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Do antithyroid antibodies affect hearing outcomes in patients with pediatric euthyroid Hashimoto's thyroiditis?

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ABSTRACT

Objectives: Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disease in children. HT is a multifaceted disease with a variable clinicopathological presentation, including hearing impairment. It is known that hearing function is negatively affected in patients with thyroid disorders. The literature includes a very limited number of studies on hearing function in euthyroid pediatric patients with HT. The aim of this study was to determine the relationship between cochlear function and HT, independent of thyroid function.

Materials and Methods: The study included 48 children and adolescents (42 females and 6 males) aged 9–18 years that were diagnosed as HT, and 30 gender- and age-matched healthy controls. Hearing was assessed via otoscopy, tympanometry, pure-tone audiometry, and measurement of distortion product otoacoustic emissions.

Results: There weren't any significant differences in pure tone thresholds between the 2 groups based on pure-tone audiometry, except in the right ear at 6 kHz and 8 kHz. Distortion product otoacoustic emissions signal to noise ratios were significantly lower in the HT group than in the control group at 4 different frequencies (6 kHz [left ear], 8 kHz [left ear], 1.5 kHz [right ear], and 6 kHz [right ear]) ($P < 0.05$). The signal to noise ratios at all frequencies were <6 dB in 3% of left ears and 2.5% of right ears in the control group, versus 12.5% of left ears and 9.6% of right ears in the HT group. Distortion product amplitudes were significantly lower in the HT group than in the control group for both left and right ears at 1 kHz, 1.5 kHz, 3 kHz, and 8 kHz, and at 2 kHz for left ears only ($P < 0.05$).

Conclusions: The present findings show that cochlear function was lower in the HT group than in the control group. Accordingly, we think that hearing in patients with HT should be monitored periodically, even if their hearing thresholds are within normal limits. Thyroid autoimmunity appears to play an important role in a decrease in cochlear activity in pediatric HT patients.

1. Introduction

Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disease in children and is the most common cause of hypothyroidism. It is a well-known clinical entity characterized by serum thyroid antibodies and goiter [1]. High thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) titers are seen in 90% of HT cases. HT has a female predominance in middle-aged woman. When HT is suspected, thyroid antibody testing, and measurement of serum thyroxin (T4) and thyroid-stimulating hormone (TSH) concentrations are required to confirm the diagnosis. Children with HT may be asymptomatic, or have hypothyroid or hyperthyroid symptoms and findings. Thyroid function at presentation can vary from euthyroidism to hypothyroidism or hyperthyroidism. HT is a multifaceted disease with variable clinicopathological manifestations, including hearing impairment [2].

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The inner ear is thought to have immunoprivileged status, as it is protected by the blood-labyrinthine barrier. The inner ear has a strong tendency to be immune responsive [3]. The strongest evidence of being immune-responsive is that of organ-specific and systemic immune diseases. It is known that hearing is negatively affected in patients with thyroid disorders. Thyroid hormone is essential for the development of the auditory system [4]. Numerous studies have reported hearing loss in patients with early-onset congenital hypothyroidism, endemic cretinism, resistance to thyroid hormone, and Pendred syndrome, and in humans and rodents with environmentally based iodine deficiency [5–9]; however, to the best of our knowledge there is only one study on the effect of antibodies in euthyroid pediatric HT patients [10].

Otoacoustic emissions (OAEs) are acoustic signals generated by the outer hair cells in the cochlea that are transmitted through the middle ear to the ear canal. OAEs are an epiphenomenon—not a process of hearing, but a byproduct of it. OAEs can be used to assess auditory function up to the cochlea (outer hair cells). OAE testing is an effective, objective, and non-invasive method for assessing cochlear function. Both spontaneous and evoked emissions can be recorded, but evoked emissions are most useful in clinical practice. There are two types of evoked OAEs that are used in clinical practice: transient evoked OAEs (TEOAEs) and distortion product OAEs (DPOAEs). DPOAEs are evoked by two simultaneously presented pure tones. There are several clinical applications for DPOAEs, such as neonatal hearing screening, auditory neuropathy, in patients that are difficult to test, intraoperative monitoring, monitoring for ototoxicity, noise exposure or in cases of suspected pseudohypacusis [11]. DPOAEs can also provide objective cochlear sensitivity data [12]. Several studies reported that DPOAEs are more sensitive for monitoring cochlear function and diagnosing subclinical cochlear damage than pure-tone audiometry (PTA) [13–16]. As such, the aim of the present study was to determine the relationship between cochlear function and HT, independent of thyroid function. Hearing in euthyroid pediatric HT patients was examined to evaluate audiological functions and to determine the effect of autoimmune antibodies on the function of the cochlea.

