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ORIGINAL ARTICLE

Serial Assessment of Cochlear Changes Using Transient Evoked and Distortion Product Otoacoustic Emissions in Children Receiving Platinum-Based Chemotherapy

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Abstract

Background: Advances in platinum-based chemotherapy have improved childhood cancer survival, but ototoxicity remains a major complication, particularly in younger children. This prospective study evaluated serial cochlear changes using TEOAE and DPOAE to objectively detect early, frequency-specific hearing impairment during platinum therapy and compare changes according to platinum agent and age, facilitating timely audiological surveillance and intervention. **Methods:** This prospective longitudinal observational study included 31 children receiving cisplatin- or carboplatin-based chemotherapy. Baseline and serial TEOAE and DPOAE assessments were performed using standardized protocols to detect early cochlear changes. Audiological findings were compared across follow-up visits, treatment groups, and age categories. Data was analyzed using IBM SPSS Statistics version 26.0, with a p-value <0.05 considered statistically significant. **Results:** Among 31 children (67.7% cisplatin, 32.3% carboplatin), serial otoacoustic emission monitoring demonstrated frequency-specific cochlear changes. DPOAE reductions occurred predominantly above 6 kHz in the cisplatin group, whereas TEOAE showed significant intergroup differences at 4 kHz during the first follow-up (30.0% vs. 0%; p=0.036) and at 1 kHz during the second follow-up (28.6% vs. 8.3%; p=0.049). Younger children showed greater cochlear changes, supporting serial TEOAE and DPOAE as useful tools for early detection of platinum-induced ototoxicity. **Conclusion:** The study identified serial, frequency-specific cochlear changes through TEOAE and DPOAE monitoring. High-frequency DPOAE reductions were more evident with cisplatin, supporting regular otoacoustic emission surveillance for early detection of chemotherapy-related ototoxicity, especially in younger children overall.

Keywords: Pediatric Neoplasms, Cisplatin, Carboplatin, Platinum-Based Chemotherapy, Ototoxicity, Transient Evoked Otoacoustic Emissions (TEOAE), Cochlear Dysfunction

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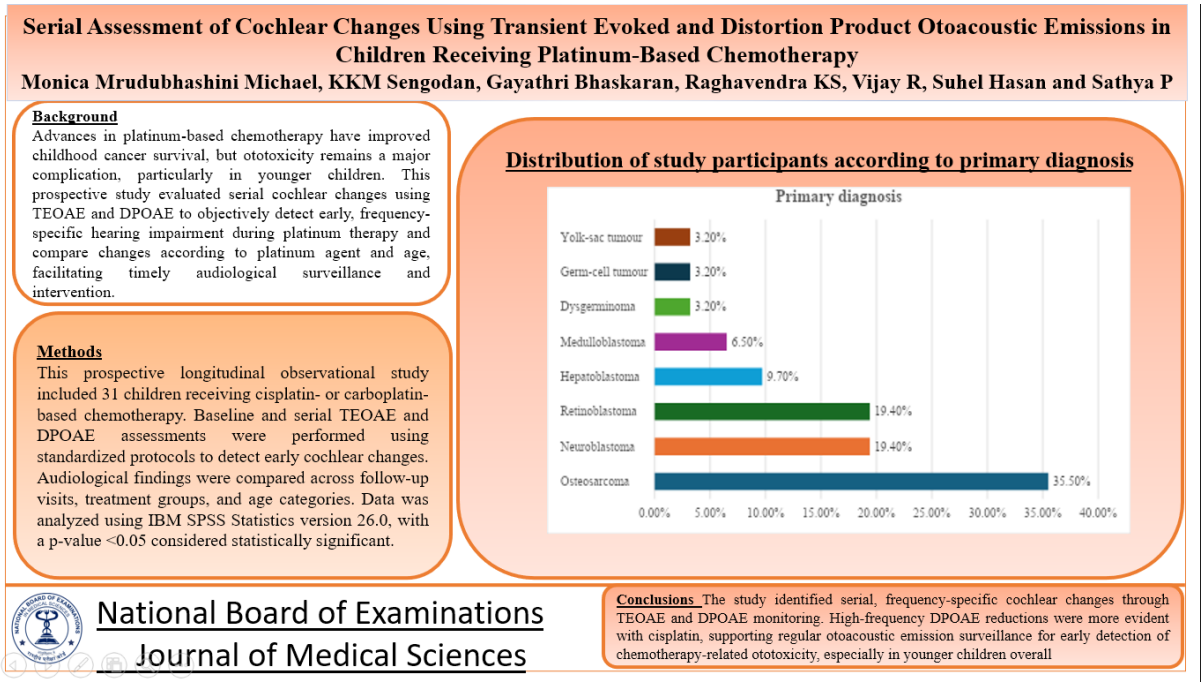
Graphical Abstract



