Original Research Article

High frequency audiometry to detect sensorineural hearing loss in patients undergoing cisplatin-based chemotherapy

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Abstract

Background: Cisplatin is a cell cycle-nonspecific cytotoxic drug and has a toxic profile that is different from other important cytotoxic drugs. High doses of cisplatin cause nephrotoxicity, gastrointestinal toxicity, neurotoxicity and ototoxicity. In present study, we aimed to study high frequency audiometry to detect sensorineural hearing loss in patients undergoing cisplatin based chemotherapy at a tertiary hospital. **Material and Methods:** Present study was a cross sectional, prospective and observational study conducted in patients, of age group 19–80 years of age, irrespective of the type of cancer, planning to receive platinum-based chemotherapy with or without concurrent Radiotherapy. **Results:** In present study, 30 cancer patients were studied for ototoxicity. Mean age of male patients was 57.62 ± 11.24 years while mean age of female patients was 49.22 ± 9.35 years. majority were male (63.33 %) as compared to female (36.67 %). majority patients had personal history of alcohol consumption (23.33 %), smoking (20 %), history of smoking + alcohol (16.67 %). In present study comorbidities noted were hypertension (43.33 %), diabetes mellitus (23.33 %), ischemic heart disease (13.33 %) and bronchial asthma (6.67 %). In present study, major malignancies noted were Head and neck carcinoma (36.67 %), Lung carcinoma (20.00 %) Stomach carcinoma (13.33 %) and Carcinoma cervix (13.33 %). Incidence of ototoxicity in present study was 26.67 %. Patients with head and neck malignancy (75 %), patients with concurrent radiation (55.56 %) had increased incidence of ototoxicity. In present study, Ototoxicity in conventional frequencies (20 %) and Ototoxicity High frequency audiometry (23.33 %) was noted. **Conclusion:** In present study, a significant percentage (26.67 %) of patients undergoing cisplatin-based chemotherapy had high frequency sensorineural hearing loss noted on high frequency audiometry.

Keywords: High frequency audiometry, sensorineural hearing loss, cisplatin, chemotherapy.

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INTRODUCTION

The platinum compounds cisplatin and carboplatin are essential components in the chemotherapeutic treatment of a variety of life-threatening common cancers including testicular, gynaecologic, bladder, head and neck, and non-small cell lung cancer.[1] The use of platinum drugs has contributed to increases in the long-term survival in patients with cancer. Cisplatin is a cell cycle-nonspecific cytotoxic drug and has a toxic profile that is different from other important cytotoxic drugs. High doses of cisplatin cause nephrotoxicity, gastrointestinal toxicity, neurotoxicity and ototoxicity.[2] Cisplatin accumulation is consistently high in the stria vascularis, the region of the cochlea that maintains the ionic composition of endolymph. Breglio AM *et al.*, demonstrated long-term retention of cisplatin in the human cochlea, and they point to the stria vascularis as an important therapeutic target for

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preventing cisplatin ototoxicity.[3] Cisplatin cytotoxicity is thought to be mediated primarily through DNA crosslinking, as well as reactive oxygen species production following binding to cytoplasmic proteins and biomolecules.[4,5] In present study, we aimed to study high frequency audiometry to detect sensorineural hearing loss in patients undergoing cisplatin based chemotherapy at a tertiary hospital.

MATERIAL AND METHODS

Present study was a cross sectional, prospective and observational study conducted in the Department of ENT in a tertiary teaching hospital in rural area of Konkan region. Study duration was of 1 year. An Institutional ethical committee clearance was obtained before the commencement of the study.

Inclusion Criteria: Patients, of age group 19–80 years of age, irrespective of the type of cancer, planning to receive platinum-based chemotherapy with or without concurrent Radiotherapy who have given consent for participation

Exclusion Criteria: Palliative Chemoradiotherapy. Previous Ear surgery, trauma or disease leading to conductive or sensorineural HL, prior severe to profound sensory-neural hearing loss. Patients with prior history of ear disease, ear surgery, noise exposure, trauma, Patients suffering with chronic diseases such as diabetes/ hypertension. Patients undergoing chemotherapy with other platinum group of drugs. Refusal to give consent, Moribund and frail patients.

