



Assessment of auditory brainstem responses in hypothyroidism and hyperthyroidism

Evaluation of hearing in thyroid disease

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Abstract

Aim: This study aimed to determine the effect of thyroid hormone changes on hearing pathways by assessing audiometry and auditory brainstem responses of hypothyroid and hyperthyroid patients and to determine whether hypothyroidism and hyperthyroidism patients are at risk for hearing loss. **Material and Method:** Between June 2008-July 2009, 25 hyperthyroidism (Graves, Multinodular Goitre) and 25 hypothyroidism (Hashimoto hypothyroidism) patients who were newly diagnosed in the endocrinology clinic of Düzce University Medical Faculty between the ages of 20-50 were taken into study. Audiometry and Auditory brainstem response (ABR) measurements were performed for each patient. **Results:** In audiometry findings of hyperthyroid patients, a sensorineural hearing loss was detected especially at high frequency when compared to normal control group. There was no significant difference in the ABR results when compared with the control group. When audiometric findings were interpreted in hypothyroid patients, a sensorineural hearing loss was detected especially at high frequencies when compared to the control group. When the ABR measurements of the control group were compared with the hypothyroid group, the wave latencies I., III., V. and I-III, I-V interpeak latencies were higher in the hypothyroid group, but the difference between the first wave latency and III-V and I-V interpeak latencies was not statistically significant ($p > 0,05$), but the difference between III., V. wave lattices and I-III interpeak latency was statistically significant ($p < 0,05$). These changes in ABR waves suggest that there are retrocochlear problems in hypothyroid patients. **Discussion:** The results of our study suggest that both hyperthyroidism and hypothyroidism may have an impact on the hearing pathways.

Keywords

Hyperthyroidism; Hypothyroidism; Audiometry; ABR; Hearing Loss

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Introduction

The thyroid gland produces two hormones, triiodothyronine (T3) and tetraiodothyronine or thyroxine (T4), which are iodine derivatives of tyrosine. Thyroid T3 and T4 secretion is under the control of thyroid stimulating hormone (TSH) secreted from the anterior pituitary. Thyroid hormone has an important physiological role in protein synthesis, cell growth, and differentiation, the continuation of cardiovascular functions, central nervous system, and maturation of musculoskeletal system [1].

Hyperthyroidism is an endocrine disorder characterized by the elevation of serum T3 and T4 hormones due to excessive secretion of thyroid hormones. The most common cause is Graves' disease, an autoimmune disorder. It is thought that oxidative stress plays a role in the pathogenesis of this disease.

Free oxygen radicals resulting from the oxidative damage of the molecules play a role in the pathogenesis of many diseases including neurodegenerative disorders, diabetes mellitus, cardiovascular diseases and different types of cancer [2].

Because thyroid hormones affect all organs in the body, hyperthyroidism is associated with various symptoms such as fatigue, nervousness, impaired concentration, weight loss, arrhythmia, tremor, insomnia, hot intolerance. Graves' disease is eight times more common in women than in men. It most commonly occurs in the 3rd or 4th decade of life [3].

Hypothyroidism is a common hormone insufficiency syndrome that can easily be diagnosed easily by laboratory tests, which can often be overlooked clinically. Hypothyroidism is classified as congenital and acquired according to the time of onset. The most common cause of acquired hypothyroidism is autoimmune thyroiditis called Hashimoto's disease. Antimicrosomal and antithyroid peroxidase antibodies are 95% positive [4].

In hypothyroidism, the lack of effects of thyroid hormones, such as regulation of oxygen consumption in tissues, and associated organ-specific effects are seen. Thyroid hormones are effective on ion transport in target tissues, and thyroid hormone disorders cause biochemical and mechanical changes in tissues. Common symptoms are cold intolerance, weight gain, constipation, bradycardia. Atypical symptoms and signs such as hypothermia, pericardial and pleural effusion, ileus, intestinal obstruction and neurological manifestations such as depression, psychosis, and ataxia may also be seen. The mean age of diagnosis is 60 years old, and it is seen four times more common in women [4].

Peripheral and central nervous system dysfunction are important clinical features of congenital and acquired hypothyroidism. Hearing loss is the most common otolaryngological finding associated with thyroid dysfunction. Various studies have shown that congenital and acquired hypothyroidism may be associated with hearing loss, which is estimated to be 10-55% in different studies [5]. Hilger first documented the hearing loss in 1956 audiometrically in acquired hypothyroidism [6].

Auditory brainstem response (ABR) is a good method for assessing the effects of thyroid diseases on the brain's hearing pathways.

