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Original Article

Vestibular Dysfunction in Euthyroid Children with Hashimoto's Thyroiditis

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BACKGROUND: A relationship exists between autoimmune thyroid disorders and vestibular dysfunction. This study aimed to analyze cervical-evoked myogenic potentials (cVEMP) and video head impulse test (vHIT) results between children with Hashimoto thyroiditis (HT) and healthy controls to determine vestibular end-organ problems.

METHODS: Thirty-six children with HT and 30 healthy subjects were recruited. The main inclusion criteria for the healthy group were the presence of normal thyroid function and no clinical history of vestibular problems. Each participant (both HT and healthy groups) was assessed using audiovestibular tests, cVEMP, and vHIT.

RESULTS: There was no significant difference between the groups in terms of cVEMP (p1 and n1) latencies for both ears. There was no significant difference in cVEMP amplitudes (p1-n1 peak-to-peak) between the groups. There were statistically significant differences in the VOR gain of the right and left ears between the groups ($P < .001$, $P < .001$). When we considered lower cutoff value as 0.80 for VOR gain, 29 of 36 patients with HT (80.6%) had lower VOR gain scores. Only 1 of 30 healthy participants (3.3%) had a lower VOR gain score. This difference was statistically significant ($P < .001$).

CONCLUSION: Subclinical vestibulopathy may occur in children with HT. The vHIT seems to be a valuable tool for identifying and screening preclinical vestibular pathologies in this patient group.

KEYWORDS: Hashimoto thyroiditis, autoimmune thyroid disorders, cervical-evoked myogenic potentials, video head impulse test

INTRODUCTION

Hashimoto's thyroiditis (HT) is the most common autoimmune disorder in children. HT is frequently associated with other organ-specific autoimmune disorders, such as type 1 diabetes mellitus, Addison's disease, multiple sclerosis, and celiac disease.[1,2] In addition to the very well-described Pendred's syndrome,[3-5] which involves congenital bilateral hearing loss and thyroid dysfunction, the relationship between HT and the auditory system has also been investigated in several studies.[6,7]

The relationship between the thyroid and vestibular systems has received increasing attention in recent years, and an increasing number of studies have investigated the relationship between HT and vestibular dysfunction in the adult population. Vestibular deterioration to a certain level has been observed in patients with HT.[8-10] Several studies have shown a relationship between vestibular disorders and thyroid autoimmunity, regardless of thyroid function.[11] The association between Meniere's disease and Benign Paroxysmal Positional Vertigo and HT has also been studied in the adult population in several studies. Immune complex precipitation in the vestibular system with autoimmune microangiitis has been postulated as a pathological mechanism of HT for this

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vestibular dysfunction.[12] However, there are no available data regarding HT and vestibular dysfunction in the pediatric population in the current literature.

Cervical vestibular evoked myogenic potentials (cVEMP) are short-latency electromyographic responses of the ipsilateral sternocleidomastoid muscle to air-conducted high-intensity sound stimuli. This reflects the function of the saccule and inferior vestibular nerve. This electrophysiological test shows the function of the vestibulocollic reflex.[13] Its reliability has also been demonstrated in pediatric age groups.[14]

The video head impulse test (vHIT) involves an unpredictable and high-acceleration head movement with an amplitude of 10°-20° that permits examination of the vestibulo-ocular reflex (VOR) of the semicircular canals. VOR stabilizes the image on the retina during head movement by shifting the eye in a direction opposite to the direction of the head. This maintains the image in the center of the visual field.[15] The anatomical pathway for the VOR includes the semicircular canals in the inner ear, vestibular and ocular motor nuclei in the brain stem, and extraocular muscles.

We aimed to focus on the relationship between vestibular dysfunction and HT in euthyroid pediatric patients. We analyzed and compared vestibular function between euthyroid HT patients and age-matched healthy subjects using electrophysical tests with VEMP and vHIT. To our knowledge, this is the first study on this topic conducted in the pediatric population.

