

Meniett Device in Meniere Disease: Randomized, Double-Blind, Placebo-Controlled Multicenter Trial

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Objective: To evaluate the efficacy of portable Meniett low-pressure pulse generator (Medtronic Xomed, Jacksonville, FL) in Meniere disease.

Study Design: Randomized, double-blind, placebo-controlled, multicenter trial carried out in 17 academic medical centers.

Methods: One hundred twenty-nine adults presenting Meniere disease (American Academy of Otolaryngology–Head and Neck Surgery criteria) not controlled by conventional medical treatment were included. The protocol included three phases: 1) placement of a transtympanic tube and evaluation of its effect (if resolution of symptoms, the patient was excluded); 2) randomization: 6-weeks treatment with Meniett (Medtronic Xomed) or placebo device; 3) removal of the device and 6-week follow-up period. The evaluation criteria were the number of vertigo episodes (at least 20 minutes with a 12-hour free interval) and the impact on daily life as assessed by self-questionnaires.

Results: Ninety-seven patients passed to the second phase of the study: 49 and 48 patients received the Meniett (Medtronic Xomed) or the placebo device, respectively. In the placebo group, the number of vertigo episodes decreased from 4.3 ± 0.6 (mean \pm standard error of the mean) during the first phase to 2.6 ± 0.5 after 6 weeks of treatment, and to 1.8 ± 0.8 after the removal of the device. Similar results were observed in the Meniett device (Medtronic Xomed) group: 3.2 ± 0.4 episodes during the first phase, $2.5 \pm$ after 6 weeks of Meniett device (Medtronic Xomed) treatment, and 1.5 ± 0.2 after the third phase.

Conclusion: An improvement of symptoms was evidenced in all patients, with no difference between the Meniett (Medtronic Xomed) and the placebo device groups. The decrease in the number of vertigo episodes could be explained by an effect of the medical care.

Key Words: Transtympanic tube, inner ear, placebo, endolymphatic hydrops, vertigo.

Level of Evidence: 1b.

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INTRODUCTION

Meniere disease is a chronic illness that affects approximately 0.2% of the world's population. The estimated annual incidence of the disease is two per 1,000.¹ Its origin is an imbalance in inner ear hydrodynamics. To date a poorly understood physiopathology, this syndrome is characterized by sudden and repeated vertigo, hearing loss, feeling of pressure in the ear, and tinnitus.² Vertigo can last hours or even days, during which time the patient is often bedridden. The disease can

have a significant effect on quality of life, including a not insignificant risk of workplace injury.³

Because of the natural history of Meniere disease, benefit of each treatment should be compared to a spontaneous improvement and to the well-known placebo effect. Symptoms for a long time have been treated by medications such as betahistine, steroids, and diuretics; however, their effect on hearing loss and the long-term evolution of the disease has not yet been established.⁴ In severe cases that are resistant to medical treatment, chemical or surgical labyrinthectomy is considered, but a debate on the risk–benefit ratio still exists.^{5–8} Therefore, effective and less invasive treatments eagerly are awaited.

In this context, it long has been shown that changes in local pressure in the middle ear could have a positive effect on Meniere disease.^{9–12} In vivo studies showed that the insertion of a transtympanic tube could reduce the development of endolymphatic hydrops, resulting in an improvement of symptoms.¹³ A similar effect was also noticed in patients with Meniere disease,¹⁴ where it has been shown that the inner ear hydrodynamic system balance could be corrected with low-pressure air pulses in the middle ear. The development of the miniaturized, portable Meniett device (Medtronic Xomed, Jacksonville,

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FL) may provide the accessibility of this treatment.^{15–19} The results of an initial placebo-controlled study with the Meniett device developed by Medtronic Xomed have been positive, and the trial was able to document the ease of use and safety of the device.¹⁹

The present prospective, multicenter, double-blind placebo-controlled study aims to validate the effectiveness and assess the benefits of the Meniett device (Medtronic Xomed) on number of vertigos, as well as on quality of life of patients affected by Meniere disease. Additionally, the introduction of a run-out period should permit estimation of the possible residual effects of this method. Considering both the spontaneous and unpredictable occurrence of Meniere disease and the difficulty in predicting its natural evolution over a given period, a controlled trial is crucial. Moreover, because the use of the Meniett device (Medtronic Xomed) requires insertion of a transtympanic tube, it is necessary to demonstrate that its effectiveness is not only a result of the transtympanic tube.

