

AUDIOLOGY

Effect of vitamin B12 deficiency on otoacoustic emissions

Effetti del deficit della vitamina B12 sulle otoemissioni acustiche

R. KARLI¹, A. GÜL², B. UĞUR³

¹ Department of Otorhinolaryngology, School of Medicine, Ondokuz Mayıs University Samsun, Turkey; ² Training and Research Hospital Department of Otorhinolaryngology, Diyarbakir Turkey; ³ Department of Otorhinolaryngology, School of Medicine, Karaelmas University, Zonguldak, Turkey

SUMMARY

The aim of this study was to investigate the possible association between otoacoustic emission (OAE) values and cochlear function in patients with vitamin B12 deficiency and no evidence of symptomatic hearing loss. Two groups were studied: Group 1: patients with vitamin B12 deficiency; Group 2: a matched control group of patients with normal vitamin B12 levels. There was no evidence of symptomatic hearing loss in either group. Transiently evoked OAEs (TEOAEs) and spontaneous OAEs (SOAEs) were recorded. A comparative analysis of the studied parameters revealed that results at TEOAE 1000, SOAEs 1500 and SOAEs 4000 Hz were somewhat lower in the vitamin B12 deficient group compared with the control group. According to our findings, there was a significant association between vitamin B12 deficiency and cochlear dysfunction. We recommend that routine vitamin B12 serum levels be determined when evaluating patients for symptomatic hearing loss.

KEY WORDS: Vitamin B12 deficiency • Hearing loss • Otoacoustic emission

RIASSUNTO

L'obiettivo del nostro lavoro è stato lo studio della funzione cocleare tramite le otoemissioni acustiche(OAE) in pazienti con deficit della vitamina B12 senza evidenza di ipoacusia sintomatica. Abbiamo diviso i pazienti in due gruppi; Gruppo 1: pazienti con deficit di vitamina B12; gruppo 2: pazienti con livelli normali di vitamina B12 (controllo). I pazienti di entrambi i gruppi non riferivano ipoacusia soggettiva. Sono state registrate le otoemissioni acustiche transienti (TEOAEs) e le otoemissioni spontanee (SOAEs). Un'analisi comparativa dei parametri studiati ha rivelato che le TEOAEs a 1000, le SOAEs a 1500 e 4000 Hz erano relativamente più basse nel gruppo con deficit di vitamina B12 che nel gruppo di controllo. Sulla base dei nostri dati è possibile stabilire un'associazione significativa fra il deficit di vitamina B12 e la disfunzione cocleare. Per tale motivo riteniamo sia indicato di routine il dosaggio della vitamina B12 sierica nei pazienti affetti da ipoacusia di tipo cocleare.

PAROLE CHIAVE: *Deficit della vitamina B 12 • Ipoacusia • Otoemissioni acustiche*

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Introduction

In humans, vitamin B12 deficiency may affect haematological, gastrointestinal and neurological systems. Neurological damage is the result of pathological changes, which may eventually lead to demyelination, axonal degeneration and eventual neuronal death^{1,2}. Electrophysiological studies in patients with vitamin B12 deficiency have revealed the presence of sensory motor axonopathy as a result of neurological deficits such as myelopathy, myeloneuropathy, peripheral neuropathy, axonal demyelinating and optic neuropathy³. Hearing loss is a major health problem, which results in a decrease in income, workforce and quality of life. Some studies have reported that hearing loss, tinnitus and noise-induced hearing loss (NIHL) are associated with vitamin

B12 deficiency, with a possible relationship between vitamin B12 deficiency and dysfunction of the auditory pathway^{4,9,10}. However, other investigations have failed to find any strong evidence to support such an association^{5,23,24}.

Herein, we aimed to determine the relationship between vitamin B12 deficiency and cochlear function, in particular at the level of the outer inner hair cells.