METHODS

Study Population

The study included 36 children with HT (girls = 33, 91%; boys = 3, 9%) and 30 healthy children (girls = 26, 86%; boys = 4, 14%) who were enrolled over six months (September 2022–March 2023). The patient group was composed of pediatric patients who were being followed up with the diagnosis of HT in the pediatric endocrinology outpatient clinic of our hospital. The diagnosis of HT was confirmed by the presence of serum thyroglobulin antibody (TgAb) and/or thyrotropin antibody (TPOAb). The healthy children were the children of the hospital staff. Thyroid autoantibody and thyroid function tests were conducted on these children, and subjects with normal thyroid function tests and negative thyroid autoantibodies were enrolled as the control group. Both the patient group and healthy subjects had normal thyroid function tests (serum TSH, FT_3 and FT_4 values). The subjects underwent a standardized neurological examination, and all examinations were normal. All participants underwent detailed ear, nose, and throat examinations, and audiological assessments. Audiological assessments included otoscopic examination and conventional pure-tone audiometry at 250, 500, 1000, 2000, 4000, and 8000 Hz. Examination of spontaneous and gaze-evoked nystagmus and dynamic positional tests (Dix-Hallpike test, supine roll test, and deep head hanging test) were performed on all subjects.

Participants with a history of any type of hearing loss, tympanic membrane abnormalities (adhesion, retraction, or perforation), or abnormalities in audiological assessment were excluded. Patients with symptoms of vestibular problems (dizziness, tinnitus, vertigo, or imbalance) were also excluded.

Vestibular tests, including VEMP and vHIT, were performed by a board-certified otolaryngologist and trained audiologist. All clinical equipment used in the study was calibrated and met the appropriate standards.

Written informed consent was obtained from the parents of all participants. The study was approved by the local ethics committee of the hospital (local file number: 9.9.2022-20915).

Cervical VEMP Procedure

Subjects were in a sitting position and were asked to turn their heads to the opposite side to maintain sternocleidomastoid muscle contraction during the cVEMP procedure. The active electrode was placed in the upper half of the ipsilateral sternocleidomastoid muscle. The reference electrode was located at the sternoclavicular joint. A short tone burst sound stimulation was delivered to the ipsilateral ear. The peak latencies of waves p13 and n23 and the peak-to-peak amplitudes were recorded. The same procedure was performed on the ears of all participants.

Video Head Impulse Test

The vHIT was performed in a room with adequate lighting, and all subjects were arranged in a sitting position. The subjects wore goggles joined by a gaze-driven digital camera system that recorded real-time eye movements. Each participant was calibrated to the goggles prior to collecting individual participant data. After the calibration process, the participants were asked to fixate on a target located on a wall almost 1m straight ahead. At least 20 unpredictable head impulses were performed in the planes of the horizontal semicircular canal. The software calculated the vestibulo-ocular reflex gain as the ratio of the peak slow-phase eye velocity to the peak head velocity for each horizontal semicircular canal. For the lateral canal vHIT examination, the minimum velocity was set to 150 °/s. vHIT recordings below this velocity were not included in the evaluation. Values between 150-300 °/s were included in the study.

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences, version 20, for Windows statistical software (IBM Corp., Armonk, NY, USA). Descriptive statistical data were calculated. The relevance of the variables to normal distribution was analyzed

MAIN POINTS

- This study is the first to investigate the relationship between vestibular dysfunction and Hashimoto's thyroiditis in euthyroid pediatric patients, revealing that the majority of children with HT have lower VOR gain scores compared to healthy subjects.
- The video head impulse test (vHIT) has emerged as a more sensitive clinical tool for evaluating preclinical vestibulopathy in euthyroid HT pediatric patients, demonstrating its effectiveness in assessing the function of the lateral semicircular canals.
- These findings suggest that pediatric patients with euthyroid Hashimoto's thyroiditis should be monitored for vestibular disorders throughout their lives, emphasizing the importance of using noninvasive and easy-to-perform tests such as vHIT for early detection and intervention.

using analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). Fisher's exact test was used to compare qualitative variables. The Mann–Whitney *U*-test was used to compare continuous variables between the two groups. The type 1 error level was identified at 5% for statistical significance.

RESULTS

All participants completed both cVEMP and vHIT procedures. The demographic characteristics are shown in Table 1. There were no statistically significant differences between the groups in terms of age or sex ($P > .05$). The mean duration of disease was 15.9 ±2.4 months in the HT group. No vestibular symptoms or hearing loss was observed in either group.

There was no significant difference between the groups regarding the cVEMP (p1 and n1) latencies for both ears ($P = .72$, $P = .52$). There was no significant difference in the cVEMP amplitudes (p1-n1) between the groups. The cVEMP values for both groups are shown in Table 2 ($P = .19$).