MATERIALS AND METHODS

This study was a multicenter (17 centers; see Acknowledgements), randomized, double-blind, placebo-controlled study. The protocol was approved by the local institutional boards.

Patients' Selection

An analysis with power calculation was performed for the study design. Given the lack of published data concerning the evolution of vertigos following placement of a transtympanic tube, the calculation was made considering the percentage of subjects who are free of symptom. Based on the results of previous studies,^{14,20} the percentage of patients who no longer experience vertigo following drain placement was estimated between 50 and 66. Thus, the number of 47 patients per group was adapted to detect a possible variation of 30% of the Meniett (Medtronic Xomed) over the placebo device (alpha risk 5%, beta risk 20%, two-sided test).

After giving their written consent, all patients underwent complete ear, nose, and throat (ENT) examination, and audiometry and videonystagmometry tests were conducted to confirm the diagnosis. All patients were adults over 18 years old age, affected by a stage 2 or greater unilateral definite Meniere disease, according to the American Academy of Otolaryngology–Head and Neck Surgery (AAO–HNS) criteria.² Patients were included if they experienced at least two episodes of rotatory vertigo in the preceding 2 months (vertigo lasting at least 20 minutes, with a free interval of 12 hours), with or without associated tinnitus, and/or a sensation of fullness in the ear. Moreover, the impact of vertigo on the patient's daily life had to be at level 3, at least on the functionality level according to AAO–HNS criteria. Patients who had undergone surgical treatment or chemical labyrinthectomy for Meniere disease were excluded.

Phases of the Protocol

The clinical protocol comprised three phases (Fig. 1).

First Phase. Placement of the transtympanic tube associated with the complete withdrawal of any anti-vertigo treatment, followed by a period of 8 weeks maximum (56 days), with recording of the number of vertigo episodes. The objective was to ensure the washout of any earlier anti-vertigo treatment and to document the onset of at least two episodes of vertigo. This

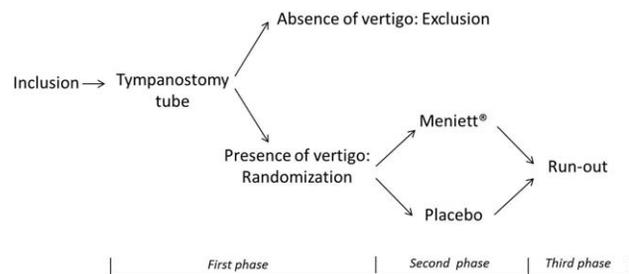


Fig. 1. Study design. Mean duration of the first phase was 35 days. The second and the third phase had duration of ~42 days each and were divided into two periods of ~21 days. Number of patients entering each phase: first phase = 129 patients; second phase = 49 Meniett (Medtronic Xomed, Jacksonville, FL) and 48 placebo devices; third phase = 47 Meniett (Medtronic Xomed) and 45 placebo devices.

phase had a mean duration of 33 days (median: 28 and 29 days, in placebo and Meniett device [Medtronic Xomed] groups, respectively). If patients had at least two episodes of vertigo, they were included in the second phase.

Second Phase. In this phase, with a duration of 6 weeks (45 days), the patients were randomly assigned under double-blind conditions to receive either the Meniett (Medtronic Xomed) or a placebo device. Randomization was performed by blocks of four. Each center received a block of four devices (2 Meniett [Medtronic Xomed] and 2 placebo). If necessary, according to the rate of inclusion in a given center, more blocks of four devices were distributed to the center. The boxes were randomly numbered and the physician did not know their content and had to distribute them to the patients. The placebo was identical in all aspects to the active device but did not generate pressure pulses. The patients were instructed to use the device three times daily for 15 minutes each; the pressure pulsed waves were at a frequency of 6 Hz and a maximum pressure of 12 cm/H₂O. Patients were seen at 3 weeks (day 21 ± 3) and at the end of the 6-week period (day 42 ± 3).

