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RESEARCH ARTICLE

COMPARISON BETWEEN PURE TONE AUDIOMETRY AND AUDITORY BRAIN-STEM RESPONSE THRESHOLD IN PATIENTS WITH PRESBYCUSIS IN CO-MORBID WITH ARTERIAL HYPERTENSION AND DIABETES MELLITUS : A PROSPECTIVE STUDY OF 56 PATIENTS AGED ≥50years old.

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ABSTRACT

Background*:* Presbycusis is age-related bilateral sensorineural hearing loss, with course acceleration highly influenced by comorbidities including arterial hypertension (AH) and diabetes mellitus (DM). Two major diagnostic approaches used include pure tone audiometry (PTA) and audiometry brain-stem response (ABR).Comparative studies regarding change in PTA and ABR threshold without age limit and co-morbidities' consideration have been published. However, literature has no reports regarding aforementioned concerns. **Objective:** In this prospective study, we aimed to ascertain and correlated the relationship between PTA and ABR thresholds in patients with presbycusis in co-morbid with arterial hypertension and diabetes mellitus, either alone or combined. ***Methods****:* In this study, 56 patients comprised of 35 females and 21 males, with mean age 64.71± 9.3(50-83) met study criteria. Depending on associated co-morbidities, the cohort was divided into 4groups, thus: group I (presbycusis alone, n=21), group II (presbycusis and DM, n=12), group III (presbycusis and AH, n=14) group IV (presbycusis and DM/AH, n=9) respectively. PTA and ABR thresholds were obtained and analysed. The statistical data analysis was performed using ANOVA-ONEWAY (SPSS-IBM), and p-value (≤0.05) was considered significant. ***Results****:* In this study, ABR and PTA threshold difference between ears was not statistically significant. The comparison between the mean threshold difference of ABR and PTA in group I and II was significant at each frequency, while group III exhibited a significant difference at high frequency only. However, group IV showed no significant difference between ABR and PTA thresholds. We also found that the mean difference in decibel was different in each group. In group I the mean difference decibel was < 20dB at high frequency and >20dB at 0.5 and 1 kHz. Group II showed a mean difference < 20dB at all frequency range. In group III we found mean difference between the two tests <20dB at 4, 8 and 2-4 kHz and >20dB at 0.5, 1, and 2 kHz. Finally in group 4 the mean threshold difference was >20dB at each frequency. ***Conclusion:*** There was a positive relationship between the ABR and PTA threshold, which appear to be insignificant in presbycusis patients with both AH and DM; this finding may be related to synergic effects of the two chronic illnesses on the cochlea.

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INTRODUCTION

Presbycusis is a bilateral sensorineural hearing loss commonly associated with advancing age. It exhibits a chronic course, and co-morbidities such as DM and AH are known to accelerate its course. Etiology is believed to be degenerative changes of cochlea hair cells and auditory nerve fibres, which elicit bilateral internal hearing loss. Studies show that 1 out of 4,1out of 3 and 1 out of 2 after 60, 65 and 70 years of age suffer from presbycusis respectively. It is usually seen after the age of 50, but sometimes earlier and more intensely in some families that have predispositions to presbycusis (Davis *et al*., 2016). Risk factors include diabetes mellitus and high blood pressure (Gates, 2005; Lee, 2013). Some studies have demonstrated that chronic diseases affecting old people such as diabetes mellitus may be related to hearing changes (Maia *et al*., 2005; Uchida *et al*., 2010). There are many implications of presbycusis, such as communication difficulties, psychological disorders and social isolation, which may negatively impact the quality of life of the individual.