The vHIT results for horizontal semicircular canals are listed in Table 3. There were statistically significant differences in the VOR gain of the right and left ears between the groups ($P < .001$ and $P < .001$, respectively).

When we considered a lower cutoff value of 0.80 for VOR gain, 29 of 36 patients with HT (80.6%) had lower VOR gain scores. Only 1 of 30 healthy participants (3.3%) had a lower VOR gain score. This difference was statistically significant ($P < .001$) (Table 4).

Among the patients with Hashimoto's thyroiditis, 13 (36.1%) had catch-up saccades. Of the cases with catch-up saccades, 10 (76.9%) had only overt saccades, 1 (7.7%) had only covert saccades, and 1 (7.7%) had both overt and covert saccades.

DISCUSSION

The relationship between the inner ear and HT has been thoroughly investigated, specifically in the auditory part. However, the effects of HT on the vestibular system have not been well described. Multiple studies have shown that cochlear damage in VEMP is a valuable tool for interpreting the vestibular system before it becomes evident in the clinic. Thus, it can provide clinicians with an idea of preclinical vestibulopathy. Changes in VEMP in chronic systemic diseases have gained attention in recent years. We used cVEMP to evaluate the saccule, inferior vestibular nerve, and vestibular nucleus. We did not use ocular VEMP (oVEMP), which evaluates the utricle and superior vestibular nerve through the vestibular ocular reflex. This is because during oVEMP testing, the subjects must keep their eyes open constantly. This is not always possible in the pediatric age group; therefore, the results may not be very reliable. There was no significant difference in the latency or peak-to-peak amplitude between the groups in our study. The latencies were lower in group 1 but not statistically significant. Only one study has investigated VEMP values in patients with HT. They just stated that 52.2% of subjects with HT had alterations in VEMPs. However, they did not emphasize what those alterations were, and they did not precisely clarify their VEMP results. It is not clear whether these alterations are in the p1 or n1 peaks or the p1-n1 amplitude. But still, Chiarella et al suggested that VEMP is a sensible tool for the assessment of preclinical vestibular dysfunction in patients with HT. We did not find any differences in the cVEMP values between the groups. This may be related to the duration of the disease. Since we studied a pediatric population, the time to reveal electrophysiological vestibular dysfunction may not be sufficient. The smaller number of participants in the patient group may be another reason for this observation. Since there are few VEMP studies in HT patients, there is an absolute need for more studies with a larger number of participants to clarify the effect of HT on otoliths.

The head impulse test is a clinically useful test of VOR; nowadays, its computerized counterpart, vHIT, enables the objective assessment of VOR. We evaluated the lateral semicircular canals, and a

Table 1. Demographic Features of the Patients

Number of Subjects		Hashimoto's Disease	Control	P
		36	30	
Sex (female/male), n		33/3	26/4	.40
Age (years)	Mean ± SD	13.64 ± 2.44	12.93 ± 1.78	.14
	Median (range)	4 (7-17)	13 (10-16)	
Time to disease (months)	Mean ± SD	15.90 ± 24.0		
	Median (range)	0.0 (0.0–96)		

Fisher's exact test and Mann–Whitney *U*-test.
$P < .05$.

Table 2. Cervical-evoked Myogenic Potential (C-VEMP) Results of Both Groups

Number of Subjects		Hashimoto's Disease N: 36	Control N: 30	P
P1 latency (seconds)	Mean ± SD	15.86 ± 1.71	15.68 ± 0.96	.72
	Median (range)	15.67 (13.33-20.0)	15.84 (13.5-17.17)	
N1 latency (seconds)	Mean ± SD	25.26 ± 2.23	25.13 ± 1.96	.52
	Median (range)	25.50 (20.5-29.17)	25.0 (22.5-32.0)	
P1-N1 amplitude (µV)	Mean ± SD	129.54 ± 75.66	112.44 ± 80.01	.19
	Median (range)	123.75 (0.0-323.55)	98.07 (0.0-399.40)	

Mann–Whitney U-test.
$^{*}P < .05$.

Table 3. Horizontal Canal Video Head Impulse Test Gain (h-vHIT gain) Results for Both Groups

		Hashimoto's Disease (N: 36)	Control (N: 30)	P
		Mean ± SD (Range)	Mean ± SD (Range)	
H-vHIT gain	Right	0.80 ± 0.19 (0.42-1.20)	0.98 ± 0.12 (0.78-1.20)	**< .001**
	Left	0.73 ± 0.14 (0.40-1.04)	0.99 ± 0.13 (0.78-1.20)	**< .001**

Fisher's exact test. Values in bold indicate statistical significance.
H-vHIT, horizontal canal video head impulse test.