Third Phase. At the end of second phase, the Meniett (Medtronic Xomed) or the placebo device was removed, and the evolution of the number of vertigo attacks was observed for an additional 6-week period. Also during this phase, the patients were seen at 3 weeks (day 21 ± 3) and at the end of the 6-week period (day 42 ± 3).

Assessment Parameters

At each visit, the permeability of the transtympanic tube was verified.

During the three phases, the patients were asked to record in a journal all the attacks they had during the day and their duration. The patients had to score their vertigo attacks by mean of a visual analog scale ranging from 1 (very weak vertigo) to 10 (unbearable vertigo attack).

The main assessment criteria of the therapeutic impact of the Meniett device (Medtronic Xomed) were the number of vertigo episodes lasting at least 20 minutes during each study phase. Two successive episodes were considered to be distinct if they occurred at a minimum asymptomatic interval of 12 hours; otherwise, they were considered a single episode.

The second parameter was the evolution of the impact of vertigo on daily life as evaluated with the AAO–HNS scale.

Randomization and Statistical Analysis

Data are given as means ± standard error of the mean. To test the homogeneity of the two study groups, a Chi-squared

TABLE I.
General Characteristics of Population.

	Age (years)	Sex	Weight (kg)	Height (cm)	BMI (kg/m ²)	Blood pressure (mm Hg)
Placebo (n = 48)	50 ± 1.9	Men: 47% Women: 53%	72 ± 2.2	168 ± 1.4	25.7 ± 2.0	Systolic: 129 ± 0.3 Diastolic: 78 ± 1.5
Meniett device* (n = 49)	52 ± 1.6	Men: 40% Women: 60%	67 ± 1.8	165 ± 1.2	24.8 ± 0.7	Systolic: 127 ± 1.8 Diastolic: 77 ± 1.3

Blood pressure were measured after a 10-minute rest period. Values are means ± standard error of the mean. The number of patients is in parentheses. No difference was observed for these data between the two groups of patients (Chi-squared test for age and sex; *t* test for mean comparison).

*Medtronic Xomed, Jacksonville, FL.

BMI = body mass index.

test was performed for age and sex, or a *t*-test for mean comparison. Two-way analysis of variance (ANOVA) (factors: treatment and time) followed by a Tukeys's honest significant difference (HSD) post-hoc test were used to analyze the influence of Meniett (Medtronic Xomed) or placebo device and time over the vertigo episodes.

All the statistical analysis was performed using IBM SPSS for Windows (V22.0, SPSS inc., Chicago, IL). For all comparisons, *P* < 0.05 was considered significant.

RESULTS

Characteristics of the Population

One hundred twenty-nine patients were enrolled and had a transtympanic tube insertion. Among them, 32 patients (26%) showed the complete absence of vertigo during the first phase of 6 weeks. Therefore, 97 patients were included in the second phase. After the randomization, 49 patients were treated with the Meniett device (Medtronic Xomed) and 48 with the placebo device. Considering the clinical data of the population (sex ratio, age, weight, height, body mass index, blood pressure), the two groups were homogeneous (Table I).

The duration of Meniere disease ranged from 0.22 to 24.5 months (mean 5 ± 0.81 months), and from 0.15 to 26.5 months (mean 7 ± 0.97 months) in the placebo and Meniett device (Medtronic Xomed) groups, respectively. The number of vertigo episodes, including dizziness, during the previous 6 months was comparable in the Meniett device (Medtronic Xomed) group (36 ± 4.6, range 4–180, median: 30) and in the placebo device group (28 ± 3.0, range 3–72, median: 23) (Student *t* test *P* = 0.07). The impact of vertigo estimated by the patient on the AAO–HNS scale was 4.3 ± 0.10 (range: 3–5, median: 4) in the placebo group and 4.5 ± 0.093 (range 3–5, median: 5) in the Meniett device (Medtronic Xomed) group.