The neurological auditory pathway extends from the spiral ganglion in the cochlea to the temporal lobe auditory cortex. ABR is an electrophysiological test that views the synchronous flow of electrical current in the area from the beginning to the midbrain of the hearing nerve. In studies conducted with superficial re-

cordings, it is observed that the responses that occurred within the first ten milliseconds consisted of seven waves. According to recent studies, I. wave originates from the distal part of the ipsilateral hearing nerve, and II. wave originates from the proximal part of this nerve. 3rd wave originates from cochlear nuclei, 4th wave from superior Olive complex, 5th wave from lateral lemniscus, and the 6th and 7th waves originates from areas where the inferior colliculus is dominant [7]. In the interpretation of the ABR, the amplitudes and latencies of these waves, as well as interpeak latencies (IPL) are important.

In some studies, peripheral and central conduction time extension was found in ABR in hypothyroidism, but no significant change was found in some.

Several studies have shown that hypothyroidism can lead to hearing loss. However, there is only one study in the literature regarding hearing assessment in hyperthyroid patients. In this study, there were no significant changes in ABR and audiometry findings in 12 hyperthyroid patients compared to the control group [5]. Free oxygen radicals resulting from oxidative damage of molecules in Graves' disease can affect hearing neurons and affect hearing pathways, leading to hearing loss.

This study aimed to evaluate the effects of thyroid hormone changes on hearing pathways by evaluating the auditory brainstem responses of patients with hypothyroidism and hyperthyroidism and to determine whether hypothyroidism and hyperthyroidism patients are at risk for hearing loss.

Material and Method

Between June 2008-July 2009, 25 hyperthyroid (Graves, Multinodular Goitre) and 25 hypothyroid (Hashimoto hypothyroidism) patients who were newly diagnosed in the endocrinology outpatient clinic of Düzce University Faculty of Medicine between 20-50 years were taken into the study. In addition to clinical characteristics and physical examinations of patients, the diagnosis was made by evaluating serum TSH, free T3 (fT3), free T4 (fT4), thyroid autoantibodies and thyroid ultrasonography. When serum TSH levels were above normal (> 4 uIU / ml) Anti-Tg (Anti-thyroglobulin) (> 115 IU/ml) and anti-TPO (Anti-thyroid peroxidase) (> 34 IU/ml) elevation as well as echogenicity reduction and parenchymal heterogeneity in the thyroid parenchyma in the ultrasonographic examination were revealed patients were categorised as Hashimoto hypothyroidism. Patients with normal fT3 and fT4 levels were considered to have subclinical hypothyroidism, and patients with normal levels were considered to be clinical hypothyroidism. Patients whose serum TSH level was below normal (<4 uIU / ml) and whose fT3 and fT4 levels were normal were considered subclinical hyperthyroidism and patients whose serum TSH levels were below normal and whose levels of fT3 and fT4 were above normal were accepted as clinical hyperthyroidism.

In this study, 50 patients, 11 with clinical hyperthyroidism, 14 with subclinical hyperthyroidism, 12 with clinical hypothyroidism and 13 with subclinical hypothyroidism were studied. The control group consisted of 30 individuals aged 20-50 years, with no thyroid disease, with hearing frequencies of 250-8000 Hz and better than 25 dB.

Detailed patient history, otoscopic examination findings, body temperatures, audiograms and ABR examinations of all the

subjects who were taken to the study were recorded with the previously prepared patient follow-up forms. Patients whose external ear and middle ear problems were detected during the routine ear examinations were not included in the study. Those who had previous autologous surgery, a history of ototoxic drug use, and systemic disease such as diabetes that would disrupt hearing, history of previous thyroid surgery were not included in the study.

Patients' air and bone conduction thresholds were measured using a clinical audiometry device (DANPLEX DA 74 Clinical Audiometer) calibrated to ISO standards. All audiological tests were done by masking the other ear.

The auditory brainstem responses of the patients were made with Nihon Kohden Neuropack μ MEB-9102 / 9104A / J / K. No medication was used to put patients to sleep during the recording, and cell phones were kept closed during the test. The BERA records were scaled, and electrodes with 4 mm diameter teflon were used. For the electrodes to respond well; the skin was first cleaned with soapy water and then treated with alcohol. EEG paste was used for good adhesion of the electrodes. When the test was performed, the active electrode was positioned on the vertex, the grounding electrode positioned between the two muscles, one of the reference electrodes was positioned on the left mastoid apex, and the other was positioned on the right mastoid apex. It was noted that the impedance values of all electrodes were below 5 Kohm. The stimulus was subjected to band-pass filtration of 150 to 3000 Hz with stimuli delivered at a rate of 80 dB and a repetition rate of 20/s. The click sound was used as the stimulus, and the results at 80 dB were taken into consideration. The latencies of I, III and V waves and I-III, III-V and I-V intercepts were determined from the auditory potentials displayed on the screen.

