Hearing evaluation with ABR in pediatric patients with celiac disease

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ABSTRACT

Background/Aims: Celiac disease (CD) is an autoimmune and genetic disease that is triggered by gluten intolerance. We aimed to investigate whether Celiac disease have any effect on Auditory Brainstem Response (ABR) waves compare to a healthy control group, and present its association with sensorineural hearing loss (SNHL).

Materials and Methods: Thirty-eight patients aged 2 to 16 years old were included in the study. The patients had confirmed diagnosis of Celiac disease through duodenal biopsies and transglutaminase Antibody (Ab) (+). The control group consisted of 18 children aged 3 to 17 years old who were all admitted to the pediatric gastroenterology department due to complaints of constipation and transglutaminase Ab (-).All children underwent Auditory-Brain-Stem-Evoked Responses (ABR). The data were gathered using click stimulus at 10/s frequency 90dB HL.

Results: The results of ABR examination did not show any difference between the patient group and control group as regards the latency of the waves I, III, V. No difference was observed between the two groups in the interpeak latecies I-III, I-V and III-V. None of the patients was observed to have clinical hearing loss.

Discussion: The exact pathogenesis of neurological damages observed in Celiac disease is still unknown. Humoral immune mechanisms are the most frequently attributed cause.

Conclusion: Although no significant difference was found in hearing values between the study group and healthy control group, there is a need for further research on this subject.

Keywords: Sensorineural hearing loss, celiac disease, auditory brainstem response

INTRODUCTION

Celiac disease (CD) is an autoimmune and genetic disease that is triggered by gluten. The disease typically manifests as abdominal pain and chronic diarrhea. However, the CD can present in atypical forms of extraintestinal symptoms, such as anemia, growth failure, elevated liver transaminase levels, and neurological disorders (1). Contrary to previous reports, recent studies have indicated nervous system impairment is common in CD and can be considered as one of the most frequent extraintestinal presentations. It was proposed that the involvement of the nervous system was associated with autoimmunity owing to the interaction between the antibodies related to CD and nervous system proteins and cells (2). Furthermore, various neurologic disorders, such as hypotonia, peripheral neuropathy, developmental delay, learning disorders, attention deficit hyperactivity disorder, cerebellar ataxia, migraine, and night blindness, are considered to be the extraintestinal manifestations of CD (3). Therefore, it is hypothesized that the hearing pathways could be affected through a similar autoimmune mechanism in pediatric patients with CD (4).

In this study, we aimed to compare the auditory brainstem response (ABR) waves between patients with CD and the healthy control group to prove the association of CD and sensorineural hearing loss (SNHL). Notably, only few studies have assessed the hearing functions in patients with CD by using the test with a subjective component (2,5-8). In this study, we aimed to demonstrate the hearing functions in patients with CD by using the ABR test that was based on an objective assessment, which was not reported previously in the literature.

MATERIALS AND METHODS

This study was conducted by the Department of Otolaryngology and Department of Pediatric Gastroenterology.

Presented in: This study was presented at the 9. Cochlear Implantation Otology-Neurotology Audiology Congress, 7-10 December 2017, Antalya, Turkey.

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Ethical approval was obtained from our Institute's Ethical Committee, bearing the approval protocol number 09.04.2013/88.

This study included 38 patients aged 2 to 16 years who were diagnosed with CD through duodenal biopsies and transglutaminase antibody (TGA) positivity. The control group consisted of 18 children, aged 3 to 17 years, who were admitted to the pediatric gastroenterology department for an etiologic investigation of chronic constipation and were negative for TGA. Written consent was obtained from parents of all patients in both groups. Individuals with a history of metabolic disease, diabetes mellitus, hypoxia, perinatal infection, prematurity, ototoxicity, past ear surgery, as well as outer, middle, and inner ear disease were excluded from the study.