Evolution of the Number of Vertigo Episodes Lasting More Than 20 Minutes During the Different Phases

A decrease of the number of the vertigo episodes lasting more than 20 minutes occurred in both groups in the second phase compared to the first one and persisted during the third phase when the devices were removed (Fig. 2). In the placebo group, the number of vertigo

episodes decreased from 4.3 ± 0.6 during the first phase to 2.6 ± 0.5 after 6 weeks of treatment, and to 1.8 ± 0.8 after the third phase. Similar results were observed in the Meniett device (Medtronic Xomed) group: 3.2 ± 0.4 episodes during the first phase, 2.5 ± after 6 weeks of Meniett device (Medtronic Xomed) treatment, and 1.5 ± 0.2 after the third phase. A decrease of vertigo episodes was observed in both groups if comparing the first phase to the end of the second phase, and if comparing the episodes recorded after the first 21 days of the second phase and the third phase (Figure 2) (Tukeys's HSD post-hoc test). However, there was no significant difference between the two study groups at all the phases of the study (two-ways ANOVA, *F* = 2.57, *P* = 0.11).

Considering the individual evolution, a decrease in the number of vertigo episodes was observed in both groups during the second and the third phase compared to the first phase. Table II shows the number of patients who have improved, worsened, or who were stable for each period of 21 days. No difference was found between the two groups (Fisher's exact test). Overall, 10% of patients aggravated their symptoms; 30% were stable; and 60% improved their symptoms. It should be noticed

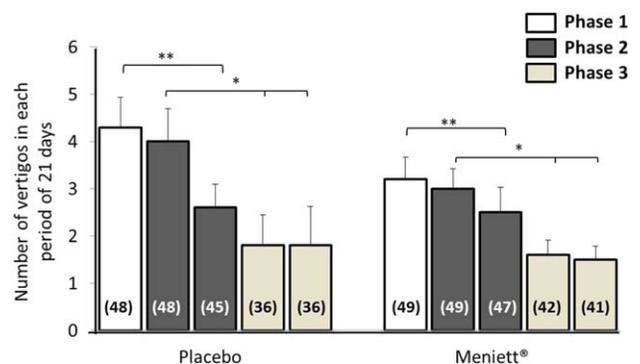


Fig. 2. Number of vertigo episodes at the different endpoints for Meniett (Medtronic Xomed, Jacksonville, FL) and placebo device groups. The first phase had a mean duration of 35 days. The second and the third phase had duration of ~42 days each and were divided into two periods of ~21 days. Values are means ± standard error of the mean. Number of patients in parentheses. Two-way analysis of variance (factors: treatment and time) followed by a Tukeys's honest significant difference post-hoc test. **P* < 0.005; ***P* < 0.03. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE II.
Evolution of the Number of Vertigo Episodes Lasting More Than 20 Minutes in Patients With Placebo or Meniett Device,* Compared to Those Recorded During the First Phase.

		Placebo	Meniett Device*
Second Phase			
1st period	Worsening	12/48	16/49
	No change	12/48	8/49
	Improved	24/48	25/49
	Lost	0	0
2nd period	Worsening	10/45	17/47
	No change	9/45	4/47
	Improved	26/45	26/47
	Lost	3	2
Third Phase			
1st period	Worsening	2/36	7/42
	No change	11/36	5/42
	Improved	23/36	30/42
	Lost	9	5
2nd period	Worsening	5/36	2/41
	No change	11/36	12/41
	Improved	20/36	27/41
	Lost	0	1

The second and third phases had duration of ~42 days each, and were divided in two periods of ~21 days. The values are number of patients/total.

*Medtronic Xomed, Jacksonville, FL.

that five patients interrupted the treatment after the end of the second phase (3 placebo, 2 Meniett [Medtronic Xomed]) and 15 patients during the third phase (9 placebo, 6 Meniett [Medtronic Xomed]).

