Transient Evoked and Distortion-Product Otoacoustic Emissions in Normal Ear of Patients with Sudden Unilateral Sensory Neural Hearing Loss

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ABSTRACT

Background: Outer hair cells are specialized sensory cells of the mammalian cochlea that contribute to cochlear amplification. Otoacoustic emissions have great potential to detect cochlear impairment, especially in nonlinear mechanical functions of the outer hair cells (OHCs).

Objective: To assess the hearing in normal ear by determining cochlear function, as evaluated by TEOAE and DBOAE in patient with unilateral sensory hearing loss with sudden onset.

Patients and Methods: This case control study included **study** group, which included patients with history of SSNHL with normal ear and **control** group that included similar number of matched subjects included in the same period with bilateral normal hearing. Every participant was subjected to full audiological history taking, otoscopic examination, pure tone audiometer, immittancemetry and otoacoustic emissions.

Results: There was a statistically significant difference among the two groups concerning TEOAE of the left ear frequency in Freq 1.0 NF, Freq 1.0 TE NF, Freq 1.5 NF, Freq 2.0 NF, and Freq 2.0 TE NF, among DBOAE of the right ear in F 1641 DP NF, F2 2016 NF, F 2484 DP NF, F2 3000 NF, F 3281 DP NF, F 4922 DP NF, F 6516 DP NF, F1 609 DP, and F 609 DP NF and among DBOAE of the left ear, F1 4922 DP, F 4922 DP NF, F2 2016 NF, F 1641 DP NF, F2 1500 NF, and F2 750 NF.

Conclusion: The study supported the use of otoacoustic emissions as a noninvasive and sensitive tool for assessing cochlear health, particularly in cases of sudden hearing loss.

Keywords: Outer Hair Cells, Sudden Sensorineural Hearing Loss, Immittancemetry, Transient-Evoked Otoacoustic Emissions, Distortion Product Otoacoustic Emissions.

INTRODUCTION

Outer hair cells (OHCs) are specialized sensory cells of the mammalian cochlea that contribute to cochlear amplification. They respond to receptor potentials evoked by sound induced transduction currents with length changes of their cell body ^[1]. OHCs generate active cochlear mechanical processes, which can be monitored by distortion product otoacoustic emission (DPOAE) **[2]** .

Investigations using otoacoustic emissions (OAEs) have great potential to detect cochlear impairment, especially in nonlinear mechanical functions of the OHCs. The clinical utility of OAEs has been described as a noninvasive objective test to predict audiometric status **[3]**. OAE can be classified into several categories according to the type of stimulation used to evoke them. On this basis, four distinct but interrelated classes can be distinguished including spontaneous, transiently evoked, stimulus-frequency, and DPOAE **[4]** .

Transiently evoked emissions grow linearly with stimulus levels below about 10 dB SPL but exhibit a strong saturating nonlinearity at higher stimulus levels such that they rarely evidence growth above stimulus levels of 20–30 dB SPL. To evoke DPOAEs, two stimulus tones of moderate level (55–75 dB SPL), separated in frequency, are presented to the ear **[5]** . In humans, the most pronounced DPOAE is found at the cubic difference frequency $fDP = 2f1-f2$ and is assumed to be comprised mainly of two components generated by different mechanisms at different sites along the basilar membrane **[6]** .

Sudden sensorineural hearing loss (SSNHL) is defined as hearing loss of at least 30 dB in three sequential frequencies in the standard pure-tone audiogram over 3 days or less **[7]**. Estimate of incidence ranges from 5 to 20 per 100.000 individuals, and bilateral involvement is very rare, it increases in the older patients (>65 year) (77 per 100.000) then in younger population (<18 year) (11 per 100.000) **[8]** .

The causes of SSNHL are speculative and probably multifactorial, but various etiological theories have been proposed. Viral infection, vascular impairment, autoimmune disorders, trauma, inner ear anomaly, and central nervous system (CNS) disease have all been implicated, but in many patients no obvious cause is found (idiopathic) **[9]** .

The aim of this study was to assess the hearing in normal ear by determining cochlear function, as evaluated by transient evoked and distortion-product otoacoustic emission (DPOAE) in patient with unilateral sensory hearing loss with sudden onset.

SUBJECTS AND METHODS

The present study was a case control study performed in ORL Department, Audiology Unit. This study included all patients visited the Audiology Unit in Mansoura University Hospital during 1 year period from January 2022 to January 2023.