2. Material and methods

2.1. Participants

The HT group included 48 patients aged 8.1–18 years who were referred due to HT to Antalya Research and Education Hospital, Department of Pediatric Endocrinology, Antalya, Turkey, between January 2013 and March 2015. HT was diagnosed based on findings of seropositivity for TPOAb and/or TgAb, as well as typical thyroid hypoechogenicity (based onultrasonography) and abnormal thyroid function. Patients in the HT group were treated with levothyroxine, the dose of which was increased until the TSH level was normal. As such, only euthyroid HT patients without hearing symptoms were included. Children with a chronic systemic disease, a history of otological and audiological problems, ototoxic medication use, exposure to noise, ear surgery, acute or chronic otitis media, effusion with otitis media, and head trauma, and those that were unable to cooperate with audiological testing were excluded from the study.

The control group included 30 volunteers aged 9–17 years who presented to the hospital for routine check-ups or such minor illness as conjunctivitis, dermatitis, and enuresis nocturna. None of the controls had an endocrine disorder, thyroid illness, or any autoimmune-related disease, or were using any medications. None of the participants had a history of chronic disease, asthma, or other allergic disorders, and none had active infections, diabetes mellitus, kidney failure, a neoplastic disease, or inflammatory disease (including non-thyroid autoimmune disease). Written informed consent was obtained from the families of each participant and the study was approved by the Antalya Education and Training Hospital Ethics Committee.

2.2. Blood sampling

Venous blood samples were obtained at 0800–0900 from each participant for the measurement of serum TSH, free thyroxine (fT_4), free triiodothyronine (fT_3), TgAb, and TPOAb levels. Serum was separated via centrifugation and stored at −20 °C until assayed.

2.3. Hormonal evaluation

Hormonal analysis was performed in all participants. Serum TSH, fT_4, TgAb, and TPOAb levels were measured using commercially available assay kits (Beckman Coulter) and an autoanalyzer (Access DxI800; Beckman Coulter Diagnostics, CA, USA). TSH (assay range: 0.003–100 μIU mL^{-1}; reference value: 0.36–5.8 μIU mL^{-1}), fT_4 (assay range:0.25–6.0 ng dL^{-1}; reference value:0.6–1.49 ng dL^{-1}), TgAb (assay range:0.9–2500 IU mL^{-1}), and TPOAb (assay range:0.25–1000 IU mL^{-1}) serum levels were evaluated via the two-site immunoenzymatic (sandwich) assay method, whereas fT_3 (assay range: 0.88–30 pg/ml) assay is a competitive binding immunoenzymatic assay. The coefficient of variation (CV) was <10% for these assays.

2.4. Otologic evaluation

All the participants underwent careful otologic examination to identify any abnormalities that could negatively effect audiometric testing. Participants with any one of the following findings were excluded from the study: (1) otoscopic evidence of tympanic membrane pathology (perforated tympanic membrane, retraction pockets, or adhesion of the tympanic membrane) or other middle-ear pathologies; (2) a flat tympanogram or absence of acoustic reflexes at 1 kHz in response to contralateral stimulation; (3) air-bone gap of 10 dB at any frequency.

2.5. Audiometric procedures

All audiological procedures, including tympanometry and evaluation of middle ear function via immittance and acoustic reflex testing, PTA, and DPOAE testing, were performed by an expert audiologist. Tympanometry was performed using an impedance audiometer (AZ26, Precision Acoustics, New York, USA) and an 85 dB sound pressure level tone set at 226 Hz to measure middle ear function. Patients and controls with normal peak compliance, peak pressure, gradient, and ear canal volume, according to American Speech-Language-Hearing Association criteria, were included in the study [17]. After evaluation of the middle ear, PTA using (AC-40 Clinical Audiometer, Interacoustics, Denmark) was performed in a soundproof booth by the audiologist. The audiometer was calibrated according to International Organization for Standardization [18] and American National Standard Institute standards [19]. PTA thresholds were measured bilaterally at 0.5, 1, 1.5, 2, 3, 4, 6, and 8 kHz using the modified Hughson–Westlake procedure [20]; this procedure is detailed in ANSI S3.21-1978 (R-1992) [21]. All thresholds were measured in dB HL.

Calibration of DPOAE testing equipment was performed and a correct fit of the probe in each participant's external ear canal was confirmed before each evaluation. DPOAEs were recorded and analyzed using a Madsen Capella diagnostic OAE device. Two simultaneous pure-tone signals at two different frequencies (f1, f2) were presented to the ear. The greatest intensity of the distortion product response was recorded at a frequency of 2f1–f2 (the cubic distortion tone). The ratio of f2:f1 was 1:22, because on average,