Introduction

Advances in multimodal therapy have substantially improved survival rates in childhood cancer, with platinum-based chemotherapeutic agents, particularly cisplatin and carboplatin, forming an integral component of treatment protocols for a wide range of pediatric malignancies, including solid tumors and central nervous system neoplasms [1-3]. Despite their therapeutic efficacy, platinum compounds are frequently associated with ototoxicity, which represents one of the most clinically significant dose-limiting adverse effects of treatment. Platinum-induced ototoxicity typically manifests as bilateral, progressive, irreversible sensorineural hearing loss that initially affects the higher frequencies before extending to lower frequencies with increasing cumulative exposure [2,4]. In children, hearing impairment has far-reaching consequences because it may adversely affect speech and language acquisition, cognitive development, communication, educational achievement, psychosocial well-being, and overall quality of life [1,5]. Several factors influence the risk of ototoxicity, including cumulative platinum dose, younger age at treatment, renal dysfunction, concurrent administration of other ototoxic medications, cranial irradiation, and individual genetic susceptibility [3,6].

The cochlea is particularly susceptible to platinum-induced injury because platinum compounds generate excessive reactive oxygen species, resulting in oxidative stress, mitochondrial dysfunction, inflammation, and apoptotic death of outer hair cells, especially within the basal turn of the cochlea where high-frequency sounds are encoded [2,6]. Conventional pure-tone audiometry remains the standard clinical method for hearing assessment; however, its usefulness in young children is often limited because reliable behavioral responses are required. Objective audiological techniques, particularly otoacoustic emissions (OAEs), provide a practical alternative by directly

evaluating outer hair cell integrity without requiring active patient participation. Transient evoked otoacoustic emissions (TEOAEs) assess cochlear responses predominantly within conventional speech frequencies, whereas distortion product otoacoustic emissions (DPOAEs) enable assessment across a wider frequency spectrum, including higher frequencies that are affected earliest by platinum-induced cochlear injury. Serial evaluation of otoacoustic emission signal-to-noise ratios may therefore facilitate the early detection and longitudinal monitoring of cochlear dysfunction during chemotherapy, even in children who are unable to perform reliable behavioral hearing tests [5,7].

Although otoacoustic emission testing has become an increasingly valuable component of ototoxicity surveillance, evidence describing serial cochlear changes throughout successive cycles of platinum-based chemotherapy in the pediatric population remains relatively limited. Furthermore, there is insufficient information regarding the frequency-specific pattern of cochlear involvement, the earliest occurrence of significant reductions in otoacoustic emission signal-to-noise ratios, and the persistence of these changes during treatment. Comparative data evaluating differences between children receiving cisplatin and carboplatin, as well as variations across different pediatric age groups, are also scarce. Improved characterization of these longitudinal cochlear changes may facilitate earlier identification of auditory dysfunction and contribute to more effective audiological surveillance and timely rehabilitative interventions in children receiving potentially ototoxic chemotherapy [5,7].

Accordingly, the present study was undertaken to evaluate serial cochlear changes using transient evoked otoacoustic emissions and distortion product otoacoustic emissions in children receiving platinum-based chemotherapy. The primary objective was to assess serial changes in TEOAE and DPOAE signal-to-noise ratios following chemotherapy. The secondary objectives were to determine the frequency-wise onset and persistence of significant reductions in signal-to-noise ratios across successive follow-up visits and to compare these changes according to the platinum agent administered and the age group of the study participants.

Methodology

This prospective observational study was conducted over 11 months, from August 2018 to June 2019, in the Department of ENT–Head and Neck Surgery at a tertiary care centre in South India. The sample size was estimated based on a previous study that reported a reduction in otoacoustic emission amplitude from 8.1 dB at baseline to 0.9 dB after treatment, with corresponding standard deviations of 9.2 dB and 12.9 dB. Assuming a 5% level of significance and 90% power, the minimum required sample size was calculated as 27 participants. After accounting for an anticipated 20% attrition, the estimated sample size was 34, which was rounded to 35. During the study period, 31 eligible children (≤18 years) with malignancies receiving platinum-based chemotherapy were enrolled.

Children with newly diagnosed malignancies scheduled to receive cisplatin- or carboplatin-based chemotherapy were included. Patients with pre-existing hearing impairment, chronic middle-ear disease, congenital profound

sensorineural hearing loss, primary tumors involving the auditory system, metastatic involvement of the auditory pathway, or baseline hearing thresholds exceeding 25 dB HL were excluded.

