

Provocation of Endolymphatic Hydrops With a Prick Test in Meniere's Disease

Bülent Topuz, MD
Gülşen Ögmen, MD
Fazıl Necdet Ardiç, MD
Cüneyt Orhan Kara, MD

Department of Otolaryngology Head and Neck Surgery
Pamukkale University
School of Medicine
Denizli, Turkey

ABSTRACT

This study was conducted to test the hypothesis that antigenic challenge is an important stimulative factor for an episode of endolymphatic hydrops. The study was held in a tertiary care center for patients with probable or definite Meniere's disease. The prick test, which included dietary and inhalant allergens, was applied to all patients with a Multi-Test Applicator (Lincoln Diagnostics, Decatur, Ill). Patients were tested with electrocochleography before and after the prick test. The positive allergen was diluted in 1/10 of a prick test dose, and patients were provoked and tested again. A negative summing potential/action potential (SP/AP) amplitude ratio greater than 0.5 was used as the main outcome measure. Pretest, posttest, and postprovocation SP/AP amplitude ratios were compared. A total of 80 diseased and 16 normal ears of 48 patients with Meniere's disease were assessed. All patients were found to be atopic, but none had allergic symptoms. No symptom like vertigo or fullness was seen after the prick test was performed. In all, 30 patients had tinnitus and fullness in the diseased ear, and 6 patients had vertigo after the provocation. The SP/AP ratio was greater than 0.50 in 23 diseased (29%) and 3 normal (19%) ears before the prick test. After the prick test, 62 diseased (78%) and 13 normal (81%) ears had endolymphatic hydrops. These numbers did not change much after the provocation. Results reported here support the role of antigenic stimulation for episodes of Meniere's disease. Endolymphatic hydrops was the atopic reaction that occurred in most study patients.

Keywords: | Meniere's disease; prick test; allergy

INTRODUCTION

Meniere's disease is an inner ear disorder that is characterized by episodic vertigo, tinnitus, aural fullness, and hearing loss. An episodic hydrostatic pressure increase in the endolymphatic compartment of the inner ear is responsible for this unique clinical picture of the disease.¹ The causes of endolymphatic hydrops (EH) have been extensively investigated. One of these involves an immunologic response to external allergic stimulation.

Evidence of allergic origin can be found in recent studies reported in the literature. Derebery and Berliner² reported a high incidence of allergic symptoms in patients with Meniere's disease. Positive skin test findings for specific allergens and a good response of Meniere symptoms to specific treatments have been described.^{3,4} A screening radioallergosorbent test (RAST) was positive in nearly 40% of patients with neurotologic symptoms.⁵ Levels of circulating immune complexes and total serum immunoglobulin E (IgE) levels were found to be higher in 42 of 59 patients than in the normal population.⁶

These studies and earlier case reports have revealed the role of allergy in the pathogenesis of Meniere's disease.^{7,8} Investigators planned a 2-stage investigation to determine the role of allergic stimulation in Meniere's disease. First, researchers tested patients with Meniere's disease to ascertain the prevalence of atopy. Second, investigators used the provocation test to find out whether this type of provocation is a triggering factor for an endolymphatic hydrops attack.

SUBJECTS AND METHODS

This study was conducted in collaboration with vertigo and allergy outpatient centers at a tertiary hospital. A total of 48 patients were included, all of whom were classified as having probable or definite Meniere's disease according to AAO-HNS (American Academy of Otolaryngology-Head and Neck Surgery) criteria.⁹ Patients were invited to the center by phone; the study was explained and written consents were obtained. No patients were using antihistamines, antidepressants, or steroids, and no eczematous skin lesions were reported at the testing site. All patients were in remission for neurotologic symptoms.

First, all patients completed a survey about their symptoms; then, pure tone audiometry, determination of speech discrimination score, and electrocochleography (EChoG) were performed. The prick test, which included dietary and inhalant allergens, was applied to all patients. Patients were tested with EChoG 30 to 45 min after the prick test was given again.

In the second phase, 1 to 2 hours after the prick test, patients were stimulated with antigens to which they had a positive reaction and correlation with patient history. If there was no correlation with patient history, the antigen that had the greatest induction was used for provocation. EChoG was then performed again.