In general, pure tone audiometry (PTA) and the auditory brainstem response (ABR) are used in the assessment of auditory sensation in patients with suspected presbycusis. PTA is a subjective test to assess the degree of the hearing loss, measuring peripheral and central auditory hearing loss (Harold, 1993). In this test, a continuous tone stimulus (duration, 0.3 s) of variable frequency is used. PTA explores the patient's ability to hear beeps (white noises) in low to high frequencies via air and bone conduction: the former reflecting the transmission of sound vibration from the ear pinna to the inner ear, the latter, and the electrical perception of sound from the inner ear to the brain. Presbycusis initially affects hearing at higher frequencies; PTA results of the patient with presbycusis shown symmetrical sensorineural hearing loss at high frequency (Khan *et al*., 2012). ABR represents an objective examination, where the goal is to recognize the level of hearing, especially when the subjective test is unpredictable or unreliable (Mccreery *et al*., 2015). The recorded electrical response is generated up to the midbrain. This objective test uses click as types of stimulus sound, Most often the stimuli used in ABR is at 1-2ms in duration and approximately 200-2000ms stimuli is used to produce behavioral responses, with this spectrum containing all the audible frequencies (Boettcher *et al*., 2002). Looking at hearing frequency or intensity, the electrophysiological hearing threshold for clicks is not strictly accurate. There are researches that have looked into PTA hearing level and its association with electrophysiological threshold, and found that subjective threshold is estimate by the objective threshold found on ABR. Some studies have demonstrated that depending on stimulus frequency there is a difference ranging from some decibels at higher frequencies to as low as 15-20 dB at lower frequencies between behavioral threshold and ABR (Gorga *et al*., 2014; Lu *et al*., 2017). Reduction in number of spiral ganglion fibers in older patients can be a reason that explains the age related difference in ABR and behavioral thresholds (Stapells, 2000). Although several studies have tried to identify the relationship between DM, AH with the hearing disorder, these correlations have not yet been clarified (Uchida *et al*., 2010; Marchiori *et al*., 2006). However, some studies have demonstrated that DM or AH can aggravate hearing loss and may cause the abnormality in the ABR (Maia, 2005; Marchiori, 2006). So, how far can DM and AH affect the relation between PTA and the ABR results in presbycusis. Therefore, the aim of this study is to evaluate the relationship between PTA threshold and ABR results in presbycusis patients with DM and AH.

MATERIALS AND METHODS

Subjects: This study was approved by the institutional review board of the second hospital of Shandong University. The study was carried out in the audiology center of the second hospital of Shandong University. This was a prospective hospital-based study of 60 patients with presbycusis conducted by collecting data of individuals who underwent a hearing evaluation test at the audiological center from October2017 to September 2018. A verbal consent was obtained from the patient after explaining to them the nature and the general content of the study. Patients≥50 years old with clinical diagnosis of presbycusis confirmed with bilateral sensorineural hearing loss on diagnostic pure tone audiometry and those who had associated chronic diseases like DM, AH or both were selected for the study. An otological inspection was made and audiological assessment was conducted to exclude patients with middle ear disorders. The patients who had ear surgery or trauma were not included in the study. Questionnaires were administered to the patients and information obtained included the demographic data, symptoms, history of noise exposure, use of alcohol and smoking, use of ototoxic drugs and presence of other chronic diseases like DM and AH. Among the 60 patients selected for the study, only 56 patients with mean age 64.71± 9.3(50-83)who had complete data records were used for analysis. We divided the participants into groups as follows: group I (presbycusis alone, n=21), group II (DM, n=12), group III(AH, n=14) and group IV(DM/AH, n=9)

PTA measurement: The PTA machine used was an AD229E interacoustic diagnostic audiometer (Audiometer: EN 60645-1, ANSI S3.6, Type 2, Calibration: AC: ISO389-1(TDH39), ISO389-2(EARTone5A), BC: ISO 389-3.) with maximum output levels of 120 dB HL in the concerned frequency region. For purposes of comparison to ABR threshold data, only behavioral thresholds for octave frequencies 500–8000 Hz were included in the analysis.