After obtaining written informed consent from parents or legal guardians, demographic and clinical details were recorded using a structured proforma. All participants underwent baseline otological evaluation before initiation of chemotherapy, followed by serial audiological assessments before each subsequent chemotherapy cycle for a maximum of three follow-up visits, depending on treatment completion and patient availability.

Otoacoustic emissions were assessed in a sound-treated room using the Neuro-Audio Neurosoft system. Transient evoked otoacoustic emissions (TEOAE) were recorded using click stimuli, while distortion product otoacoustic emissions (DPOAE) were obtained using paired primary tones with an F2/F1 frequency ratio of 1.22. DPOAE responses were analyzed across frequencies below and above 6 kHz, whereas TEOAE responses were evaluated at 1, 2, 3, 4, and 5 kHz. The signal-to-noise ratio (SNR) was recorded at each frequency during baseline and follow-up assessments, and serial changes in SNR were used to assess cochlear function throughout chemotherapy. Participants received platinum-based chemotherapy according to standard institutional treatment protocols. Serial TEOAE and DPOAE findings were analyzed according to the platinum agent administered (cisplatin or carboplatin), the available follow-up visits, and the age group of the participants to characterize the frequency-wise pattern, onset, and persistence of cochlear changes during treatment.

Continuous variables were summarized as mean ± standard deviation or median with interquartile range, as appropriate, while categorical variables were expressed as frequencies and percentages. Comparisons between cisplatin and carboplatin groups were performed using the Chi-square test or Fisher's exact test for categorical variables. A two-sided p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS software (IBM SPSS Statistics, version 20.0; IBM Corp., Armonk, NY, USA).

Results

Table 1. Baseline demographic and anthropometric characteristics of the study participants

Characteristic	Category	Value
Age	**Mean ± SD, years**	7.01 ± 6.16
	Median (range), years	3.0 (0.08–18.0)
Age group	**<3 years**	16 (51.6%)
	≥3 years	15 (48.4%)
Gender	**Male**	17 (54.8%)
	Female	14 (45.2%)
Body surface area	**Mean ± SD, m²**	0.80 ± 0.44
	Median (range), years	0.60 (0.50–0.98)

The study included 31 children with a mean age of 7.01 ± 6.16 years and a median age of 3.0 years. Participants were almost evenly distributed between the <3-year and ≥3-year age groups. Males constituted 54.8% of the cohort, while females accounted for 45.2%. The mean body surface area was 0.80 ± 0.44 m², with a median of 0.60 m^2 (Table 1).