The included subjects were divided into **study** group and **control** group, which included similar number of matched subjects included in the same period with bilateral normal hearing sensitivity at frequencies (250-500-1000-2000-4000-8000khz) according to puretone audiometry (PTA). This study included patients aged between 15 to 40 years with severe to profound SSNHL according to the criteria defined in "Clinical Practice Guideline: Sudden Hearing Loss, and normal ear according to PTA and immittance measures **[10] ,** and with normal MRI and other studies. But we excluded patients who had medical or neurological problems that were known to affect the auditory system, with family history of hearing impairment, with history of ototoxic drug intake, with previous history of noise exposure, with history of anomalies or middle ear diseases, with history of otological complaints or previous ear operation and with otoscopic evidence of ear-drum abnormalities.

METHODS

Every participant was subjected to full audiological history taking and otoscopic examination. The equipment used were sound treated room (locally made), pure tone audiometer (Madsen-Itera II, Denmark), immittancemetry (interacoustics-AT235, Denmark) and otoacoustic emissions (Biologic Scout OAE, Natus hearing diagnostic version 4. 0 USA).

Immittancemetry included tympanometry that was done at varying pressures ranging from +200 to 400 mm $H₂O$ to evaluate the middle ear pressure and acoustic reflex threshold measurements that were elicited ipsilaterally at 1000 and 2000 Hz and contralaterally using pure tones of 500, 1000, 2000, and 4000 Hz. Basic audiological evaluations included pure tone audiometry where air conduction threshold was done in the frequency range (250-8000 Hz) and bone conduction threshold in the frequency range (500-4000 Hz), and speech audiometry included speech recognition threshold (SRT) using Arabic spondee words and speech discrimination score: using Arabic phonetically balanced words. Otoacoustic emissions (OAEs) included *transient-evoked otoacoustic emissions* (TEOAEs) induced by clicks (80 dB pe SPL) at 1, 1. 5, 2, 3 and 4 kHz in a 20-ms window; and TEOAEs were considered present if response signal to noise ratio was 6 dB with reproducibility > 70% at least in three frequencies with overall SNR 6 dB SPL and overall reproducibility > 70%, and *distortion product otoacoustic emissions* (DPOAEs) in the form of a DP-Gram over f2 750, 984, 1500, 2016, 3000, 3984, 6000 and 7969 Hz. DPOAE responses were recorded in f2 but are equal to 2f1-f2. DPOAEs were considered present if SNR 6 dB at least in four frequencies.

Ethical approval:

The Ethics Committee of the Faculty of Medicine at Mansoura University approved the study. Each adult participant or the caregiver of any child who participated in the study, received a full summary of the study's aims prior to signing an informed consent form. The Helsinki Declaration was followed at all stages of the inquiry.

Statistical analysis

The study was performed at 95% level of significance and power of 80%. The collected data were coded, processed and analysed using the SPSS (Statistical Package for Social Sciences) version 26 for Windows® (SPSS Inc, Chicago, IL, USA). Qualitative data were presented as number (frequency) and percent. Comparison between groups was done by Chi-Square test (χ^2) . Quantitative data were presented as mean \pm SD. Mann-Whitney U-test was used to compare between two groups. P value $\langle 0.05 \rangle$ was considered significant.

RESULTS

There was no statistically significant difference detected between the two groups regarding their gender (**Table 1)**.

There were no statistically significant differences among the two groups regarding the left ear affection, except for the left TEOAE. As regards the TEOAE and DBOAE of the affected ear, statistically significant differences were determined among the two groups, except for DBOAE of the left ear (**Tables 1 and 2).**

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Table (2): Comparison between the two studied groups (case and control) according to TEOAE and DBOAE of the affected ear

There were statistically significant differences among the two groups regarding TEOAE in Rt Freq 1.0 NF, Rt Freq 1.0 TE NF, Rt Freq 1.5 TE, Rt Freq 1.5 TE NF, and Rt Freq 2.0 TE NF. A statistically significant difference was recognized among the two groups concerning TEOAE of the left ear frequency in Freq 1.0 NF, Freq 1.0 TE NF, Freq 1.5 NF, Freq 2.0 NF, and Freq 2.0 TE NF. There were statistically significant differences among the two groups regarding DBOAE of the right ear in F 1641 DP NF, F2 2016 NF, F 2484 DP NF, F2 3000 NF, F 3281 DP NF, F 4922 DP NF, F 6516 DP NF, F1 609 DP, and F 609 DP NF.