ABR measurement: The Intelligent Hearing Smart EP/Universal Smart Box was used to evaluate ABR. Two recording channels were made using vertex and ipsilateral mastoid electrodes, and a ground electrode was placed on the forehead. The parameters were as follows: Stimulus sound type: click; Transuder: earphone; Stimulus sound duration: 100s; Repetition rate: 19.3/s; Number of sweeps: 1024 times/s; filter settings: 100-3000Hz. Some ABR measurements were initiated with an 80 dBnHL click, others was initiated with a 60 dBnHL depending on the patient's PTA dB response on high frequency. If a well-formed ABR was measured, the intensity was decreased in 20-dB steps until the response was no longer evident.

Data analysis: The statistical data analysis was performed using ANOVA-ONEWAY (SPSS-IBM), and p-value (≤0.05) was considered significant. Numerical variables were conforming to the normal distribution. Since there was no significant difference between ears, the ears were grouped and we used the average threshold of ABR and PTA for analysis. The relationship between the click-evoked ABR thresholds (2-4 kHz frequency) and behavioral PTA thresholds at frequencies of 0.5, 1, 2, 4, 8 and 2-4 KHz was analysed. Mean difference threshold, the standard deviation, the standard error was obtained. Pearson bivariate correlation analysis was used to assess the correlation coefficient between ABR and PTA.

RESULTS

Subject background: In this study, we compared ABR and PTA in people with presbycusis. There were 35 females and 21 males, aged from 50 to 83 years with a mean age of 64.71± 9.3. Among them, some patients presented with other symptoms like tinnitus, dizziness, ear fullness and other aggravating factors (Table 1).

Group I: We first assessed the mean threshold difference between ABR and PTA in group I. We found a mean threshold within 20 dB at high frequencies and mean threshold >20 dB at lower frequencies with a standard deviation >15. A significant statistical mean threshold difference was obtained at each frequency. A strong correlation was present at all range frequencies, with the strongest correlation at 2 kHz (Table 2).
Group II We then evaluated the mean threshold difference in group II, there was a significant mean difference between ABR

Table 1. The general demographic data of 56 patients

Indices	N	Percentage
Age		
50-59	21	37.5
60-69	19	33.9
70	16	28.57
Gender		
Female	35	62.5
Male	21	37.5
Associated Symptoms		
Tinnitus	38	67.9
Ear fullness	19	33.9
Vertigo	22	39.3
Possible risk factors		
Smoke	9	16.1
Alcohol	9	16.1
Diabetes	12	21.4
Hypertension	14	25
Diabetes and hypertension	9	16.1
No diabetes/hypertension	21	37.5

Table 2. Statistical results of the relationship between ABR (2-4 kHz) and PTA threshold (T) (at 0.5 to 8 kHz and 2-4 kHz) in group I

relation ABR-PTA.T	PTA frequency, kHz					
	0.5	1	2	4	8	2-4
Mean difference dB	20.47	21.19	17.38	15.83	15.71	15.65
SD	13.88	13.61	10.79	13.21	13.53	10.58
SE	3.03	2.97	2.37	2.88	2.95	2.31
r	0.679	0.706	0.741	0.576	0.525	0.678
P	0.001	<0.0001	<0.0001	0.006	0.015	0.001

SD, standard deviation of mean difference dB; SE: standard error of mean difference dB; r, correlation coefficient of mean difference dB; P, P-value of the correlation coefficient.

Table 3.Statistical results of the relationship between ABR (2-4 kHz) and PTA threshold (T) (at 0.5 to 8 kHz and 2-4 kHz) in group II

Relation ABR-PTA.T	PTA frequency, kHz					
	0.5	1	2	4	8	2-4
Mean difference dB	17.5	13.95	12.08	12.91	13.12	10.83
SD	14.84	12.12	9.81	11.06	8.33	10.66
SE	4.28	3.50	2.83	3.19	2.40	3.07
r	0.610	0.693	0.759	0.702	0.798	0.742
P	0.035	0.012	0.004	0.011	0.002	0.006

SD, standard deviation of mean difference dB; SE: standard error of mean difference dB; r, correlation coefficient of mean difference dB; P, P-value of the correlation coefficient.