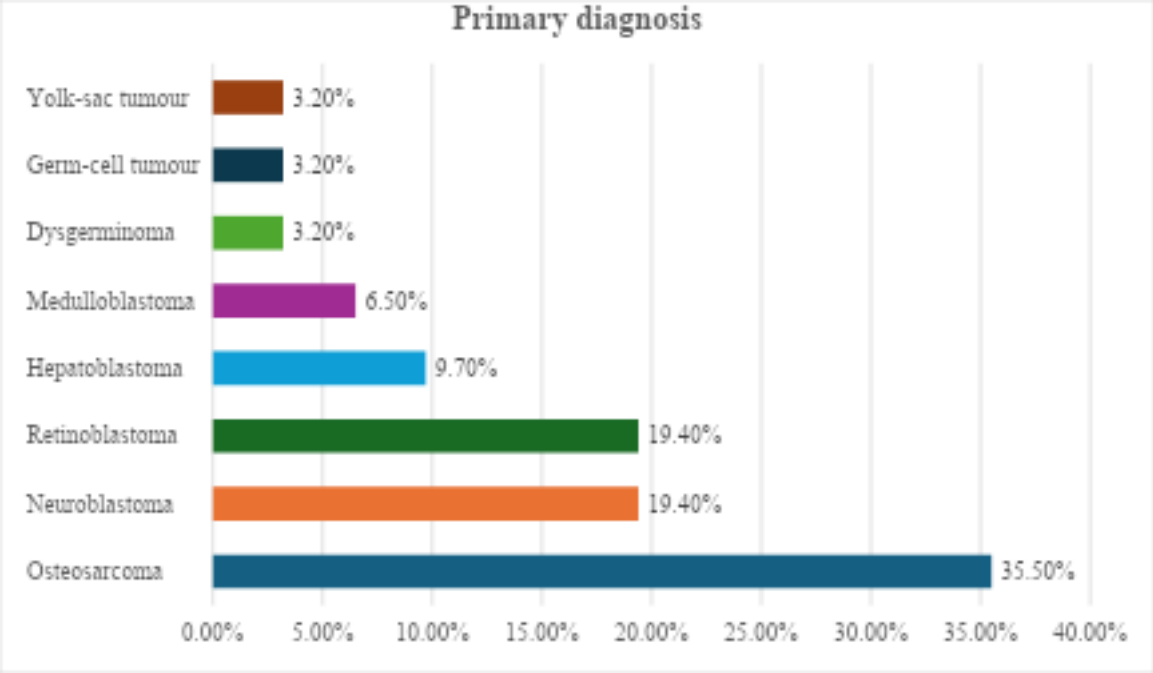


Figure 1. Distribution of study participants according to primary diagnosis

Osteosarcoma was the most common malignancy, affecting 11 children (35.5%). Neuroblastoma and retinoblastoma were each diagnosed in 6 participants (19.4%), followed by hepatoblastoma in 3 (9.7%) and medulloblastoma in 2 (6.5%). Dysgerminoma, germ-cell tumour, and yolk-sac tumour were each observed in one participant (3.2%) (Figure 1).

Table 2. Distribution of platinum-based chemotherapy and concomitant treatment regimens

Characteristic	Category	Value
Platinum compound administered	**Cisplatin**	21 (67.7%)
	Carboplatin	10 (32.3%)
Mean platinum dose	**Cisplatin, mg/m²**	62.11 ± 10.71
	Carboplatin for retinoblastoma, mg/kg/day	28.45 ± 5.59
	Carboplatin for other malignancies, mg/m²	560.10 ± 75.23
Other chemotherapy regimen administered	**DOX and MTX**	7 (22.6%)
	DOX	7 (22.6%)
	VCR and ETO	6 (19.4%)

	ETO, CPM and DOX	3 (9.7%)
	ETO and BLM	2 (6.5%)
	AMI, VCR and CPM	2 (6.5%)
	ETO	2 (6.5%)
	DOX, VBL and BLM	1 (3.2%)
	ETO and CPM	1 (3.2%)

DOX – Doxorubicin; MTX – Methotrexate; VCR – Vincristine; VBL – Vinblastine; ETO – Etoposide; CPM – Cyclophosphamide; BLM – Bleomycin; AMI – Amifostine.

Cisplatin was administered to 21 participants (67.7%), while 10 (32.3%) received carboplatin. The mean cisplatin dose was 62.11 ± 10.71 mg/m². Carboplatin dosing differed by indication, averaging 28.45 ± 5.59 mg/kg/day for retinoblastoma and 560.10 ± 75.23 mg/m² for other malignancies. Doxorubicin with methotrexate and doxorubicin alone were the most common additional regimens, each used in 7 participants (22.6%), followed by vincristine with etoposide in 6 (19.4%) (Table 2).

Table 3. Follow-up distribution of participants according to platinum compound

Follow-up assessment	**Total participants (N=31)**	**Cisplatin (n=21)**	**Carboplatin (n=10)**
At least one follow-up	26 (83.9%)	16 (76.2%)	10 (100.0%)
At least two follow-ups	19 (61.3%)	12 (57.1%)	7 (70.0%)
Three follow-ups completed	10 (32.3%)	6 (28.6%)	4 (40.0%)
No follow-up available	5 (16.1%)	5 (23.8%)	0 (0.0%)

Among the 31 participants, 26 (83.9%) completed at least one follow-up, 19 (61.3%) completed at least two follow-ups, and 10 (32.3%) completed all three follow-ups. Follow-up completion was consistently higher among carboplatin recipients than cisplatin recipients. All participants receiving carboplatin underwent at least one follow-up, whereas 5 cisplatin-treated participants (23.8%) had no follow-up data available (Table 3).

Table 4. Serial changes in distortion product otoacoustic emission (DPOAE) signal-to-noise ratio (SNR) according to platinum compound

DPOAE frequency range		SNR finding	Cisplatin	Carboplatin	p-value#
At least one follow-up (16 vs 10)	<6 kHz	Significant reduction	1 (6.3%)	0 (0.0%)	0.723
		No significant reduction	12 (75.0%)	8 (80.0%)	
		Invalid response	3 (18.8%)	2 (20.0%)	
	>6 kHz	Significant reduction	2 (12.5%)	0 (0.0%)	0.549
		No significant reduction	6 (37.5%)	6 (60.0%)	
		Invalid response	8 (50.0%)	4 (40.0%)	
At least two follow-ups (12 vs 7)	<6 kHz	Significant reduction	0 (0.0%)	0 (0.0%)	0.563
		No significant reduction	10 (83.3%)	5 (71.4%)	
		Invalid response	2 (16.7%)	2 (28.6%)	
	>6 kHz	Significant reduction	2 (16.7%)	0 (0.0%)	0.423
		No significant reduction	3 (25.0%)	3 (42.9%)	
		Invalid response	7 (58.3%)	4 (57.1%)	
Three follow-ups completed (6 vs 4)	<6 kHz	Significant reduction	0 (0.0%)	0 (0.0%)	0.389
		No significant reduction	5 (83.3%)	4 (100.0%)	
		Invalid response	1 (16.7%)	0 (0.0%)	
	>6 kHz	Significant reduction	1 (16.7%)	0 (0.0%)	0.170
		No significant reduction	1 (16.7%)	3 (75.0%)	
		Invalid response	4 (66.7%)	1 (25.0%)	