Skin prick tests were performed with the Multi-Test Applicator (Lincoln Diagnostics, Decatur, Ill). Allergens used for testing included mite, grass, tree, weed, and epidermal mixes, and 32 types of food allergens. Negative control was provided by 50%

glycerosaline, and positive control was established by histamine phosphate (1 mg/mL histamine base) in 50% glycerosaline.

Skin prick tests were applied to the skin 3 cm distal to the elbow crease on the volar surfaces of the forearms. Tests were evaluated after 15 min. The wheal was first circled with a thin, felt-tipped pen and was then measured directly at the site with the use of a transparent, flexible ruler. If the wheal size of histamine was equal to or smaller than the wheal size of glycerosaline, the patient was excluded. If the wheal of an allergen was 1 mm larger than that of the negative control, the patient was classified as atopic. All wheal sizes were measured as the mean of the 2 longest perpendicular diameters.

The positive allergen was diluted in 1/10 of the prick test dose and was used for provocation. Then, 1 mL of the allergen was injected into the dermis of the left arm with an insulin injector.

Multisystem evoked potential unit (ICS CHARTR and CHARTR EP 1.44) software programs (GN Otometrics, Bloomington, Minn) were used for EChoG recordings. An average of 1024 90-dB alternating click stimuli were recorded (rate: 7.7/s; low-frequency cutoff: 10 Hz; high-frequency cutoff: 3 KHz). Electrode sites were cleaned with a special gel. Elefix Cream (Nihon Kohden, Tokyo, Japan) was used between skin and electrodes for good conduction. A gold-coated, tiptrode recording electrode was placed into the external ear canal. Inverting and ground electrodes were placed on the contralateral mastoid and forehead, respectively. Each test was repeated 3 times to establish stability of the waveforms. Summating potential (SP) and compound action potential (AP) amplitudes were measured. Amplitude was defined as the difference between baseline measurements and the peak of the wave.

The SP/AP amplitude ratio was used as the main outcome measure. According to normative data and the laboratory protocol, the SP/AP ratio (0.50) was accepted as abnormal. Results were compared with the use of a Student *t* test.

RESULTS

A total of 48 patients (38 female, 10 male) were included in the study. The average age of patients was 44.16 ± 11.1 y (range, 15–61 y). Meniere's disease was unilateral in 16 patients and bilateral in the rest. A total of 80 diseased ears and 16 normal ears were assessed. The average duration of the disease was 54.15 ± 46.5 mo (range, 11–240 mo). The average number of Meniere attacks was 2.58 ± 1.5 (range, 1–10). None of the patients had visited a doctor previously for an allergic incident.

All but 2 patients were atopic for more than 1 antigen. One patient was only atopic for egg white and another only for mite mix. Inhalant antigens were used for provocation in 29 patients, and dietary antigens were used in 19 patients.

After the provocation, 30 patients (12 food, 18 inhalant allergen positive) reported tinnitus and fullness in the diseased ear. Six patients (1 food, 5 inhalant allergen positive) had vertigo that lasted for minutes. In patients with vertigo, the wheals of allergens were larger than 5 mm. None of the above symptoms was observed after the prick test.

The SP/AP ratio was greater than 0.50 in 23 diseased (29%) and 3 normal (19%) ears, before the time of the prick test. After the test, endolymphatic hydrops had developed in 62 (77.5%) diseased ears (Table 1) and 13 (81.2%) normal ears (Table 2). Pre- and post-prick test SP/AP ratios were statistically different in diseased ears ($P<.001$).

Table 1. SP/AP Values of Diseased Ears and Changes After a Prick Test and Provocation (n=80)

	Number of Ears With SP/AP ≥ 0.50	Mean $\pm$ Std SP/AP	Min–Max SP/AP
Before prick test	23 (28.7%)	0.41 $\pm$ 0.12	0.11–0.64
After prick test	62 (77.5%)	0.61 $\pm$ 0.18	0.14–0.97
After provocation	58 (72.5%)	0.61 $\pm$ 0.17	0.14–0.94

In normal ears, statistically significant differences in SP/AP ratios were reported after prick tests ($P<.001$) (Table 2). The same statistical result was valid between pretest and postprovocation results ($P<.001$); however, no statistical difference was reported between the post-prick test and postprovocation SP/AP ratios.