Materials and methods

Fifty-three patients were included in the study. The vitamin B12 deficiency group (Group 1) comprised 33 patients between 18 and 69 years with a mean age of 44.6 [females, 19 (57.6%); males, 14 (42.4%)]. The remaining 20 patients in the control group (Group 2) were between

20 and 57 years with a mean age of 42.4 [females, 18 (54.5%); male, 15 (45.5%)]. This prospective study included 33 patients (66 ears) with vitamin B12 deficiency and normal hearing. All subjects (patients and controls) gave informed consent prior to inclusion in the study. The control group included 20 healthy subjects (40 ears) with normal hearing and normal vitamin B12 levels. Pure tone audiometric threshold averages in the (0.5, 1, 2, 4, 6 kHz) lower than 30 dB HL were accepted in the study.

To ensure reliability of results, all patients underwent an otoscopic examination before performing the test. Patients with a clean external ear channel and normal eardrum were included. Pure tone audiogram (PTA), TEOAE and SOAEs measurements were performed bilaterally in both groups. Subsequently, the average of the OAE values obtained for each single patient was calculated. Patients in whom emissions could not be obtained or with remarkable medical histories (i.e. family history of hearing impairment or history of noise exposure, prescription of ototoxic drugs) were excluded. During the study, background noise was lower than 50 dB. OAEs were measured with the DPE choport IL-O292 (Otodynamics Ltd.) through the use of an adult probe. TEOAEs were measured at 1000, 1500, 2000, 3000 and 4000 Hz using standard techniques. PTAs were measured at 250, 500, 1000, 2000, 4000 and 6000 Hz. The same device was used in all cases for measurement of TEOAEs. A nonlinear mode of click stimulation of intensity (75+/-85) dB SPL was produced. The presence of TEOAE measurement method is the normal case of standard; reconstructed form reproducibility (correlation) value was accepted only when better than 70%¹⁵.

In analysis of TEOAE measures, parameters of reproducibility percentage, response (emission strength) value (dB) and S/N rate (signal to noise ratio) were evaluated. The averages and standard deviations (SD) of the OAE results were calculated. The differences between the OAE results of the B12 deficiency group and the control group were compared statistically using the Mann Whitney U test.

SOAE

Otoacoustic emissions (OAEs) are evident as sound emanating from the healthy cochlea, which may be recorded using a sensitive microphone placed in the ear canal. Without an external stimulus individuals emit sounds that can be recorded by the external ear, but which not are believed to originate from outer hair cells of the cochlea. These spontaneously-emitted sounds are called spontaneous otoacoustic emission (SOAE)¹⁶. This type of emission is narrow-band low intensity acoustic signals. Their incidence is around 38% in a population with normal hearing¹⁷.

TEOAE

A commonly-studied OAE is elicited in response to a brief transient sound, such as a click or a tone burst. This

is referred to as transient-evoked otoacoustic emission (TEOAE), and can be measured as electromotive activity emitted in outer hair cells of cochlea after a specific latent period in response to an acoustic stimulus from external ear. This type of emission is widely used in clinical practice. TEOAE is present in all ears with normal hearing and almost normal cochlear function¹⁹.

Statistical analysis

All analyses were conducted using SPSS 15.0 (SPSS® for Windows 15.0, Chicago, USA). The data were distributed non-parametrically according to the one-sample Kolmogorov-Smirnov test. Comparisons of all parameters were done using the Mann Whitney U test. Variables were expressed as mean \pm SD. A two tailed $p < 0.05$ was considered statistically significant.

Results

The results for the two groups and comparison with the Mann Whitney U test are shown in Tables I-IV. In the vitamin B12 (Group 1), the following values were obtained: min: 121 pg/mL, max: 157 pg/mL (mean 140.52 pg/mL). In Group 2: min: 210 pg/mL, max: 435 pg/mL (mean 262.5 pg/mL). There were no significant differences in terms of gender or age between the two groups. The PTA thresholds in decibels are presented in Table I. There was no statistically significant difference between the groups in terms of audiological results ($P > 0.05$).

