments in Amala Institute of Medical Sciences, Thrissur, Kerala during the period between June, 2014 to June, 2015. Controls were 54 age and sex matched healthy volunteers with no history of ionizing radiation exposure (0 to 3mSv/year). [11.] Since calculating individual radiation exposures were impractical we made an assumption based on the report by the United Nations Scientific Committee on the effects of atomic radiation in 2008 that the estimated global annual average individual effective dose from all sources of radiation is approximately 3.0 mSv in public.[12] Hence the controls were taken to have been exposed to <3 mSv. Subjects in both groups were made sure to have normal otoscopic evaluation and normal pure tone audiogram with standard frequencies between 250 to 8000 Hz.

History of hearing problems, systemic illness like diabetes mellitus, hypertension, kidney diseases, chronic neurologic diseases, using ototoxic agent like aminoglycosides, head injury, hearing loss in their families, pregnancy, neoplasia and psychiatric illness were excluded from the study. Informed consent was obtained from the subject and the study was approved by the institutional ethics committee. Demographic data and details about the duration of exposure, symptoms related to radiation exposure like hearing loss, tinnitus, vertigo, ear block, loss of appetite, fatigue, head ache, their addictions, exposure to ototoxic drugs and certain implicated co-morbidities were collected using questionnaire. Otoscopic evaluation was done to confirm normal tympanic membrane and removal of wax debris was done when indicated.

Audiological tests

Audiological tests were carried out in the standard acoustically controlled rooms. Gardiner-Brown Tuning forks of 256, 512 and 1024 Hz were used for performing tuning fork tests GSI 61 Clinical audiometer (Grason-Stadler Inc.), GSI tympstar and GSI audioscreener plus were used for audiologic evaluation. TDH 50 earphone (Telephonics 296d 200-2) was used for standardised audiometry assessment. HDA 200 (Sennheiser) digital earphone was used for high frequency measurement. B-71 (radio ear) bone vibrator for bone conduction assessment. The audiometer was calibrated by Larson Davis sound level metre or real time analyser, Larson Davis CAL 250 acoustic calibrator, 1/2" preamplifier -7-pin LEMO and ½" microphone –RI-200V. The hearing thresholds at 250, 500, 1000, 2000, 4000, 6000, 8000, 10,000, 12,500, 14000, 16 000 and 20 000 Hz were assessed using the standard ascending/descending modified Hughson-Westlake procedure (after attenuation to inaudibility in 5–10 dB steps, the signal to be increased "until the tone is heard") at octave intervals from 250 to 20 000 Hz and from 500 to 4000 Hz for air conduction and bone conduction, respectively. Tympanometric tests were performed at a probe tone frequency of 226 Hz GSI middle ear analyser. OAE measured using GSI Audio screener version 3.21.

1. Tuning fork tests- Rinne's test, Weber's test, absolute bone conduction test
2. Tympanometry
3. Stapedial reflex
4. TEOAE- at 1000, 2000 and 4000 Hz was conducted
5. Pure tone audiogram

For frequencies from 250 to 8000 Hz standard audiometry was used and for frequencies 10000 to 20000 Hz high frequency audiometry used.

Threshold for hearing loss

For frequencies from 250 to 8000 Hz by standard audiometry more than 15 dB was taken as threshold.[13] From frequencies 10,000 to 16,000 Hz, by high frequency audiometry normative thresholds from studies

were used. 10,000 Hz- 25±10dB; 12,500 Hz- 25±10dB; 14,000 Hz-30±10dB; 16000-50±10 dB; 20000Hz-60±10 dB.[14-16] It was found that the thresholds of 20 000 Hz were at or above the limit levels of the machine in most of the subjects. Seventy decibel was considered the 20 000 Hz thresholds for those subjects.

Normal tympanogram-Type A curve.[13,17] Normal otoacoustic emissions at 1000Hz, 2000Hz and 4000Hz-presence of response.[18]

Normal acoustic reflex- ipsilateral and contralateral reflexes present at 500 Hz to 4000 Hz.[13]

Statistical analysis

Analysis was done using SPSS for Windows version 10.0 computer program. Paired Student's t-test, $\chi 2$-test, Fisher exact test and Mann-Whitney u test were done for the parametric data. Correlation was done using Spearman and Pearson correlation analysis. P<0.05 was considered as significant.