Table 4. Statistical results of the relationship between ABR (2-4 kHz) and PTA threshold (T) (at 0.5 to 8 kHz and 2-4 kHz) in group III

Relation ABR-PTA.T	PTA frequency, kHz					
	0.5	1	2	4	8	2-4
Mean difference dB	28.92	27.50	20.71	9.28	11.60	12.85
SD	19.50	18.10	14.59	6.68	8.52	10.52
SE	5.21	4.83	3.89	1.78	2.27	2.81
r	0.131	0.159	0.210	0.771	0.719	0.595
P	0.655	0.587	0.472	0.001	0.004	0.025

SD, standard deviation of mean difference dB; SE: standard error of mean difference dB; r, correlation coefficient of mean difference dB; P, P-value of the correlation coefficient

Table 5. Statistical results of the relationship between ABR (2-4 kHz) and PTA threshold (T) (at 0.5 to 8 kHz and 2-4 kHz) in group IV

Relation ABR-PTA.T	PTA frequency, kHz					
	0.5	1	2	4	8	2-4
Mean difference dB	31.66	30.27	26.38	23.05	24.16	22.50
SD	17.85	17.29	18.03	19.51	19.96	20.39
SE	5.95	5.76	6.01	6.50	6.65	6.79
r	0.251	0.161	0.183	0.186	-0.012	0.185
p	0.514	0.679	0.638	0.632	0.976	0.634

SD, standard deviation of mean difference dB; SE: standard error of mean difference dB; r, correlation coefficient of mean difference dB; P, P-value of