A statistically significant decrease in the emission values was observed at 1 kHz in TEOAEs ($P < 0.05$) (Tables II, III) and 1500-4000 Hz in SOAEs ($P < 0.05$) (Table IV) between the vitamin B12 deficiency and control groups.

Discussion

OAEs are sounds recorded in the external ear, generated by the outer hair cells⁷. The measurement of OAEs provides an indicator of the functioning of the peripheral auditory organ. Both the cochlea components of hearing loss can be monitored, and a subclinical dysfunction of hearing presenting no audiological evidence can be detected by OAE tests, which are objective and non-invasive⁸.

According to the findings of our study, the results of TEOAE 1000 and SOAEs 1500, 4000 Hz were lower in the vitamin B12 deficiency group. This finding suggests that vitamin B12 deficiency has a negative effect on hearing at the cochlear level. The significant results at different frequencies in our TEOAE and SOAEs analysis depends on the characteristics of these types of emission. In previous studies, the incidence of SOAEs was around 30-40%^{18,17} and with a clinical value that was more limited than TEOAE^{20,21}.

Table I. Pure tone audiometric thresholds (PTA).

	250 Hz Mean \pm SD	500 Hz Mean \pm SD	1000 Hz Mean \pm SD	2000 Hz Mean \pm SD	4000 Hz Mean \pm SD	6000 Hz Mean \pm SD
B12 group	19.47 \pm 7.34	14.70 \pm 7.64	12.05 \pm 8.27	13.41 \pm 11.37	20.15 \pm 17.45	24.85 \pm 20.15
Control	19.00 \pm 6.99	15.63 \pm 6.01	12.13 \pm 4.37	12.00 \pm 5.86	16.00 \pm 6.99	19.75 \pm 9.26
P	0.79	0.30	0.31	0.73	0.77	0.90

Table II. Changes in TEOAEs.

TEOAE	TEOAE 1 kHz Mean \pm SD	TEOAE 1.5 kHz Mean \pm SD	TEOAE 2 kHz Mean \pm SD	TEOAE 3 kHz Mean \pm SD	TEOAE 4 kHz Mean \pm SD
B12 group	6.00 \pm 6.01	11.27 \pm 10.78	18.33 \pm 18.78	12.33 \pm 13.81	14.14 \pm 23.05
Control	10.23 \pm 5.13	9.60 \pm 7.59	14.60 \pm 5.59	11.28 \pm 6.05	6.73 \pm 6.41
P	0.001	0.18	0.91	0.72	0.12

Table III. Changes in the TOAE signal-to-noise ratio (dB).

	TOAE 1 kHz Mean \pm SD	TOAE 1.5 kHz Mean \pm SD	TOAE 2 kHz Mean \pm SD	TOAE 3 kHz Mean \pm SD	TOAE 4 kHz Mean \pm SD
B12 group	15.46 \pm 5.09	9.22 \pm 6.23	4.35 \pm 7.80	26.21 \pm 3.99	22.82 \pm 5.09
Control	23.35 \pm 5.28	12.51 \pm 4.49	5.76 \pm 7.38	24.43 \pm 4.64	21.16 \pm 3.93
P	0.02	0.34	0.47	0.14	0.26

Table IV. Changes in SOAEs.

	SOAE 1 kHz Mean \pm SD	SOAE 1.5 kHz Mean \pm SD	SOAE 2 kHz Mean \pm SD	SOAE 3 kHz Mean \pm SD	SOAE 4 kHz Mean \pm SD
B12 group	9.79 \pm 20.26	14.97 \pm 6.25	15.85 \pm 12.45	14.36 \pm 16.91	16.00 \pm 25.11
Control	10.60 \pm 21.08	11.93 \pm 5.58	13.53 \pm 6.29	10.38 \pm 6.55	6.33 \pm 5.98
P	0.71	0.024	0.29	0.31	0.021

According to a study on the reliability of TEOAE results, hearing scanning was performed on 31,092 newborns with TEOAE and clinical consultation/examination and ABR were required only in 0.8% of cases. This study demonstrates the efficiency of TEOAE measurements²².