Chi-square test

Significant DPOAE SNR reductions were observed predominantly at frequencies above 6 kHz among cisplatin recipients, occurring in 12.5%, 16.7%, and 16.7% of participants across the one-, two-, and three-follow-up cohorts, respectively. No significant reductions were recorded among carboplatin recipients. Invalid responses were more frequent above 6 kHz, particularly in the cisplatin group. However, DPOAE findings did not differ significantly between cisplatin and carboplatin recipients at any follow-up level or frequency range (all $p>0.05$) (Table 4).

Table 5. Serial changes in transient evoked otoacoustic emission (TEOAE) signal-to-noise ratio (SNR) according to platinum compound

DPOAE frequency range		SNR finding	Cisplatin	Carboplatin	p-value[#]
At least one follow-up (16 vs 10)	1 kHz	Significant reduction	4 (25.0%)	1 (10.0%)	0.223
		No significant reduction	9 (56.3%)	4 (40.0%)	
		Invalid response	3 (18.8%)	5 (50.0%)	
	2 kHz	Significant reduction	3 (18.8%)	2 (20.0%)	0.241
		No significant reduction	12 (75.0%)	5 (50.0%)	
		Invalid response	1 (6.3%)	3 (30.0%)	
	3 kHz	Significant reduction	1 (6.3%)	0 (0.0%)	0.711
		No significant reduction	11 (68.8%)	7 (70.0%)	
		Invalid response	4 (25.0%)	3 (30.0%)	
	4 kHz	Significant reduction	0 (0.0%)	3 (30.0%)	0.036*
		No significant reduction	5 (31.3%)	4 (40.0%)	
		Invalid response	11 (68.8%)	3 (30.0%)	
	5 kHz	Significant reduction	0 (0.0%)	0 (0.0%)	0.063
		No significant reduction	0 (0.0%)	1 (10.0%)	
		Invalid response	16 (100.0%)	9 (90.0%)	
At least two follow-ups (12 vs 7)	1 kHz	Significant reduction	1 (8.3%)	2 (28.6%)	0.049*
		No significant reduction	11 (91.7%)	3 (42.8%)	
		Invalid response	0 (0.0%)	2 (28.6%)	
	2 kHz	Significant reduction	3 (25.0%)	3 (42.8%)	0.598
		No significant reduction	8 (66.7%)	3 (42.8%)	
		Invalid response	1 (8.3%)	1 (14.3%)	
	3 kHz	Significant reduction	2 (16.7%)	1 (14.3%)	0.977
		No significant reduction	8 (66.7%)	5 (71.4%)	
		Invalid response	2 (16.7%)	1 (14.3%)	
	4 kHz	Significant reduction	2 (16.7%)	3 (42.8%)	0.087
		No significant reduction	2 (16.7%)	3 (42.8%)	
		Invalid response	8 (66.7%)	1 (14.3%)	

	5 kHz	**Significant reduction**	0 (0.0%)	0 (0.0%)	0.147
		No significant reduction	0 (0.0%)	2 (28.6%)	
		Invalid response	12 (100.0%)	5 (71.4%)	
Three follow-ups completed (6 vs 4)	**1 kHz**	**Significant reduction**	1 (16.7%)	3 (75.0%)	0.091
		No significant reduction	4 (66.7%)	0 (0.0%)	
		Invalid response	1 (16.7%)	1 (25.0%)	
	2 kHz	**Significant reduction**	2 (33.3%)	3 (75.0%)	0.232
		No significant reduction	3 (50.0%)	0 (0.0%)	
		Invalid response	1 (16.7%)	1 (25.0%)	
	3 kHz	**Significant reduction**	2 (33.3%)	2 (50.0%)	0.659
		No significant reduction	3 (50.0%)	2 (50.0%)	
		Invalid response	1 (16.7%)	0 (0.0%)	
	4 kHz	**Significant reduction**	1 (16.7%)	2 (50.0%)	0.108
		No significant reduction	1 (16.7%)	2 (50.0%)	
		Invalid response	4 (66.7%)	0 (0.0%)	
	5 kHz	**Significant reduction**	0 (0.0%)	1 (25.0%)	0.434
		No significant reduction	0 (0.0%)	0 (0.0%)	
		Invalid response	6 (100.0%)	3 (75.0%)	