RESULTS

The study group was comprised of 114 subjects of 60 cases and 54 controls. Mean age group of the subjects was 31.04±5.513 years which included 94 males and 20 females. Sixty workers exposed to low-dose ionizing radiation (31.32±5.649 years). There were 11 women and 49 men. In the study group, the working duration of subjects ranged from 3 to 19 years (10.48±5.06 years).

Table 1: Correlation between duration of exposure and thresholds at each frequency.

Frequency (Hz)	Correlation coefficient (r)	P value
250	0.161	0.109
500	0.283	0.014
1000	0.116	0.190
2000	0.109	0.204
4000	-0.063	0.318
8000	-0.147	0.131
10000	0.217	0.048
12500	-0.166	0.102
14000	-0.049	0.354
16000	0.069	0.30
20000	-0.003	0.491

The control group was comprised of 54 healthy subjects including 9 women and 45 men (30.72±5.392 years). There was no statistically significant difference between groups in terms of sex (Chi square p=0.815) and age (Independent sample t test p=0.568). The maximum number of subjects were in the age group 26 to 30 years. In the study group, the correlation analysis, between the duration of low-dose radiation exposure and hearing loss showed that hearing loss at 500 Hz (r=0.014, p<0.05)and 10 000 Hz (r=0.217, p<0.05) was significantly correlated with the duration of radiation exposure (Table 1 and Figure 1).

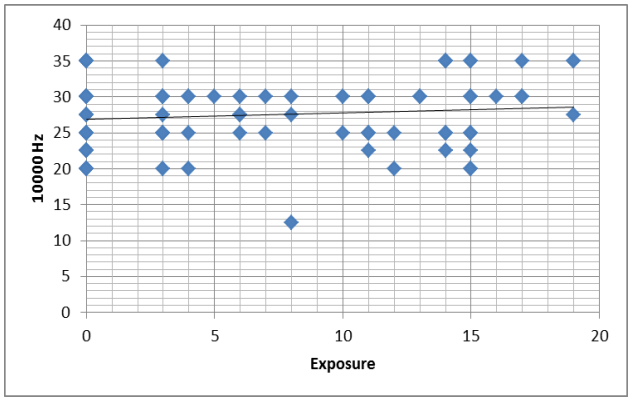

Figure 1: Correlation between duration of exposure and thresholds at 10000 Hz.

Table 2: Mean pure tone hearing thresholds.

Freq (Hz)	Group		P value
	Control (54)	Case (60)	
250	8.65±3.78	8.91±3.45	0.632 (Mann Whitney u test)
500	9.44±3.68	9.54±3.91	0.922 (Mann Whitney u test)
1000	8.38±3.15	8.41±3.56	0.851 (Mann Whitney u test)
2000	10.23±4.07	10.37±4.26	0.826 (Mann Whitney u test)
4000	9.16±3.46	9.04±3.50	0.795 (Mann Whitney u test)
8000	12.50±2.83	12.12±3.11	0.504 (independent sample t test)
10000	27.17±4.55	27.54±4.72	0.676 (independent sample t test)
12500	26.11±4.84	29.00±3.54	0.0001(independent sample t test)
14000	36.29±3.17	37.16±2.74	0.119 (independent sample t test)
16000	53.98±4.02	58.50±4.42	0.0001(independent sample t test)
20000	62.82±4.58	62.91±5.02	0.919 (independent sample t test)

Symptoms like tinnitus, vertigo, hard of hearing, loss of appetite and ear block were studied. No statistically significant difference was found between cases and controls (p>0.05).

We observed that mean pure tone hearing thresholds were markedly increased for all frequencies assessed among cases compared to the control group except at 4000 Hz (Table 2). But significant difference (p<0.005) was obtained only at 12500 Hz (p=0.001) and 16000 Hz (p=0.001). All had air-bone gap of less than 5 dB.

Table 3: Symptoms in cases and controls.