The investigators did not compare normal and diseased ears because of huge differences between the numbers. When a total comparison (diseased + normal) was made between pretest and posttest results, the difference was significant ($P<.001$). No difference was reported between post-prick test and postprovocation results.

Both prick test and provocation showed stimulative effects on most ears. It is interesting to note that the SP/AP ratio was decreased in some ears (Table 3).

Table 2. SP/AP Values of Normal Ears and Changes After a Prick Test and Provocation (n=16)

	Number of Ears With SP/AP ≥ 0.50	Mean $\pm$ Std SP/AP	Min–Max SP/AP
Before prick test	3 (18.7%)	0.34 $\pm$ 0.11	0.13–0.55
After prick test	13 (81.2%)	0.65 $\pm$ 0.18	0.30–0.89
After provocation	14 (87.5%)	0.59 $\pm$ 0.21	0.09–0.88

Table 3. Changes in the Number of Ears With Endolymphatic Hydrops After a Prick Test and Provocation

		Meniere's Disease (n=80)	Normal (n=16)
At the beginning	Mean SP/AP ratio	0.41±0.12	0.34±0.11
	Ears with SP/AP higher than 0.5, n	23	3
Pretesting– posttesting	Mean increase in SP/AP ratio	0.21	0.31
	Ears with increased SP/AP ratio, n	78	15
	Ears with decreased SP/AP ratio, n	12	3
Pretesting– postprovocation	Mean increase in SP/AP ratio	0.20	0.25
	Ears with increased SP/AP ratio, n	77	17
	Ears with decreased SP/AP ratio, n	13	1
Posttesting– postprovocation	Mean increase in SP/AP ratio	0.00	–0.06
	Ears with increased SP/AP ratio, n	35	8
	Ears with decreased SP/AP ratio, n	45	10

DISCUSSION

The EChoG recording, especially the SP/AP ratio, was the best available test to show endolymphatic hydrops in the diagnosis of Meniere's disease.¹⁰⁻¹² A correlation between symptoms of the disease and the SP/AP ratio has been shown.¹³ Therefore, studies that seek to prove endolymphatic hydrops must use this test. Investigations of the relationship between antigen challenge and Meniere's disease most often depend on clinical chart reviews. A few studies have used EChoG in limited numbers of patients.^{7,8}

Viscomi and Bojrab⁷ used EchoG to test 5 selected patients with Meniere's disease. Patients reported dizziness, tinnitus, hearing loss, and aural fullness with dietary antigen provocation, or a decrease in symptoms with neutralization therapy. Investigators identified an increase in the SP/AP ratio during the attack period.⁷ Gibbs et al⁸ used a nasal provocation test on patients with Meniere's disease with known allergic symptoms. They found at least a 15% increase in the SP/AP ratio in 4 of 7 patients.⁸ Upon provocation of hydrops with a prick test, the investigators reported an increase in inner ear symptoms in the same patients.

The investigators found an increment in endolymphatic pressure in most ears. This pressure change was noted after the prick test and occurred at the same level after the provocation. Findings led investigators to believe that the provocative effect of the prick test was sufficient to promote an inner ear reaction. In the prick test, 38 different antigens were used at the same time; on the other hand, only 1 (but with a greater amount of antigen) was used in the provocation test. The investigators believed that ears do not need a high antigen dose for stimulation, and that provoked ears cannot respond electrophysiologically to additional stimulation, even when the stimuli are more powerful. Therefore, no difference was reported between post-prick test and

postprovocation EChoG results. On the other hand, although no symptoms were reported after the prick test, inner ear symptoms were described in more than half of patients after provocation (65%). Symptomatic effects seemed more likely to be related to the antigen dosage.

The basic effect of the prick test and provocation was to increase the release of histamine. This reaction is not limited to the provocation site; it can occur in any part of the body, including the inner ear. Symptoms in the inner ear can be explained as histaminergic reactions that lead to inflammation of the sac or stria vascularis and irregular circulation of the endolymph.

An interesting finding of this study was the reaction of normal ears to provocation. Nearly 80% of normal ears had an increase in the SP/AP ratio. It is anticipated that these nonsymptomatic ears will develop Meniere's disease in the future.