Study was explained to patients and a written informed consent was taken for participation. Demographic data, patients history (past/medical) was documented in case record proforma. Patients were evaluated with necessary investigations including complete haemogram, liver and renal function tests to undergo chemotherapy. Fit patients for chemotherapy, were further evaluated by thorough ENT examination, audiological evaluation including conventional frequencies and High frequency audiometry. Serial audiograms were taken at the end of each cycle up to 6 cycles of chemotherapy. Follow-up audiograms are taken at 3 months and 6 months after completion of chemotherapy. All patients were treated for 3 days with three divided doses of cisplatin. Dose was different as for head and neck carcinoma patients (40-60 mg/sqm), for lung, stomach and neuroectodermal carcinoma patients (60 mg/sqm), ovarian, nasopharyngeal carcinoma patients with malignant Brenner tumour (75 mg/sqm), breast and pancreatic carcinoma patients (maximum of 50 mg/sqm), oesophageal and cervical carcinoma patients (40–60 mg/sqm). During study period, 4 patients were defaulters for further treatment and 3 patients died during the course of treatment. Statistical analysis was done using descriptive statistics.

RESULTS

In present study, 30 cancer patients were studied for ototoxicity. Mean age of male patients was 57.62 ± 11.24 years while mean age of female patients was 49.22 ± 9.35 years. majority were male (63.33 %) as compared to female (36.67 %). majority patients had personal history of alcohol consumption (23.33 %), smoking (20 %), history of smoking + alcohol (16.67 %). In present study comorbidities noted were hypertension (43.33 %), diabetes mellitus (23.33 %), ischemic heart disease (13.33 %) and bronchial asthma (6.67 %).

Table 1: Baseline characteristics

Characteristics	No. of patients / Mean ± SD (n=30)	Percentage
Mean age (years)		
Male	57.62 ± 11.24	
Female	49.22 ± 9.35	
Gender		
Male	19	63.33
Female	11	36.67
Personal history		
Alcohol consumption	7	23.33
Smoking	6	20.00
Smoking + Alcohol	5	16.67
No addiction	12	40.00
Comorbidity		0.00
Hypertension	13	43.33
Diabetes mellitus	7	23.33
Ischemic heart disease	4	13.33
Bronchial asthma	2	6.67

In present study, major malignancies noted were Head and neck carcinoma (36.67 %), Lung carcinoma (20.00 %) Stomach carcinoma (13.33 %) and Carcinoma cervix (13.33 %).

Table 2: Incidence of various types of cancer in the study

Types of cancer	No. of patients	%
Head and neck carcinoma	11	36.67
Lung carcinoma	6	20.00
Stomach carcinoma	4	13.33
Carcinoma cervix	4	13.33
Ovarian carcinoma	2	6.67
Oesophageal carcinoma	1	3.33
Carcinoma breast	1	3.33
Pancreatic carcinoma	1	3.33

Incidence of ototoxicity in present study was 26.67 %. Patients with head and neck malignancy (75 %), patients with concurrent radiation (55.56 %) had increased incidence of ototoxicity.

Table 3: Correlation of radiation, ototoxicity and malignancy site

Site of malignancy	Total (n=30)	Patients with concurrent radiation (n=22)	Patients without concurrent radiation (n=8)	Patients who developed ototoxicity (n=8)	Patients developed ototoxicity with concurrent radiation (n=9)
Head and neck	11 (36.67 %)	9 (40.91 %)	2 (25 %)	6 (75%)	5 (55.56 %)
Non head and neck	19 (63.33 %)	13 (59.09 %)	6 (75 %)	2 (25 %)	4 (44.44 %)

In present study, Ototoxicity in conventional frequencies (20 %) and Ototoxicity High frequency audiometry (23.33 %) was noted.

Table 4: Ototoxicity

Characteristics	No. of patients (n=30)	Percentage
Ototoxicity in conventional frequencies	6	20.00
Ototoxicity High frequency audiometry	7	23.33