Symptoms	Case (60) N (%)	Control (54) N (%)
Tinnitus	15.0	7.4
Vertigo	15.0	7.4
Hard of hearing	3.3	1.9
Ear block	3.3	3.2
Loss of appetite	3.3	1.9

Symptoms like tinnitus, vertigo, hard of hearing, loss of appetite and ear block were studied. No statistically significant difference was found between cases and controls (p>0.05) (Table 3). With impedance audiometry, static compliance levels ranged from 0.7 to 1.5 cm^3 in the study group and in the control group with an average of 1.026±0.237 in cases and 1.038±0.254 in controls (p=0.791), which is statistically not significant (Table 4).

Table 4: Mean compliance in cases and controls.

Compliance	Group	Number	Mean	Std. Deviation	Independent t test (P value)
	Control	54	1.038	.254	0.791
	Case	60	1.026	.237	

Among the cases, the middle ear pressures on the right and left ears were 21.38±18.34 mmH_2O and 20.80±20.25 mmH_2O, respectively; and in control group they were 17.56±25.879 mmH_2O and 21.26±19.995 mmH_2O. The difference was not significant. Among the cases, tympanograms were as follows: right ear –95% A and 5% Ad; left ear 96.7%−A and 3.3% Ad. In the control group, tympanograms were as follows: right ear −94.4% A and 5.6% Ad; left ear −96.3% A, 3.7% Ad. There was no statistically significant differences between the two groups (p>0.05). There was no statistically significant difference between the study and the control groups with regard to ipsilateral and contralateral acoustic reflexes Transient evoked OAEs at 2000, 3000 and 4000 Hz were done. There was no statistically significant difference between pass and refer among cases and controls. The difference in cigarette smoking and alcoholism between the cases and control groups was not statistically significant.

DISCUSSION

High frequency audiometry was done to evaluate the hearing loss at frequencies above 8000 Hz as early SNHL due to radiation exposure was seen to occur at these frequencies in various studies in literature. Such studies were done in patients with head and neck malignancies who had undergone radiotherapy.[3-5] Studies on high dose radiation exposed head and neck oncology cases also showed that high frequency was the earliest to be affected in them.[4,19] Study by Kwong et al in subjects with radiation therapy for nasopharyngeal carcinoma concluded that transient and persistent SNHL occurred after radiotherapy, more commonly and at the earliest affecting high frequency.[1]

In our study adults above 40 years were avoided as high frequency loss is seen in early age related hearing loss.[10,20] Charlotte et al in their study found only modest hearing loss in mean age group patients who received full-course intensity-modulated RT (range, 56–70 Gy), with a median cochlear dose of 11.4 Gy. But older population showed significant hearing loss.[3] But in another study, there was no relation found between patient age and increased risk of developing hearing impairment after radiation for head and neck malignancies.[4] Younger age group assured reduced risk of other factors like noise exposure.[21-23] Other risk factors that are theorized to cause high frequency hearing loss in literature are diabetes mellitus, hyperlipidemia and coronary artery diseases.[20,24,25]

Since it was a case control study all previous differences between cases and controls were matched that might have led to variations in results like age, sex and external ear and middle ear status. Acoustic reflex is a very sensitive parameter for middle ear pathology. Even when patient has no hearing loss it might be absent if there is slightest abnormality of tympanic membrane or middle ear. Absence lacks specificity especially at 4000 Hz reflex as it may be found absent even in normal population too.[17] In our study there was no significant difference in this parameter between the two groups.

With a normal impedance audiometry including tympanogram, middle ear pressure and normal acoustic reflexes, it was made sure that the subjects had no middle ear pathology. Transient evoked OAE was performed at 2000, 3000, 4000 Hz using 80 decibel intensity sounds. Responses obtained were graded as either pass when response is present to sound given or else as refer. No statistically significant difference was seen in cases and controls in the results of OAE. TEOAEs are very sensitive hence its absence does not necessarily denote pathology. They show status of outer hair cell function at these frequencies. A normal middle ear and cochlear function is a pre-requisite for obtaining the response.[18]