Evolution of Short Duration Vertigo and Dizziness

The number of the short duration vertigos (5–20 minutes) and the number of dizziness episodes (vertigos of less than 5-minute duration) remained stable in both

groups during the three phases (Table III). The decrease of the number of 20-minute vertigos during the treatment and the run-out periods was clearly not associated to an increase in shorter vertigos or dizziness.

Impact of Vertigo in Daily Life

Concerning the impact of vertigo on quality of life, whatever the treatment—Meniett device (Medtronic Xomed) or placebo—the quality of life of the patient was improved, and this even after the treatment was removed, with no significant difference between the two groups of patients (Table IV).

DISCUSSION

This study shows that after placement of a transtympanic tube, there was an overall improvement of symptoms in patients with Meniere disease, and this improvement persisted after Meniett (Medtronic Xomed) or placebo device treatment without significant difference between these two later groups.

The improvement of the symptoms was evident immediately after placement of the transtympanic tube; indeed, after the first phase, 26% of the patients were excluded from the study due to the absence of vertigo episodes. A transtympanic tube effect had been first evidenced in guinea pigs,²¹ where the middle-ear ventilation reduced the development of endolymphatic hydrops induced by the blockage of the endolymphatic duct. The authors proposed that inhibition of the hydrops was due to pressure release into the middle ear and/or improved oxygenation of the middle and inner ears. In patients with Meniere disease, Barbara et al.¹⁷ evidenced a major effect of the transtympanic tube, the number of vertigo decreasing from 9 to 1 after a 40-day period.

During the subsequent phase of the study, an overall improvement in the number of vertigo episodes was evidenced, without difference between the group treated with middle ear pressure therapy by the Meniett device (Medtronic Xomed) and the group that received a placebo device. Moreover, this improvement persisted about a

TABLE III.
Number of Vertigo Episodes Lasting Less Than 20 Minutes.

	First Phase	Second Phase		Third Phase
	With tube only ~33 days	1st period ~21 days	2nd period ~42 days	~42 days
N vertigo 5–20 minutes/3 weeks				
Placebo	0.7 ± 0.38 (48)	1.0 ± 0.32 (48)	0.4 ± 0.20 (45)	0.05 ± 0.036 (36)
Meniett device*	0.5 ± 0.19 (49)	0.7 ± 0.19 (49)	0.4 ± 0.16 (47)	0.2 ± 0.08 (41)
N vertigo < 5 minutes/3 weeks				
Placebo	0.4 ± 0.16 (48)	1.2 ± 0.72 (48)	2.0 ± 1.01 (45)	0.5 ± 0.23 (36)
Meniett device*	0.6 ± 0.46 (49)	0.7 ± 0.40 (49)	1.3 ± 0.67 (47)	0.4 ± 0.20 (41)

Values are means ± standard error of mean. The number of patients is in parentheses.

During the third phase, after the removal of the device, the number of the vertigo episodes lasting less than 20 minutes were collected during the whole first + second period (i.e., ~45 days). For easier comparison with the previous phases, the indicated data was the number of vertigo registered during the third phase expressed on a 21-day period. For easier comparison between the different columns, the number of vertigos during the run-out period are referred to a 3-week period.

*Medtronic Xomed, Jacksonville, FL.

TABLE IV.
Impact of Vertigo in Daily Life.

	Initial	End of First Phase	End of Second Phase ~42 days	End of Third Phase ~42 days
Placebo	4.3 ± 0.10 (48)	4.0 ± 0.12 (48)	2.6 ± 0.21 (45)	2.8 ± 0.22 (36)
Meniett device*	4.5 ± 0.09 (49)	4.2 ± 0.12 (49)	2.8 ± 0.21 (47)	2.8 ± 0.25 (41)

Values are means ± standard error of the mean. The number of patients is in parentheses.

The impact of the vertigo was estimated by the patient on the visual analog scale.

*Medtronic Xomed, Jacksonville, FL.

month and a half after the end of the treatment; and after the third phase, 60% of all the patients showed an improvement in symptoms, suggesting a positive effect of the transtympanic tube and/or of the medical care in general.