Statistical package program was used to analyze the data (SPSS 13, Statistical Package for Social Sciences, Chicago, Illinois, USA). Values were given as mean \pm standard deviation and p values less than 0.05 were considered significant. Student's t-test was used to compare audiometry results of both ear audiometry, I, III, and V wave latencies at 80 dB, I-III, III-V, and I-V interpeak latencies and body temperatures of the control group with hyperthyroidism group and the hypothyroid group and the control group. Analysis of categorical variables was done by Chi-square test.

Results

In hyperthyroidism group total of 25 patients; 6 male (24%) and 19 female (76%) were studied. The mean age of the patients was 37.4 (\pm 10.75) years, and their ages ranged from 20 to 50 years.

Twenty-five patients, including 3 men (12%) and 22 women (88%), were studied in the hypothyroid group. The mean age of the patients was 40.76 (\pm 9.18) years, and their ages ranged from 20 to 50 years.

The control group consisted of 25 patients; 11 men (44%) and 14 women (56%). The average age of the control group was 35.48 (\pm 9.32), and their ages ranged from 20 to 50 years.

When the airway thresholds (HYE) values of the control group compared with the hyperthyroid group, there was no statistically significant difference between 500Hz, and 1000Hz (p >

0,05) when the airway thresholds were higher in the hyperthyroid group in all frequencies and hyperthyroidism group was significantly higher at 2000Hz, 4000Hz, and 8000Hz (p <0,05). Pure voice averages were calculated as 9.46 dB (\pm 3.47) in the hyperthyroid group, and 7.32 dB (\pm 4.48) in the control group and the difference between pure averages was statistically significant (p <0.05).

When the ABR measurements of the control group were compared with the hyperthyroid group, no statistically significant differences were found between the groups in the I, III, V, wave latencies and I-III, III-V, I-V interpeak latencies (p > 0,05). Although airway thresholds were higher in hypothyroid group at all frequencies when audiometric thresholds of the control group were compared with the hypothyroid group, there was no statistically significant difference at 500Hz, 1000Hz, 2000Hz, 4000Hz (p > 0,05) and it was significantly higher in the hypothyroid group at 8000 Hz (p <0,05).

The pure sound average was calculated as 7.32 dB (\pm 4.48) in the control group, and the mean of the hypothyroid group was 9,78 dB (\pm 7.99) while the difference between the pure sound averages was statistically significant (p <0,05). When the ABR measurements of the control group were compared with hypothyroidism group, it was found that there was no statistically significant difference between groups I., III., V., wave latency and I-III, I-V, interpeak latencies although interpeak latencies were high in the hypothyroid group, whereas the difference between III., V. wave latencies and I-III interpeak latency was statistically significant (p <0.05).

Discussion

Peripheral and central nervous system dysfunction are important clinical features of congenital and acquired hypothyroidism. Various studies have shown that congenital and acquired hypothyroidism may be associated with hearing loss. However, studies investigating hearing loss due to acquired hypothyroidism have also been performed [8]. It is known that electrophysiological changes are seen in thyroid diseases. Calcium absorption decreases in hypothyroidism. Calcium is effective on synaptic transmission in the nervous system [5]. Hearing loss due to brain stem pathologies may occur in hypothyroidism.

The ABR, an electrophysiological test that subtracts the synchronous flow of electrical current from the beginning to the midbrain of the auditory nerve, is a good way to assess the effects of thyroid diseases on the brain's hearing pathways.

Interpic latencies (IPL) are important in interpreting ABR as well as the amplitudes and latencies of the waves. Retrocochlear hearing loss is prolonged in III., V. wave latencies, and I-III, III-V, I-V interpeak latencies.

Auditory brainstem responses to thyroid diseases in adults and children have been reported in various studies. Hypothyroidism changes the normal development of hearing receptors [9]. In congenital hypothyroid patients, Hebert et al. reported shortening of I-V interpeak latency and Himelfarb et al. reported an extension of I-V interpeak latency [10].