Both the patient and control groups underwent systemic and ear, nose, throat examinations. Furthermore, they underwent detailed otomicroscopic examination. Patients observed to have tympanic membrane perforation or sclerotic plaques were excluded from the study. For the audiological examination, middle ear pressures and compliance of all patients were initially measured (AZ26 Interacoustics). The pressure and compliance values of both the patient and control groups were determined to be within the normal range. An attempt was made for all children included in the study to undergo a pure tone audiogram. The test failed because seven children from the patient group, and four from the control group did not cooperate. With the exception of these children, air conduction thresholds of 250, 500, 1000, 2000, 4000, and 6000 Hz frequency and bone conduction thresholds of 500, 1000, 2000, and 4000 Hz frequency were measured in all children (AC40 Interacoustics).

Table 1. Descriptive statistical data related to age and sex in study and control groups.

	Control	Celiac	Total	p
Number of cases (n)	18	38	56	
Age mean (SD)	7.39 (±4.654)	9.87 (±4.326)	9.07 (4.544)	0.039*
Sex (female/male)	9/9	23/15	32/24	0.457

*p<0.005.

All children underwent ABR (Epic-Plus Labat). Data were gathered using click stimulus at 10/s frequency 90 dB HL (hearing level). Chloral hydrate sedation was administered to uncooperative children before the measurement to prevent motion artifacts.

The descriptive statistics were expressed as count, mean, median, mode, standard error, standard deviation (SD), variance, minimum (min), and maximum (max) values.

Statistical analysis

The normal distribution of continuous variables was tested using the Shapiro–Wilk test, and they were not observed to be normally distributed. Therefore, the Mann–Whitney U test was employed to analyze the difference between the measured values of the two groups. Because sex was a categorical variable, the Pearson chi-square test was used to analyze the sex distribution in patient and control groups.

The statistical analyses were performed using The Statistical Package for the Social Sciences (SPSS) 21.0 software package (IBM Corp.; Armonk, NY, USA), and p values lower than 0.05 were considered to be statistically significant.

RESULTS

The patient group consisted of 23 girls (60.5%) and 15 boys (39.5%) with a mean age of 9.87±4.326 years (median: 10.0 years; min-max: 2-16 years). The control group

Table 2. Auditory brainstem response results in both groups.

	Control	Celiac			
	Mean±SD	Median (Range)	Mean±SD	Median(Range)	p
I LATENCY	1.46±0.09	1.46(1.2-1.72)	1.5±0.11	1.5(1.24-2)	0.014*
III LATENCY	3.61±0.09	3.62(3.42-3.74)	3.64±0.18	3.64(3.28-4.42)	0.368
V LATENCY	5.42±0.11	5.42(5.18-5.64)	5.51±0.24	5.44(5.08-6.82)	0.113
I-III Interwave Intervals	2.15±0.11	2.14(1.94-2.38)	2.14±0.19	2.14(1.7-2.98)	0.453
III-V Interwave Intervals	1.82±0.14	1.84(1.44-2.08)	1.87±0.24	1.82(1.42-2.7)	0.768
I-V Interwave Intervals	3.91±0.36	3.96(1.94-4.22)	3.99±0.28	3.97(3.06-5.38)	0.894

*p<0.05.

consisted of 9 girls (50%) and 9 boys (50%) with a mean age of 7.39±4.654 years (median: 5.50 years; min-max: 3-17 years). The age of children in the patient group was noted to be statistically higher than those in the control group (p=0.039). However, no intergroup difference was observed regarding the distribution of sex (p=0.457) (Table 1). The analysis of pure tone audiogram results did not reveal any statistically significant intergroup difference related to the hearing frequency values. The results of the ABR examination did not reveal any intergroup difference regarding the latency of the waves I, III, and V. Notably, no intergroup difference was observed regarding the latency of the waves I-III, I-V, and III-V. None of the patients was observed to have clinical hearing loss (Table 2).