Chi-square test; * Statistically significant

TEOAE SNR reductions varied across frequencies and follow-up cohorts. At the first follow-up, carboplatin recipients showed significantly more reductions at 4 kHz than cisplatin recipients (30.0% vs 0.0%; p=0.036). Among those completing at least two follow-ups, significant differences were observed at 1 kHz, with reductions in 28.6% of carboplatin recipients versus 8.3% of cisplatin recipients (p=0.049). No significant between-group differences were observed among participants completing all three follow-ups. Invalid responses were frequent at 4 and 5 kHz (Table 5).

Table 6. Association of age group with significant TEOAE and DPOAE signal-to-noise ratio reductions among cisplatin recipients

Follow-up cohort	Age group	TEOAE SR, n/N (%)	p-value#	DPOAE <6 kHz SR, n/N (%)	p-value#	DPOAE >6 kHz SR, n/N (%)	p-value#
One follow-up	<3 years	1/16 (6.3)	0.300	1/16 (6.3)	0.149	2/16 (12.5)	0.106
	>3 years	0/16 (0.0)		0/16 (0.0)		0/16 (0.0)	
Two follow-ups	<3 years	2/12 (16.7)	0.102	1/12 (8.3)	0.121	2/12 (16.7)	0.788
	>3 years	1/12 (8.3)		0/12 (0.0)		0/12 (0.0)	
Three follow-ups	<3 years	1/6 (16.7)	0.269	0/6 (0.0)	0.121	1/6 (16.7)	0.472
	>3 years	0/6 (0.0)		0/6 (0.0)		0/6 (0.0)	

SR – Significant Reduction; # Chi-square test

Across all follow-up cohorts, significant TEOAE and DPOAE SNR reductions were observed predominantly among children aged <3 years. However, no statistically significant association was found between age group and significant reduction in TEOAE, DPOAE below 6 kHz, or DPOAE above 6 kHz at any follow-up level (all p>0.05). The highest proportion of reduction was observed for DPOAE above 6 kHz among children aged <3 years in the one- and two-follow-up cohorts (Table 6).

Table 7. Association of age group with significant TEOAE and DPOAE signal-to-noise ratio reductions among carboplatin recipients

Follow-up cohort	Age group	TEOAE SR, n/N (%)	p-value#	DPOAE <6 kHz SR, n/N (%)	p-value#	DPOAE >6 kHz SR, n/N (%)	p-value#
One follow-up	<3 years	0/10 (0.0)	0.257	0/10 (0.0)	0.301	0/10 (0.0)	1.000
	>3 years	0/10 (0.0)		0/10 (0.0)		0/10 (0.0)	
	<3 years	0/7 (0.0)	0.301	0/7 (0.0)	0.439	0/7 (0.0)	0.273

Two follow-ups	**>3 years**	0/7 (0.0)		0/7 (0.0)		0/7 (0.0)	
Three follow-ups	**<3 years**	1/4 (25.0)	0.513	0/4 (0.0)	0.441	0/4 (0.0)	0.046*
	>3 years	0/4 (0.0)		0/4 (0.0)		0/4 (0.0)	

SR – Significant Reduction; # Chi-square test; * Statistically significant

No significant TEOAE or DPOAE SNR reductions were observed in either age group among participants completing one or two follow-ups. Among those completing three follow-ups, TEOAE reduction occurred in one child aged <3 years, while no DPOAE reductions were recorded. Although the reported comparison for DPOAE above 6 kHz was statistically significant (p=0.046), this finding should be interpreted cautiously because no significant reduction occurred in either age group (Table 7).

Discussion

Early identification of platinum-induced ototoxicity is essential in children because hearing impairment may be irreversible and adversely affect speech, language, learning, and quality of life. Objective monitoring is particularly important in younger children who may not reliably perform conventional audiometry. Therefore, this prospective longitudinal observational study evaluated serial cochlear changes in 31 children receiving cisplatin- or carboplatin-based chemotherapy using Transient Evoked Otoacoustic Emissions (TEOAE) and Distortion Product Otoacoustic Emissions (DPOAE).