These observations lead to pose some questions concerning the diagnosis of Meniere disease. The clinical diagnosis of Meniere's disease is universally accepted to be based on AOS-HNS criteria. Nevertheless, an instrumental diagnosis of endolymphatic hydrops can be realized by means of electrocochleography (ECoG).^{22,23} Although for some authors the only reliable diagnosis of Meniere's disease is clinical,²⁴ the symptoms of the disease are very variable and heterogeneous; to assess the effectiveness of a device, an objective instrumental finding concerning the condition of the inner ear appears to be necessary. A weakness of the present study is the lack of an objective assessment of inner ear status at the inclusion phase, for example, by means of ECoG. Indeed, the diagnosis of Meniere disease only was defined by clinical parameters, as recommended by AAO-NHS. We can hypothesize that some patients did not have an active endolymphatic hydrops. Considering the whole population at the end of the protocol, 60% of the patients had a decrease in the number of long-duration vertigo episodes. This percentage can be considered high and may raise some issues concerning the patients selection.

The relationship between the middle ear (which is easily accessible) pressure changes and the inner ear pressure changes, in connection with endolymphatic approaches, has been the subject of several experimental and clinical studies.²⁵ Most of these studies support the hypothesis that continuous or intermittent pressure to the middle ear could prevent the development of endolymphatic hydrops (in animal)²⁶ or could improve both the clinical symptoms and the electrophysiological hearing parameters in patients with Meniere disease.²⁷ Nevertheless, evaluation of the effectiveness of treatments for Meniere disease incurs considerable difficulties because of the natural course of the disease, characterized by spontaneous remissions and placebo effect. This may explain the different conclusion of several literature reviews concerning the Meniett device (Medtronic Xomed), some of them assessing a positive effect of this treatment^{28,29} and others the inefficacy of it.^{30,31}

Many randomized controlled studies were realized in order to investigate the expected placebo effect. The

first published study¹² reported improvement concerning the frequency and intensity of vertigo, and also hearing and electrocochleographic recordings, in 31 patients compared to 25 who had a placebo device. Unfortunately, these very encouraging results were not reproduced in the following studies. Gates et al.¹⁰ studied 67 patients and reported less severe vertigo, fewer days with definite vertigo, and fewer days lost from work, but no difference in hearing and electrocochleographic results between the two groups of patients. One year later, Thomsen et al.⁹ evidenced an improved functionality level in the 20 treated patients compared to the 20 who received the placebo, but the difference in the frequency of the vertiginous attacks was clearly not significant. However, the central issue is the selection criteria of the patients. Gates et al. included medical treatment-resistant patients and a median duration of treatment of 4.5 years. The patients in Thomsen's study had variable disease duration, ranging from less than 1 year to 37 years, with a median between 5 and 10. In the present study, the patients had disease duration much shorter, less than 2 years.

One suggestion could be that local pressure treatment should be indicated, and effective, in case of well-established and resistant disease at an early stage.

CONCLUSION

The benefit of the treatment assessed in about the 60% of the patients in both study groups, Meniett (Medtronic Xomed) or placebo device, strongly suggests a positive effect of the medical management in patients suffering from Meniere disease independently from the treatment. Nevertheless, because this effect persisted at the end of the active treatment phase, a pressure effect of the transtympanic tube can be suspected. Moreover, this effect has been rapidly evidenced in 32 patients who were not included after the first phase. Further studies are necessary to investigate this beneficial effect of the transtympanic tube and to determine patients who would improve their symptomatology by this procedure. Special attention is needed considering the heterogeneity of this disease in order to define the hydrops evolutivity. Indeed, it is clear from this study that the clinical classification is not sufficient: electrophysiological data (e.g., ECoG) would be needed to more precisely select the patients.