DISCUSSION

The prevalence of SNHL below the age of 18 years is 0.6% (9, 10), and could be caused by congenital or acquired diseases. CHARGE syndrome, Pendred syndrome, and Waardenburg syndrome are the most prominent congenital causes, whereas inner ear infections, trauma, and autoimmune diseases are the most common causes of acquired SNHL. Cogan syndrome, juvenile idiopathic arthritis, Wegener's granulomatosis, Sjogren's syndrome, Behçet's disease, and Hashimoto's thyroiditis are the most prominent autoimmune causes of SNHL (11). Notably, the prevalence of hearing loss associated with autoimmune diseases increases with age, reaching a peak in adolescence (12).

The exact pathogenesis of neurological damages observed in CD is still unknown. Humoral immune mechanisms are the most frequently attributed cause (13). Furthermore, the cellular immune response may cause neurological symptoms by causing tissue damage (14). Even though hypovitaminosis, because of malabsorption, has been inculpated for the emergence of neurological symptoms, vitamin replacement treatments were noted to be futile (15).

Few studies have been conducted regarding SNHL in patients with CD (5, 7). These studies have revealed that hearing functions of patients with CD are affected compared with healthy controls. These evaluations were performed using a pure tone audiogram. Şahin et al. reported that the mean bone conduction thresholds in the patient group were significantly lower compared with the control group, whereas no difference was noted regarding the mean air conduction thresholds. Although mean bone conduction thresholds were significantly lower, no obvious clinical hearing loss was observed in the patient group (6). On the other hand, in a similar study, Hizli et al. reported that the prevalence of SNHL in patients with CD was statistically significantly higher compared with the healthy control group. They indicated that their findings supported the hypothesis that an immune-related pathology could be responsible for the involvement of the inner ear in the development of mild SNHL in pediatric CD cases. The hearing was evaluated using pure tone audiogram in both studies (5). Notably, the pure tone audiogram is a hearing test with a subjective component. Hearing thresholds are determined based on patients' responses. Therefore, the reliability of this test in the pediatric population is lower because of the lack of cooperation (16). Notably, limited studies exist concerning the hearing function in patients with CD, and all these determined hearing thresholds by using pure tone audiogram (5-7, 17).

Unlike all these studies, we used ABR to evaluate the inner ear functions. ABR is a surface recording that measures the activity of the distal portion of the auditory pathway. ABR is recorded using differential amplification with the active electrodes positioned at the vertex or forehead and with the reference electrodes positioned at the mastoids. Five to seven peaks occurring within a timeframe of less than 10 msec constitute the ABR. All these waves provide information regarding the neural auditory pathway (18) and provide accurate estimations of the threshold. Toneburst and click ABRs are the most common tests to estimate auditory sensitivity. Both these tests aid in determining the hearing threshold, identifying the differential diagnosis of hearing losses, localizing lesions, and diagnosing some neurological diseases involving the brain stem (19-22).

We preferred ABR because it is a more objective test to specify hearing thresholds in children and enable us to evaluate central pathways of hearing. This preference is one of the advantages of our study. Contrary to other studies, we did not observe any intergroup differences (5-7, 17). Moreover, no hearing loss was observed, either clinically or on laboratory tests, in both study groups.

Generally, hearing loss positively correlates with age in CD (2). In our study, the mean age of the patient group was significantly higher than the control group, but no hearing loss was observed in both groups. This finding is another advantage of our study and brings to mind questions regarding the reliability of findings of previous studies on SNHL in patients with CD.

Nevertheless, we believe it would be of merit to conduct such studies with more number of patients. The small study sample size seems to be the only limitation of our study, but the sample size was similar to the previously referred studies (5-7, 17, 23). An adult study regarding this topic with a higher number of patients seems to illuminate the literature.

In conclusion, ABR is clinically ideal as an objective test to determine SNHL. Although our study observed no significant intergroup differences regarding hearing values, further research is warranted on this subject, keeping in mind limitations, such as a lesser number of patients and lack of similar studies on adult patients with CD, before arriving at a definitive conclusion.

Ethics Committee Approval: : Ethics committee approval for this study was received from the Ethical Committee of Akdeniz University School Of Medicine, the approval protocol number 09.04.2013/88.

Informed Consent: Informed consent was obtained from the patient who participated in this study.

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