Normal pure tone audiometry at frequencies was obtained at 250 Hz-8000 Hz using standard audiometer. Higher frequencies from 10000 to 20000 Hz were measured using high frequency audiometer. Human cochlea responds to even frequency up to 24 kHz as shown by various studies.[20,26,27] High frequencies of audiometry are

frequencies at or above 8000 Hz i.e., above speech frequencies. High frequency audiometry may be done after incorporating a separate audio-oscillator in the pure tone audiometer and using special head phones.[17] Their use have been implicated in noise induced hearing loss, presbyacusis, ototoxicity and also in diabetes and hyperlipidemia.[10,15,24,28,29]

Normative threshold for high frequency audiometry was obtained from literature. Beiter and Talley found normative thresholds for high frequency by analysing various studies including their own study and reached a mean value for high frequencies.[14,16,30,31] It has been recommended by researchers that the experimental values may be used as an interim standard until such time as official standard values are promulgated.[27] For frequencies 10000 to 20000 Hz normative thresholds by high frequency audiometry from various studies used are as follows 10000 Hz- 25±10 dB; 12500 Hz- 25±10 dB; 14000 Hz- 30±10 dB; 16000-50±10 dB; 20000 Hz- 60±10 dB. It was found that the thresholds of 20000 Hz were at or above the limit levels of the machine in most of the subjects. Seventy decibel was considered the 20000 Hz thresholds for those subjects.

Air bone gap was less than 5 dB in all cases and controls. No statistically significant difference was found between cases and controls in hearing thresholds at speech frequencies from 500 Hz to 2000 Hz and higher frequencies from 4000 Hz to 8000 Hz measured using standard pure tone audiometer. In the high frequency audiometry from frequencies 10000 Hz to 20000 Hz only at 12500 Hz and 16000 Hz there were statistically significant difference between thresholds of cases and controls. This is in contrast to the study results obtained by Karlidag et al observed a statistically significant differences between subjects with low dose ionizing radiation exposure and the control groups in the mean hearing threshold at 4000–8000 Hz and 14000–16000 Hz.[32] But in our study, even though not statistically significant at all frequencies except at 4000 Hz, there was higher thresholds recorded for cases than controls.

There was also no correlation between duration of exposure and thresholds of hearing loss except at 500 Hz and 10000 Hz unlike seen in prior studies.[32] This might be due to the lesser duration of exposure among workers as we had taken only younger age group to avoid changes due to ageing. There have only been very few studies regarding ill effects of low dose ionising radiation exposure in radiation workers and hearing loss in them. Proper pre-placement and periodic monitoring with high frequency audiometry is warranted for such subjects. Even though there was no compelling evidence in our study that there is solid association between hearing loss and low dose ionising radiation, this is not an issue that can be evaded by health authorities.

It is important to note that tinnitus, vertigo, hearing loss, ear block and loss of appetite were all more for workers exposed to low-dose radiation for a long period. A periodical follow-up (at least once a year) is warranted in them not only by standard audiometry but also by high-frequency audiometry. Protective devices like ear plugs or ear muffs can also be advised. If there is evidence of early onset high frequency loss then they can be transferred to another department with lesser exposure. They can be given anti-oxidants as these have been shown to have a protective effect. Antioxidants and other anti-apoptotic medications can be applied topically in the middle ear.[8]

Pre-placement hearing status was not available in this study. But with a prospective design, additional hearing losses might have been detected. There must be criteria to be fulfilled to assess the compliance of using a radiation monitor by all medical personnel. Also the controls must be monitored for at least an year with dosimeters to know their exact annual radiation exposure doses. PTA is quite a subjective test. Moreover high frequency audiometry has high inter and intra individual variations as per various studies.[14,33] So a more objective test has to be used for assessment of high frequency hearing loss. The normative threshold value used in this study for high frequency are from various studies as no definitive high frequency normative thresholds has been yet defined conclusively. A more comprehensive study has to be done to evaluate effects of noise and mobile phone exposure.

CONCLUSION

No significant difference was observed between the high frequency audiometry of radiation workers and normal population, except at 12500 Hz and 16000 Hz. Meanwhile for all but one among the frequencies the mean thresholds of hearing were more for cases than in controls. If a larger group is studied prospectively for longer durations these changes might become significant. Cases were also more symptomatic than controls. All these might necessitate pre placement and periodic evaluation in such workers.

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