DISCUSSION

Although there are different degrees of hearing loss, any impediment in conduction of sounds to the auditory nervous system signifies loss of message content, and this may give rise to emotional and social limitations and/or restrictions. Drug-induced hearing loss is generally irreversible and occurs in a dose-related and cumulative fashion. Monitoring audiological evaluations during treatment and the one- and three-month follow-up evaluations include case interview, otoscopy, and immittance audiometry as well as air conduction pure tone and objective testing.[6] In study by Kalyanam B *et al.*,[7] among 59 patients with squamous cell carcinomas of head and neck, who received cisplatin chemotherapy, hearing loss was observed in 12 patients at speech frequencies and those at higher frequencies were 12 (4000 Hz), 18 (6000 Hz), and 28 (8000 Hz). The hearing loss was symmetrical, sensorineural, and showed a strong correlation with the low serum albumin levels at the end of the third cycle. Dizziness was seen in eight patients, at the end of the study. The commonly observed adverse effects were nausea, vomiting, hair loss, fatigue, and tinnitus. Madisetti S.,[8] conducted audiological evaluation among the 72 patients before the commencement of chemotherapy showed that 52 patients had normal hearing with air thresholds ranging from 10 to 20 dB with a mean of 14.45 ± 1.05 dB, bone thresholds ranging from 05 to 10 dB with a mean of 09.45 ± 0.35 dB. The pure tone average was ranging from 15 to 20 dB with a mean of 17.15 ± 1.75 dB. The speech discrimination score was 80 to 85%. The DPOAE values were present and normal in all the patients (100%). Among the 52 patients with normal hearing 13.46% had developed moderate hearing loss and among the 20 patients with pre-existing hearing loss, 04 (20%) patients had developed severe sensorineural hearing loss in this study. Sivasankari L[9] studied 67 patients, who underwent chemotherapy, 37% patients had normal hearing, 10% of the patients developed sensorineural hearing loss after treatment. Among 63% of the patients with prior mild sensorineural hearing loss, 11.8% developed worsening of hearing after completion of treatment. Nalini R *et al.*,[10] studied 25 patients, sequential audiogram was taken before each cycle of cisplatin therapy and post-treatment and it showed that there was a gradual increase in threshold of hearing in speech frequency and high frequency when compared to pre-treatment audiogram in both ear. The audiogram of speech frequency after treatment showed that 52% and 56% of patients had moderate hearing loss in the right and left ear, respectively. In a study of ototoxicity monitoring in children receiving cisplatin chemotherapy, High-frequency audiometry (HFA) usually detected ototoxic changes prior to DPOAEs, although both HFA and DPOAES changed prior to thresholds in the conventional frequency range.[11] However, OAEs may still be useful as a part of an ototoxicity monitoring program, because they do not require a behavioral response and are time efficient Cisplatin may cause permanent cochlear damage by changing cochlear frequency selectivity and can lead to

irreversible sensorineural hearing loss. High-frequency audiometry (HFA) is able to assess hearing frequencies above 8,000 Hz; hence, it has been considered a high-quality method to monitor and diagnose early and asymptomatic signs of ototoxicity in patients receiving cisplatin.[12] Abujamra AL *et al.*,[13] evaluated 42 pediatric patients for hearing loss induced by cisplatin utilizing HFA, and its diagnostic efficacy was compared to that of standard pure-tone audiometry and distortion-product otoacoustic emissions (DPOAEs). The median age at study assessment was 14.5 years (range 4-37 years). Hearing loss was detected in 24 patients (57%) at conventional frequencies. Alterations of DPOAEs were found in 64% of evaluated patients and hearing loss was observed in 36 patients (86%) when high-frequency test was added. The mean cisplatin dose was significantly higher (P = 0.046) for patients with hearing impairment at conventional frequencies. The results suggest that HFA is more effective than pure-tone audiometry and DPOAEs in detecting hearing loss, particularly at higher frequencies. Conventional pure tone audiometry (PTA) remains the mainstay for the identification and categorisation hearing impairment in many ototoxicity grading systems.[14] A PTA may be all the testing that patients undergoing chemotherapy can tolerate, and this may be especially true of the paediatric population.[15] Cisplatin-associated ototoxicity usually manifests as irreversible, progressive, bilateral, high frequency sensorineural hearing loss associated with tinnitus. The degree of hearing loss is often variable and is related to the dose.[16] Comprehensive evaluation of hearing status along with self-reported impact of the cochlear and vestibular handicap should be implemented in a monitoring and surveillance program for appropriate investigation and management.[17] Monitoring the auditory functions can be helpful in detecting hearing loss at an early stage and also adopting other preventive measures such as reducing the dose or substituting cisplatin with carboplatin/oxaliplatin can be done. Therefore, pretreatment and periodic audiograms should be done in patients receiving cisplatin.

CONCLUSION

In present study, a significant percentage (26.67 %) of patients undergoing cisplatin based chemotherapy had high frequency sensorineural hearing loss noted on high frequency audiometry. Early detection of changes in hearing status, audiometric evaluation by high frequency audiometry should be included in treatment regimen of patients undergoing cisplatin-based chemotherapy especially in patients with head/neck malignancy, patients receiving concurrent radiation.

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