Baseline testing was performed before chemotherapy, followed by serial assessments during subsequent treatment visits. Signal-to-noise ratios were recorded at predefined frequencies to identify early and frequency-specific cochlear dysfunction. Demographic, clinical, diagnostic, and treatment-related details were documented using a structured proforma. Children with pre-existing hearing impairment or conditions affecting otoacoustic emission testing were excluded. Findings were compared over time, between cisplatin and carboplatin groups, and across age categories to assess treatment- and age-related differences in ototoxicity.

Clinical feasibility of OAE monitoring

In the present study of 31 children receiving platinum-based chemotherapy, serial TEOAE and DPOAE monitoring was successfully performed without sedation, overcoming the limitations of behavioural pure-tone audiometry in young children. At least one follow-up was completed by 83.9% (26/31), two follow-ups by 61.3% (19/31), and all three by 32.3% (10/31). Hecker et al. (2026) [8] similarly reported reliable behavioural PTA in only 39.2% (60/153), whereas DPOAE testing was completed in 100% (153/153). Brooks et al. (2018) [5], Knight et al. (2007) [9], and Diepstraten et al. (2024) [10] also supported OAEs as objective, rapid, ear-specific, well-tolerated, and suitable for children unable to cooperate with PTA. No

contradictory evidence was identified, supporting OAE monitoring as a practical, reliable, and sedation-free surveillance method.

Cisplatin-related DPOAE reductions

Significant DPOAE signal-to-noise ratio reductions above 6 kHz were observed among cisplatin recipients in 12.5% (2/16) at the first follow-up and 16.7% at both the second (2/12) and third (1/6) follow-ups. Knight et al. (2007) [9] reported bilateral DPOAE amplitude and dynamic-range reductions in 81.3% (26/32) of platinum-treated children. Hecker et al. (2026) [8] demonstrated significant reductions between 10 and 16 kHz ($p=0.01$), most pronounced after the second cycle ($p\leq0.02$). Lopes et al. (2020) [11] described early basal outer hair cell injury with reductions above 4 kHz, while Fetoni et al. (2016) [12] found a significant relationship with cumulative cisplatin dose ($p<0.05$) and hearing loss in 25% (6/24). Diepstraten et al. (2024) [10] reported that each 100 mg/m² increase in cisplatin dose increased the risk of Muenster grade ≥2b hearing loss by OR 1.6 (95% CI 1.4–2.0; $p<0.001$). These findings support high-frequency DPOAE monitoring as a sensitive marker of early cisplatin ototoxicity.

Carboplatin-related DPOAE reductions

No significant DPOAE SNR reductions occurred among carboplatin recipients below or above 6 kHz at any follow-up: 0/10 at the first, 0/7 at the second, and 0/4 at the third assessment, with all p-values >0.05. Hecker et al. (2026) [8] similarly reported a lower risk of sensory hearing loss with carboplatin. Diepstraten et al. (2024) [10] found no significant association with Muenster grade ≥2b hearing loss (OR 0.71, 95% CI 0.38–1.30) or SIOP grade ≥2 hearing loss (OR 1.05, 95% CI 0.57–1.91). Lopes et al. (2020) [11], citing Clemens et al. (2016) [13], reported ototoxicity in 17% of carboplatin-only survivors versus 45% of cisplatin-only survivors. Smits et al. (2006) [14] reported 0% hearing loss and no OAE changes in 25 carboplatin-treated children, while Amorim et al. (2007) [15] observed 100% TEOAE preservation. Fetoni et al. (2016) [12] found no dose–ototoxicity correlation ($p>0.05$), although 19% (9/47) developed hearing loss. Contrastingly, Bhagat et al. (2010) [16] found significant DPOAE reductions at 7996 Hz ($p=0.004$), with 40% (4/10) meeting clinical OAE reduction criteria. Macdonald et al. (1994) [17] reported hearing loss in 50%, while Simon et al. (2002) [18] and Knight et al. (2005) [9] reported hearing impairment in 40% and 38%, respectively, particularly with high-dose carboplatin. Thus, standard-dose carboplatin appears less ototoxic, although high cumulative exposure may affect ultra-high frequencies.

TEOAE reductions

At the first follow-up, carboplatin recipients showed significantly more 4-kHz TEOAE SNR reductions than cisplatin recipients, 30.0% (3/10) versus 0.0% (0/16), respectively ($p=0.036$). The difference persisted without statistical significance at the second follow-up, 42.8% (3/7) versus 16.7% (2/12; $p=0.087$), and third follow-up, 50.0% (2/4) versus 16.7% (1/6; $p=0.108$). Bhagat et al. (2010) [16] reported clinically relevant OAE reductions of more than 6 dB at frequencies ≥4004 Hz in children receiving cumulative carboplatin doses above 1800 mg/m². Brooks et al. (2018) [5] emphasized the clinical importance of monitoring 2 and 4 kHz. However, Hecker et al. (2026) [8]

found no substantial middle-frequency DPOAE changes with carboplatin, while Smits et al. (2006) [14] and Amorim et al. (2007) [15] reported no OAE deterioration and complete TEOAE preservation. The present finding therefore suggests that early subclinical 4-kHz injury may occasionally occur despite carboplatin's generally lower ototoxicity.