In all, 15% of diseased ears had decreased endolymphatic pressure after the prick test. The inner ear of these patients might be affected in a different way by allergic stimulation. Vasodilatation produced by a histaminergic reaction around the inner ear could increase endolymph circulation and decrease pressure. These patients must be studied to determine different etiologies of the condition (eg, vascular).

A notable finding of this study is the high prevalence of atopy in Meniere's disease. Forty-seven of 48 patients (97.7%) were atopic for inhalant allergens. The prevalence of inhalant allergen atopy was studied in a group of young patients (15–25 y).¹⁴ Investigators found that 127 of 277 subjects (46%) had a positive skin test response to inhalant allergens. No study included food allergens for comparison. The findings of the present study reveal that atopy seems more prevalent in patients with Meniere's disease than in the normal population, although the age groups are not comparable with previous studies.

CONCLUSION

Results reported here show that antigenic stimulation changes the SP/AP amplitude ratio in Meniere's disease. Endolymphatic hydrops seemed to occur as an atopic reaction in most study patients. Before additional interventions are provided, hydrops must be investigated in allergic patients without inner ear symptoms, with the goal of finding the specificity of the endolymphatic pressure increase in patients with Meniere's disease with a positive prick test. After this step is performed, an antigen challenge test may be useful in a routine clinical test battery for Meniere's disease, so that a new treatment protocol can be established for atopy-positive patients with Meniere's disease.

REFERENCES

1. Hallpike CS, Cairns H. Observations on the pathology of Meniere's syndrome. *J Laryngol Otolaryngol*. 1938;53:625-655.
2. Derebery MJ, Berliner KI. Prevalence of allergy in Meniere's disease. *Otolaryngol Head Neck Surg*. 2000;123:69-73.
3. Derebery MJ. Allergic management of Meniere's disease: an outcome study. *Otolaryngol Head Neck Surg*. 2000;122:174-182.

4. Derebery MJ, Valenzuela S. Ménière's syndrome and allergy. *Otolaryngol Clin North Am.* 1992; 25:213-224.
5. Howard BK, Mabry RL, Meyerhoff WL, Mabry CS. Use of a screening RAST in a large neuro-otologic practice. *Otolaryngol Head Neck Surg.* 1997;117:653-659.
6. Zhu X, Hsu L, Zhao Y. Immunoglobulin E and circulating immune complexes in endolymphatic hydrops. *Ann Otol Rhinol Laryngol.* 1990;99:535-538.
7. Viscomi GJ, Bojrab DI. Use of electrocochleography to monitor antigenic challenge in Menière's disease. *Otolaryngol Head Neck Surg.* 1992;107:733-737.
8. Gibbs SR, Mabry RL, Roland PS, Shoup AG, Mabry CS. Electrocochleographic changes after intranasal allergen challenge: a possible diagnostic tool in patients with Meniere's disease. *Otolaryngol Head Neck Surg.* 1999;121:283-284.
9. Monsell EM, Balkany TA, Gates GA, Goldenberg RA, Meyerhoff WL. Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease. *Otolaryngol Head Neck Surg.* 1995;113:181-185.
10. Ferraro JA, Tibbils RP. SP/AP area ratio in the diagnosis of Meniere's disease. *Am J Audiol.* 1999;8:21-28.
11. Ruth RA, Lambert PR, Ferraro JA. Electrocochleography: methods and clinical applications. *Am J Otol.* 1988;9(suppl 1):11.
12. Pappas DG Jr, Pappas DG Sr, Carmichael L, Hyatt DP, Toohey LM. Extratympanic electrocochleography: diagnostic and predictive value. *Am J Otolaryngol.* 2000;21:81-87.
13. Ferraro JA, Arenberg IK, Hassanein RS. Electrocochleography and symptoms of inner ear dysfunction. *Arch Otolaryngol.* 1985;111:71-74.
14. Sin A, Köse S, Terzioğlu E, Kokuludag A, Sebik F, Kabakçı T. Prevalence of atopy in young healthy population, in Izmir, Turkey. *Allergol Immunopathol (Madr).* 1997;25:80-84.