Also, **Table (3)** points out the DBOAE of the left ear in the current investigation, showing that there were statistically significant differences among the two groups in F1 4922 DP, F 4922 DP NF, F2 2016 NF, F 1641 DP NF, F2 1500 NF, F 797 DP NF, and F2 750 NF.

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Table **(4)** shows that according to TEOAE Rt, there was no significant difference between males and females of the 2 studied groups regarding 1.0 TE, 1.0 NF, 1.0 TE NF, 1.5 TE, 1.5 NF, 1.5 TE NF, 2.0 TE, 2.0 NF, 2.0 TE NF, 3.0 TE, 3.0 NF, 3.0 TE NF, 4.0 TE, 4.0 NF, 4.0 TE NF, 1.2 3.4 TE, 1.2 3.4 NF, and 1.2 3.4 TE NF. According to DBOAE Rt and DBOAE Lt, there was no significant difference regarding males and females between F1 6516 DP, F2 7969 NF, F 6516 DP NF, F1 4922 DP, F2 6000 NF, F 4922 DP NF, F1 3281 DP, F2 3984 NF, F 3281 DP NF, F1 2484 DP, F2 3000 NF, F 2484 DP NF, F1 1641 DP, F2 2016 NF, F 1641 DP NF, F1 1219 DP, F2 1500 NF, F 1219 DP NF, F1 797 DP, F2 984 NF, F 797 DP NF, F1 609 DP, F2 750 NF, and F 609 DP NF.

Table (4): Comparison between the two studied groups (males and females) according to TEOAE Rt, DBOAE Rt and Lt

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Table **(5)** revealed no significant correlation between the duration of affection and TEOAE Rt and TEOAE Lt according to studied frequencies. There were no significant correlations in the duration of affection and DBOAE Rt according to studied frequencies except F1 797 DP, F2 984 NF and F 609 DP NF. Also, there were no significant correlations in the duration of affection and DBOAE Lt according to studied frequencies except F 3281 DP NF, F2 984 NF and F2 750 NF.

DISCUSSION

Sudden sensorineural hearing loss (SSNHL) is characterized by a rapid decline in hearing, typically occurring within 72 hours and defined as a hearing loss of at least 30 dB across three consecutive frequencies on a pure-tone audiogram **[11]**. Investigating cochlear function in the "normal" ear of patients with unilateral SSNHL can provide valuable insights, as the outer hair cells (OHCs) of the cochlea are crucial for sound amplification, and their dysfunction can lead to hearing impairment. Conventional audiometric tests like pure-tone audiometry (PTA) may miss early cochlear dysfunctions, making otoacoustic emissions (OAEs) such as transient evoked OAEs and distortionproduct OAEs important tools **[12]** .

This study aimed to investigate differences in TEOAEs and DPOAEs between case and control groups, considering demographic factors such as gender, age, and duration of auditory affection. Significant differences were observed in specific TEOAE and DPOAE frequencies, as well as in the presence of otoacoustic emissions in the affected ears.

The gender distribution in this study showed a slight male predominance in the cases group, with 55% males and 45% females. The control group, however, had an equal distribution of males and females. The absence of a statistically significant difference in gender distribution between the two groups $(p=0.654)$ suggests that gender does not play a substantial role in the differentiation of the studied condition.

On the other hand, some research has suggested that gender could influence certain auditory outcomes, particularly in otoacoustic emissions. Several studies highlighted that females generally exhibit stronger otoacoustic emissions compared to males **[13,14]** , which could potentially influence diagnostic outcomes.

The comparison between the case and control groups regarding the affected side and the presence of TEOAEs and DPOAEs revealed significant differences. Specifically, over half of the cases group (55%) had a normal left ear, compared to 45% with profound affection. While no significant differences were observed for the right ear, the left TEOAE showed a statistically significant difference (p=0.007). These findings are consistent with the existing literature that indicates a potential side preference in auditory pathologies. For example, a study by **Wasano** *et al.* **[15]** found that auditory conditions often exhibit asymmetry, with one ear being more affected than the other.

The significant difference in TEOAEs between the groups could also be linked to underlying cochlear dysfunctions that are more prevalent in one ear. Studies by **Yağcıoğlu and Öztürk [16]** and **Yıldız [17]** have shown that TEOAEs are highly sensitive to cochlear integrity, with reduced or absent emissions indicating cochlear damage. Our results, particularly

the significant difference in the left TEOAE, align with these findings, suggesting that the cases group may have underlying cochlear dysfunctions that are not as prevalent in the control group.