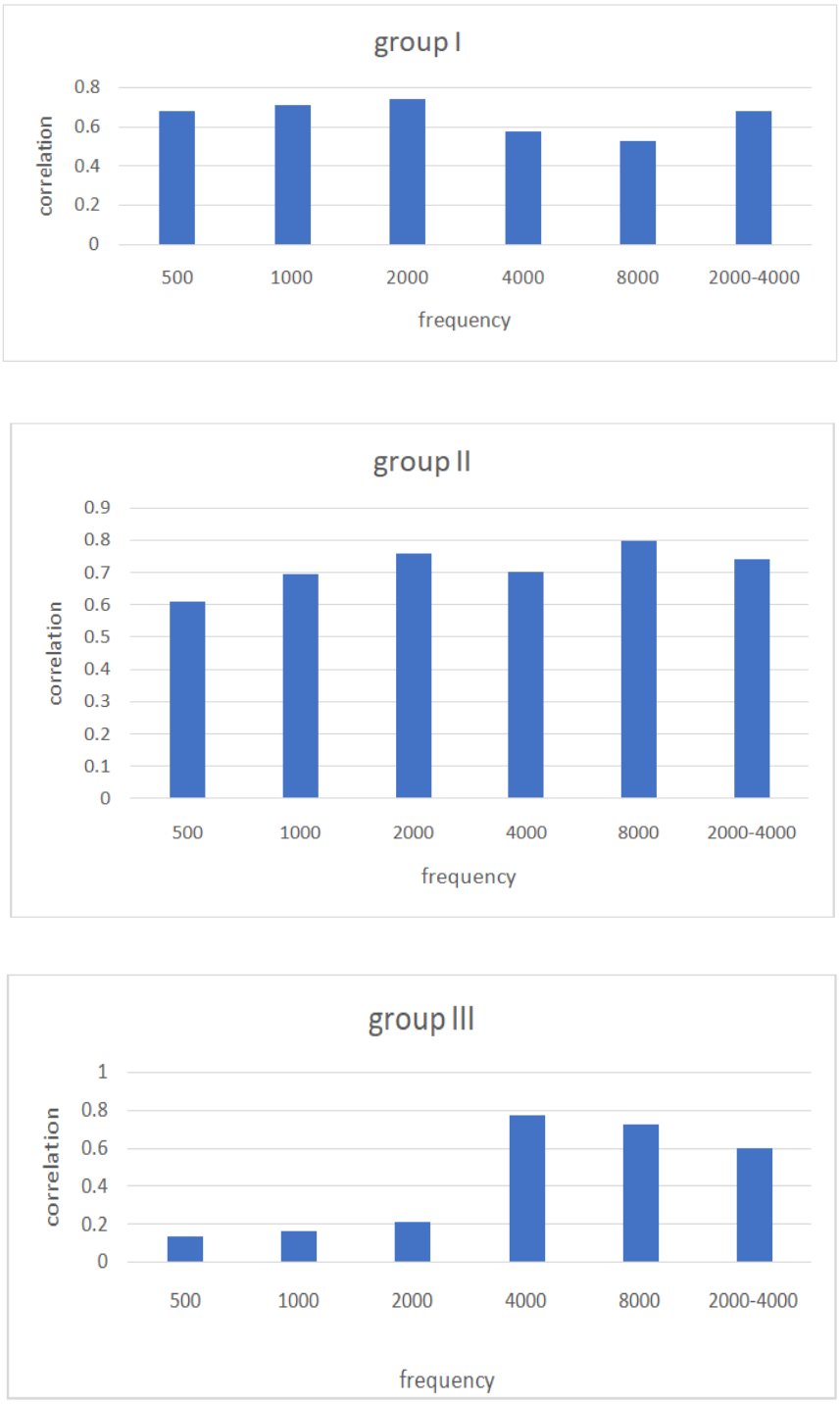

Figure 1. Correlation of threshold difference between auditory brainstem response and pure tone audiometry (a) Group I; (b) group II; and (c) group III

and PTA threshold where we obtained a difference within 20 dB at all frequencies. A positive relationship between ABR and PTA was observed, and their correlation coefficient was strong at all range with the best agreement at 8 kHz and a standard deviation less than 15 at each frequency (Table 3).
Table 3.Statistical results of the relationship between ABR (2-4 kHz) and PTA threshold (T) (at 0.5 to 8 kHz and 2-4 kHz) in group II.

Group III: The comparison made between the two tests in group III shown also a difference of mean threshold within 20 decibels at high frequencies and >20 dB at low frequencies, but in this group, the mean difference at low frequencies is very high compared to the two previous groups.

The standard deviation was also calculated for each frequency. A significant correlation between ABR and PTA in group III was observed only at 4 kHz, 8 kHz and 2-4 kHz (Table 4).

Group IV: Furthermore, we investigated 9 patients diagnosed with presbycusis associated with hypertension and diabetes grouped in group 4. The mean threshold difference in this group was totally different from the expected decibels, at all frequencies the difference was above 20 dB with a standard deviation >16. There was no significant correlation at all in each frequency; the P-value was statistically insignificant for each frequency (Table 5). Figure 1 shows the correlation of threshold difference between ABR and PTA at each frequency in different population groups.

Figure 1a, b shows individuals in group I and group II, respectively, in whom a strong correlation between PTA and ABR results are seen at all frequencies. Figure 1c represents people in group III, where a strong correlation between PTA and ABR results is observed only at high frequencies.