Table 4. This scheme shows abnormalities between two groups when 0.8 is considered as the cut-off values for vestibulo-ocular reflex (VOR) gain scores. 80.6% of patients with Hashimoto's disease had abnormal VOR gain values compared to only 3.3% in healthy subjects.

			Groups		*P*
			Hashimoto's Disease N: 36	Control N: 30	
vHIT gain	0-0.79	N	29	1	**<.001***
		%	80.6%	3.3%	
	0.8-1.2	N	7	29	
		%	19.4%	96.7%	

Fisher's exact test. The value in bold indicates statistical significance.
vHIT, video head impulse test.**P* < .05.

computer-based system calculated the VOR gain. We did not evaluate the vertical canals. There is no consensus regarding the reliability and validity of vertical canal responses for vHIT in the pediatric population.[16] Bell defined VOR gain as having a normative lower limit of 0.83 and upper limit of 1.21 for lateral semicircular canals 6[5] for adults. Our measurements in the HT groups for both ears were lower than the normal values and statistically different from those of normal healthy subjects. In the patient group, the VOR gains were statistically lower than those in the healthy group. Since the normal VOR gain cut-off limit is 0.8, when we used this cut-off value, 80.6% ($n=29$) of children with HT had VOR gains below this value. However, only one healthy subject had lower VOR gain < 0.8 value. This finding suggests that there may be subclinical peripheral bilateral vestibulopathy affecting the VOR in HT patients, particularly affecting the lateral semicircular canal. Since our patients with HT were euthyroid, we suggest that this effect is not related to blood thyroid hormone levels. Autoimmunity owing to circulating autoantibodies may play a leading role in this neuropathy. Chiarella et al. used the caloric test, head-shaking test, and VEMP values in euthyroid patients with HT to evaluate vestibular functions. They used a caloric test to evaluate semicircular canals and showed that 47.7% of HT patients had altered caloric test responses. We were also able to demonstrate differences in VOR gain between the groups. In our study, 80.6% of patients had lower VOR gain scores than the normal population. Thus, we can conclude that vHIT is a more sensitive clinical tool for evaluating preclinical vestibulopathy, specifically in euthyroid patients with HT. This is the first study to evaluate semicircular canals via vHIT in children with HT. There is an absolute need for further well-designed studies to assess this relationship. Compared to adults, children were more compliant during the vHIT test. Factors such as easier neck movements, better cooperation, and a better visual system made it easier for them to fixate on the visual target.

We were able to use it even in the pediatric population; therefore, we can recommend using vHIT for semicircular canal assessment in pediatric populations with HT. Preclinical vestibulopathy may occur, which may be beneficial in the future. However, as mentioned before, there is an absolute need for standard values for vertical canals in the vHIT in the pediatric population. Therefore, this research can be further detailed to examine vertical semicircular canals. There is also a need for follow-up studies in our group to assess further changes as patients grow older. This may clarify the impact of HT on the semicircular canals over time.

Limitations of Study

One of the limitations of this study is that we did not study oVEMP. One of the reasons for this was the technical application and interpretation problems of oVEMP in the pediatric population. Although it may be used in adolescent patients, it is not easy to use this tool specifically in preschool-aged children. We evaluated only the lateral canal responses, not the vertical canals, through vHIT. There are no available data about the VOR gain cutoff values in the pediatric population, and there is a publication stating that VOR gains of both anterior and posterior semicircular canals are quite variable.[16]

CONCLUSION

The vHIT enables an objective assessment of VOR. The test is noninvasive and easy to perform with experienced hands. Ear, nose, and throat specialists, audiologists, and audiometry technicians familiar with the battery can easily perform and interpret the results. We were able to show the decreased VOR gains in children with HT. This may be the first sign of preclinical vestibular end-organ dysfunction. Based on the results of the present study, the authors suggest that the study of VOR in children with HT might benefit from continued evaluation in older children or adults, particularly if the results reported in the present report are supported by additional investigations.

Ethics Committee Approval: This study was approved by the Ethics Committee of Umraniye Training and Research Hospital (approval number: 20915; date: 09.09.2022).

Informed Consent: Written informed consent was obtained from the parents of all participants who agreed to take part in the study.

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