The analysis of TEOAEs and DBOAEs in the affected ear showed statistically significant differences between the case and control groups, except for DBOAE of the left ear. These findings highlight the sensitivity of otoacoustic emissions as diagnostic tools for detecting cochlear dysfunctions. TEOAEs, which are responses generated by the outer hair cells of the cochlea in response to an auditory stimulus, have been widely used to assess cochlear health. Their significant difference between the groups indicates that the cases group likely has more pronounced cochlear impairments.

Interestingly, the lack of significant difference in the left ear's DBOAE suggests that distortion product otoacoustic emissions may be less sensitive or specific to the type of cochlear damage present in our cases group. This contrasts with some studies, found DPOAEs to be highly reliable in detecting cochlear damage ^[18-20]. However, our findings may indicate that in certain populations or conditions, TEOAEs are more effective at highlighting differences in cochlear function between affected and unaffected individuals. These findings, combined with the significant differences observed in TEOAEs, underscore the importance of using a combination of otoacoustic emissions to gain a comprehensive understanding of cochlear health **[21]** . The observed differences between TEOAEs and DBOAEs in our study may also reflect the varied sensitivity of these tests to different types or stages of cochlear damage.

Statistically significant differences in TEOAEs were observed between the case and control groups at several frequencies for both the right and left ears. These differences suggest that cochlear function, particularly at specific frequency bands, is compromised in the case group. This finding is consistent with earlier studies that have shown that TEOAEs are sensitive indicators of cochlear health and can detect subclinical dysfunction that might not be evident in standard audiometric tests. Several studies have demonstrated the utility of TEOAEs in detecting early cochlear damage, particularly in patients with risk factors for hearing loss ^[22,23].

The significance of the right ear TEOAE frequencies, specifically at 1.0, 1.5, and 2.0 kHz may indicate that these frequencies are more vulnerable to cochlear damage or dysfunction in the case group. This aligns with research suggesting that different regions of the cochlea may be differentially susceptible to damage due to various factors such as noise exposure, ototoxic drugs, or vascular compromise **[24,25]** .

The significant differences in DPOAEs at multiple frequencies in both the right and left ears between the case and control groups, underscoring the potential for subclinical cochlear dysfunction in the case group. DPOAEs are known to reflect the integrity of outer hair cells (OHCs) and their non-linear amplification processes ^[26]. The broad range of frequencies showing significant differences in DPOAEs, including low, mid, and high frequencies, suggests that the case group may have widespread OHC damage or dysfunction. Several studies have reported similar findings, where individuals with hearing loss or at risk of hearing loss showed reduced DPOAE amplitudes across a range of frequencies **[14,27]** .

The study found no significant gender differences in TEOAE and DPOAE measurements across most frequencies, with a few exceptions in the left ear frequencies. This finding is generally in agreement with existing literature, where gender differences in OAEs have been reported but are often small and frequency-specific **[28]**. Several works observed that females tend to have slightly higher OAE amplitudes compared to males, potentially due to hormonal influences on cochlear function **[29]**. However, the lack of significant differences in this study suggests that gender may not be a major factor affecting OAE measurements in the context of the studied condition.

The few significant differences noted in the left ear at specific frequencies could be attributed to anatomical or physiological variations between genders, but these differences were not consistent across all frequencies, which might reduce their clinical relevance. It could also reflect sample size limitations or the need for further exploration into how gender influences specific cochlear frequencies under different pathological conditions.

The absence of significant correlations between the duration of affection and OAE results (both TEOAE and DPOAE) in most frequencies suggests that the duration of the condition might not have a straightforward relationship with the degree of cochlear dysfunction, as measured by OAEs. This is an interesting finding, as one might expect that longer duration would correlate with more pronounced cochlear dysfunction. This finding contrasts with some studies, which suggested that longer exposure to damaging factors (e.g., noise, ototoxic drugs) results in more severe cochlear damage detectable by OAEs [30,31]. The discrepancies could be due to differences in the underlying pathology, where the condition affecting the case group might cause acute damage that stabilizes over time, rather than progressive deterioration.

CONCLUSION

We concluded that the significant differences in TEOAEs, particularly in the left ear, highlight the potential for early detection of cochlear dysfunction in patients with SSNHL. TEOAEs may be more sensitive than DPOAEs in detecting certain types of cochlear

damage, especially in specific frequency bands. The lack of correlation between the duration of auditory affection and OAE results raises interesting questions about the progression of cochlear dysfunction in SSNHL patients, suggesting that further research is needed to explore these relationships.

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