DISCUSSION

Through this prospective study, we made a comparison between the auditory brainstem response (ABR) threshold and pure tone audiometry (PTA) threshold. Many studies have been done on hearing threshold estimation using the auditory brainstem response and demonstrated that depending on stimulus frequency there is a difference ranging from some decibels at higher frequencies to as low as 15-20 dB at lower frequencies between PTA threshold and ABR (Boettcher, 2002; Lu *et al*., 2017). By comparing the mean difference between ABR and PTA threshold of each group, we found significant mean difference threshold in group I where patients are only affected by presbycusis, the mean difference threshold was within the norm of the interval of 20 decibels as mentioned above that the difference between ABR and PTA varies between 15-20 decibels. In group II we obtained almost similar result than group I, the mean threshold difference was<20 decibels at all frequencies. This shows that diabetes did not influence the relationship between ABR and PTA threshold if compare to group I. In group III (presbycusis and hypertension) we obtained different results compare to group I results. In this group, the relationship between ABR and PTA was only significant at high frequency with mean threshold difference within 15 decibels at high frequency and was insignificant at lower frequency with the mean difference threshold >20decibels. This finding may be due to the effect of aging process associated with hypertension effect in the cochlea. It is reported that the degeneration of auditory system may be accelerated by the effect of hypertension which can influence the physiological mechanisms of the inner ear inducing elevated blood viscosity, leading to low capillary blood flow and transportation of oxygen (16). In group IV, where patients have presbycusis with both diabetes and hypertension, the obtained results were worse if compare to those of group I and the II others groups. In group IV the mean difference between ABR and PTA threshold was not significant at each frequency with the mean difference was > 20decibels and did not respect the expected mean threshold difference value (15-20 decibels). This findings show that except of hypertension acting as an accelerating factor which can influence the mean threshold difference of ABR and PTA, at some point diabetes can play a role of aggravating factor and worsen the mean difference between ABR and PTA threshold. As known diabetes can induce auditory neuropathy and angiopathy. Diabetic neuropathy and angiopathy may cause a second degeneration of the eighth cranial nerve, causing neural hearing loss and diabetic angiopathy and resulting in diffuse thickening of the basement membrane and vascular endothelium. This may interfere directly in the supplementation of nutrients and oxygen in the cochlea due to reduced transport induced by thickening of the capillary membrane. This neuropathy can also interfere indirectly by promoting a reduced circulation caused by vascular atrophy thus causing cell and biological tissue death(6,7). Another study conducted in 2005 compared PTA, vocal audiometry and ABR in patients with type 2 diabetes with values for healthy subjects and identified hearing loss with abnormal ABR in patients with diabetes, which worsened with age(17). Rolim LP *et al* demonstrated that older patients with hearing loss associated to both hypertension and diabetes had worsen mean hearing threshold compare to those who had hypertension alone or diabetes alone or none of them(16). We also conclude that presbycusis patient with both diabetes and hypertension can worsen the mean difference between ABR and PTA threshold. Since there was no statistical significance in group IV between ABR and PTA threshold, the correlation coefficient was only calculated in the first three groups to determine the best correlation point between the ABR and PTA threshold. Studies conducted by van der Drift *et al*.(18) and Bellman *et al*.(19) on the comparison between ABR and PTA in cochlear hearing loss in adults (all ages) demonstrated that the two hearing threshold assessment method have a strongest correlation point at 2 and 4 kHz. In our study, the strongest correlation was obtained at 2 kHz, 8 kHz, and 4 kHz in group I, group II and groupIII respectively. Therefore, we think that it is important when a patient with presbycusis presents to the clinic for a hearing threshold assessment, in addition to the subjective PTA test, ABR should be performed to estimate whether the speech hearing ability of the patient differs from the hearing threshold of each frequency. This test can also help to assess whether the patient is suitable for hearing aids, providing guidance for finding a solution in the future. Thus, the search for better ways to improve the auditory speech recognition ability of patients should be the focus of future research.

Limitations of the study: In this study, one limitation is that the sample size is not enough, maybe if this comparison was made with equal patients' number in each group, the threshold difference between ABR and PTA would be clear. We suggest further study into the onset of disease (e.g. which of presbycusis, diabetes or hypertension was first found) and the intake and duration of diabetes medication, which may also have an effect on hearing disorders

Conclusion

The correlation between ABR and PTA mean threshold difference was significant in group I and group II in all ranges with a strongest correlation at 2 kHz and 8 kHz respectively. This correlation was only significant at high frequencies for subjects in group III with the best correlation at 4 kHz, and not significant in participants with both associated illness. Therefore, presbycusis alone doesn't influence the relationship between ABR and PTA threshold. Thus if associated with chronic diseases like DM and AH the relationship between ABR and PTA threshold is affected.

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