De Capua et al., in a study testing 532 consecutive newborn infants by TEOAE, confirmed the feasibility and accuracy of universal neonatal hearing screening based on recording TEOAE²⁵.

On the other hand, some authors suggest that TEOAE is not a very effective method due to its low sensitivity and specificity, false negative and false positive outcomes and discordance for some categories of hearing loss^{26,27}. We believe that the method is acceptable considering the large number of screenings, and that TEOAE measures are more reliable than SOAE. We detected anomalies by the 1000 Hz frequency band of TEOAE. Deficiencies of vitamin B12 are widespread and are responsible for major morbidity across all age groups, and may have significant consequences for quality of life as it affects multiple systems in the body. It is relatively difficult to pinpoint the relationship between the auditory pathway

and vitamin B12 deficiency because of the effect of this deficiency on hearing sensitivity and the duration of the deficiency, as well as many other systemic and/or local effects.

None of our patients were able to provide definitive information on the duration of their vitamin B12 deficiency, and the impact of this duration on the results is unclear.

According to a study by Shemesh et al. on army personnel with tinnitus and related disorders, 47% of patients had vitamin B12 deficiencies, which may be overcome by vitamin supplementation. They also reported that the personnel reported some improvement following B12 vitamin replacement therapy. According to the authors, those findings suggest a relationship between B12 deficiency and auditory dysfunction⁴.

Houston et al. investigated whether a poor vitamin B12 and folate status may be associated with age-related auditory dysfunction⁹. In another study, researchers evaluated the effects of supra-physiological vitamin B12 administration on noise-induced temporary threshold shift in 20 young volunteers, which suggested that elevated plasma levels of vitamin B12 may reduce the risk of hearing dys-

function resulting from noise exposure in healthy young subjects¹⁰. Another study investigated the effect of vitamins A, E, B12 and folic acid on NIHL and found that vitamin A, E and folic acid levels were normal while the levels of vitamin B12 were low in individuals with hearing loss due to noise¹¹. As a result, the authors recommend routine measurement of vitamin B12 in control of people working in noisy environment¹¹. Although a number of studies, as noted above, support a negative effect of vitamin B12 deficiency on hearing function, others contend no such relationship¹⁵. In a study in individuals over the age of 60, folate and vitamin B12 values in those with normal hearing at both speaking frequency and high frequency were compared to those with hearing loss. A significant decrease in folate level in those with age-related hearing loss (ARHL) was found, but a significant relationship with vitamin B12 levels was not found. As a result, it was emphasized that folate deficiency might be significant in age-related hearing loss²³. In another study in 2956 patients with presbycusis over the age of 50 years, serum folate, vitamin B12 and homocysteine levels were not found to play a role in hearing loss²⁴.

As mentioned above, despite many studies, the effects of this widespread nutritional deficiency on the auditory pathway remain unknown⁶. Vitamin B12 is integral to the myelination process, and its lack or deficiency results in abnormal myelin formation or even complete demyelination¹². Furthermore, animal experiments of B12 deficiency have revealed neuropathological effects¹³. Medial efferent fibres of the medial olivocochlear bundle originate in the medial nuclei of the superior olivary complex. The large myelinated fibres of the bundle project mainly contralaterally to the synapses at the base of the outer hair cells¹⁴.

Uğur and colleagues reported a contralateral suppression effect in children with type 1 diabetes mellitus who presented with no evidence of symptomatic neuropathy. The findings point to the presence of a dysfunction in the medial olivocochlear efferent system in diabetic children. This may be regarded as an early, central manifestation of diabetic neuropathy⁷.

Vitamin B12 deficiency is known to have negative effects on hearing by affecting myelination at any level of the retrocochlear area of the auditory system. More detailed studies are needed to determine the exact nature of these effects.

Conclusions

There appears to be a correlation between vitamin B12 deficiency and cochlear function. The level of vitamin B12 in the blood should not be ignored in assessment of auditory function.

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