At the second follow-up, TEOAE SNR reductions at 1 kHz were significantly more frequent in carboplatin recipients than in cisplatin recipients, 28.6% (2/7) versus 8.3% (1/12), respectively (p=0.049). At the first follow-up, reductions occurred in 25.0% (4/16) of cisplatin and 10.0% (1/10) of carboplatin recipients (p=0.223), while at the third follow-up they occurred in 16.7% (1/6) and 75.0% (3/4), respectively (p=0.091). Brooks et al. (2018) [5] and Lopes et al. (2020) [11] described platinum ototoxicity as predominantly high-frequency, extending to lower speech frequencies only after continued exposure. Fetoni et al. (2016) [12] reported that frequencies between 0.5 and 1 kHz were never affected, while Smits et al. (2006) [14] found no low-frequency deterioration. Therefore, the early 1-kHz reduction observed in the present carboplatin cohort was atypical and differed from the usual basal-to-apical progression of platinum ototoxicity.

Age-related vulnerability

OAE reductions were observed more frequently among cisplatin-treated children aged below 3 years. At the first follow-up, DPOAE reductions above 6 kHz occurred in 12.5% (2/16) of children aged below 3 years compared with 0.0% among those aged 3 years or older (p=0.106). However, no statistically significant age association was demonstrated at any follow-up or frequency range. Diepstraten et al. (2024) [10] found that younger age significantly increased hearing-loss risk under both Muenster criteria (OR 0.9 per year, 95% CI 0.9–1.0; p=0.049) and SIOP criteria (OR 0.9 per year, 95% CI 0.8–1.0; p<0.001). Knight et al. (2007) [9] reported bilateral hearing loss in 76.9% (10/13) of children aged 5 years or younger. Hecker et al. (2026) [8] and Lopes et al. (2020) [11] also identified children below 5 years as particularly susceptible because of immature auditory and antioxidant systems. Conversely, Fetoni et al. (2016) [12] found no significant age association (p>0.05), possibly owing to reduced doses, avoidance of cranial radiotherapy, or preferential carboplatin use in infants. The present trend therefore remains clinically relevant despite limited statistical power.

Progression and persistence across chemotherapy cycles

Cisplatin-related cochlear changes showed a progressive and persistent pattern. DPOAE reductions above 6 kHz increased from 12.5% (2/16) at the first follow-up to 16.7% at the second (2/12) and third (1/6) follow-ups. TEOAE reductions at 2 kHz increased from 18.8% (3/16) to 25.0% (3/12) and 33.3% (2/6), respectively. Fetoni et al. (2016) [12] reported progressive threshold deterioration even after chemotherapy completion in 8.6% of patients. Knight et al. (2007) [9] also demonstrated progressive reductions in OAE amplitudes and hearing thresholds across treatment courses. Diepstraten et al. (2024) [10] identified cumulative cisplatin dose as the strongest predictor, with each 100 mg/m² increase raising the risk of Muenster grade ≥2b hearing loss by OR 1.6 (95% CI 1.4–2.0; p<0.001). Lopes et al. (2020) [11] and Brooks et al. (2018) [5]

similarly described progression from higher to lower frequencies with increasing cumulative exposure. Overall, serial TEOAE and DPOAE monitoring demonstrated the cumulative, progressive, and frequency-spreading nature of platinum-induced cochlear injury.

Limitations

The relatively small sample size and invalid responses might limit the generalisability of this study, requiring more studies to corroborate similar findings in different settings.

Conclusion

The study demonstrated serial, frequency-specific cochlear changes in children receiving platinum-based chemotherapy using TEOAE and DPOAE. DPOAE reductions were predominantly observed above 6 kHz among cisplatin recipients, indicating early high-frequency cochlear involvement, while TEOAE changes varied across treatment groups, frequencies, and follow-up periods. Although younger children receiving cisplatin showed more frequent reductions, age was not significantly associated with otoacoustic emission changes. Differences between cisplatin and carboplatin were limited, and invalid high-frequency responses affected interpretation. These findings support serial otoacoustic emission monitoring for early detection of chemotherapy-related ototoxicity, particularly among younger children and those receiving cisplatin.

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Statements and Declarations

Conflict of interest

The authors declare that they do not have conflict of interest.

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