In another study of congenital hypothyroid patients, V-wave elongation was considered to be due to the maturation defect in the brainstem [10]. When the airway thresholds (HYE) values of the control group compared with the hypothyroid group,

there was no statistically significant difference between 500Hz, 1000Hz, 2000Hz, and 4000Hz ($p > 0,05$) when the airway thresholds were higher in the hypothyroid group in all frequencies hypothyroidism group was significantly higher at 8000Hz ($p < 0,05$). The pure sound average was calculated as 7.32 dB (± 4.48) in the control group, and the mean of the hypothyroid group was 9,78 dB (± 7.99) while the difference between the pure sound averages was statistically significant ($p < 0,05$).

Thornton et al. (2008) reported that our audiometry results were similarly elevated relative to the control group in the hypothyroid group in airway thresholds [5].

When the ABR measurements of the control group were compared with hypothyroidism group, it was found that there was no statistically significant difference between groups I., III., V., wave latency and I-III, I-V, interpeak latencies although interpeak latencies were high in the hypothyroid group, whereas the difference between III., V. wave latencies and I-III interpeak latency was statistically significant ($p < 0,05$).

Similarly to our study Anand et al. (1989) found, V-wave elongation in hypothyroid patients, elongation in I-III interpeak latency, and elongation in I-V interpeak latency unlike our results [11]. Khedr et al. found all wave latencies and interpeak latencies in hypothyroid patients [12]. Anjana et al. have not detected a significant difference in interpeak latencies in hypothyroid patients, but have found a significant decrease in latency to wave V [13]. Vanasse et al. did not find a significant difference in ABR outcomes when compared to the normal group in hypothyroid patients [13].

Thornton et al. have detected a prolonged ABR I-V interval in hypothyroid patients. A low metabolic rate in hypothyroid patients has been suggested to be a result of decreased body temperature, and that I-V interpeak latency may depend on this [4].

In our study, we also found that ABR changes in hypothyroid patients are not related to body temperatures since patients' body temperatures were recorded during ABR measurements and there was no significant difference between the hypothyroid group and the control group.

Various studies have shown that in a high-frequency hearing loss, there may be more prolongation of the first wave latency than the V-wave and concomitant shortening of I-V [5].

Meyerhoff detected I and II wave prolongation in congenital hypothyroidism, and this suggests that cochlea is affected by congenital hypothyroidism [6].

Although there are various studies about hearing assessment of hypothyroid patients, the studies on hyperthyroid patients are limited. Thornton et al. (2008) did not find a significant difference when compared with the normal group by evaluating the audiometry and ABR results of 12 hyperthyroid patients [5]. Oxidative stress is thought to play a role in the pathogenesis of Graves' disease, the most common cause of hyperthyroidism [1]. The audiometry and ABR results of 25 hyperthyroid patients were evaluated in our study, considering that free oxygen radicals resulting from oxidative damage of the molecules may affect the hearing pathways.

When the airway thresholds values of the control group compared with the hyperthyroid group, there was no statistically significant difference between 500Hz, and 1000Hz ($p > 0,05$)

when the airway thresholds were higher in the hyperthyroid group in all frequencies and hyperthyroidism group was significantly higher at 2000Hz, 4000Hz, and 8000Hz ($p < 0,05$).

Pure voice averages were calculated as 9.46 dB (SS = 3.47) in the hyperthyroid group, and 7.32 dB (SS = 4.48) in the control group and the difference between pure averages was statistically significant ($p < 0,05$).

When the ABR measurements of the control group were compared with the hyperthyroid group, no statistically significant differences were found between the groups in the I, III, V, wave latencies and I-III, III-V, I-V interpeak latencies ($p > 0,05$).

Conclusion

Thyroid hormones are known to be effective in peripheral and central nervous system as well as affecting all organs in the body.

In our study, when audiometric findings of hyperthyroid patients were compared with control group, sensorineural hearing loss was detected especially at high frequencies. However, when wave latencies and interpeak latencies were compared in ABR results, no significant difference was found. Changes in audiometric findings suggest that hyperthyroidism can affect many organs in the body as well as affect hearing pathways.

Peripheral and central nervous system dysfunction are important clinical features of congenital and acquired hypothyroidism. Previous studies have shown that congenital hypothyroidism affects the hearing pathways. Significant changes were found in audiometry and ABR results in previous studies in adult hypothyroid patients.

In our study, sensorineural hearing loss was detected especially at high frequencies when compared with audiometric findings group in hypothyroid patients. Findings that support retrocochlear hearing loss were found in patients with hypothyroidism, suggesting that ABR results were due to brain stem pathology when compared with the control group.

The results of our study suggest that both hyperthyroidism and hypothyroidism may have an impact on the hearing pathways. However, further work with more patients is needed for these effects to be fully demonstrated.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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