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BIBLIOGRAPHY

- Alexander TH, Harris JP. Current epidemiology of Meniere's syndrome. *Otolaryngol Clin North Am* 2010;43:965–970.
- Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease American Academy of Otolaryngology—Head and Neck Foundation, Inc. *Otolaryngol Head Neck Surg* 1995;113:181–185.
- Porter M, Boothroyd RA. Symptom severity, social supports, coping styles, and quality of life among individuals' diagnosed with Meniere's disease. *Chronic Illn* 2015;11:256–266.
- Martin Gonzalez C, Gonzalez FM, Trinidad A, et al. Medical management of Meniere's disease: a 10-year case series and review of literature. *Eur Arch Otorhinolaryngol* 2010;267:1371–1376.
- Quagliari S, Gatti O, Rebecchi E, Manfrin M, Tinelli C, Mira E, Benazzo M. Intratympanic gentamicin treatment 'as needed' for Meniere's disease. Long-term analysis using the Kaplan-Meier method. *Eur Arch Otorhinolaryngol* 2014;271:1443–1449.
- McRackan TR, Best J, Pearce EC, et al. Intratympanic dexamethasone as a symptomatic treatment for Meniere's disease. *Otol Neurotol* 2014;35:1638–1640.
- Van de Heyning PH, Wuyts F, Boudewyns A. Surgical treatment of Meniere's disease. *Curr Opin Neurol* 2005;18:23–28.
- Kim HH, Wiet RJ, Battista RA. Trends in the diagnosis and the management of Meniere's disease: results of a survey. *Otolaryngol Head Neck Surg* 2005;132:722–726.
- Thomsen J, Sass K, Odkvist L, Arlinger S. Local overpressure treatment reduces vestibular symptoms in patients with Meniere's disease: a clinical, randomized, multicenter, double-blind, placebo-controlled study. *Otol Neurotol* 2005;26:68–73.
- Gates GA, Green JD Jr, Tucci DL, Telian SA. The effects of transtympanic micropressure treatment in people with unilateral Meniere's disease. *Arch Otolaryngol Head Neck Surg* 2004;130:718–725.
- Gates GA, Green JD Jr. Intermittent pressure therapy of intractable Meniere's disease using the Meniett device: a preliminary report. *Laryngoscope* 2002;112:1489–1493.
- Odkvist LM, Arlinger S, Billermark E, Densert B, Lindholm S, Wallqvist J. Effects of middle ear pressure changes on clinical symptoms in patients with Meniere's disease—a clinical multicentre placebo-controlled study. *Acta Otolaryngol Suppl* 2000;543:99–101.
- Park JJ, Chen YS, Westhofen M. Meniere's disease and middle ear pressure: vestibular function after transtympanic tube placement. *Acta Otolaryngol* 2009;129:1408–1413.
- Montandon P, Guillemin P, Hausler R. Effets favorables des aérateurs transtympaniques sur les vertiges du syndrome de Meniere. *J Fr Otorhinolaryngol Audiophonol Chir Maxillofac* 1987;36:9–12.
- Boudewyns AN, Wuyts FL, Hoppenbrouwers M, et al. Meniett therapy: rescue treatment in severe drug-resistant Meniere's disease? *Acta Otolaryngol* 2005;125:1283–1289.
- Gates GA. Treatment of Meniere's disease with the low-pressure pulse generator (Meniett device). *Expert Rev Med Devices* 2005;2:533–537.
- Barbara M, Consagra C, Monini S, Nostro G, Harguindey A, Vestri A, Filipo R. Local pressure protocol, including Meniett, in the treatment of Meniere's disease: short-term results during the active stage. *Acta Otolaryngol* 2001;121:939–944.
- Peterson WM, Isaacson JE. Current management of Meniere's disease in an only hearing ear. *Otol Neurotol* 2007;28:696–699.
- Thomsen JC, Sass K, Odkvist L, Arlinger S. [Local overpressure treatment reduces vestibular symptoms in patients with Meniere's disease—secondary publication. A clinically randomised multicenter double-blind placebo-controlled study]. [Article in Danish]. *Ugeskr Laeger* 2006;23;168:378–380.
- Sugawara K, Kitamura K, Ishida T, Sejima T. Insertion of tympanic ventilation tubes as a treating modality for patients with Meniere's disease: a short- and long-term follow-up study in seven cases. *Auris Nasus Larynx* 2003;30:25–28.
- Kimura RS, Hutta J. Inhibition of experimentally induced endolymphatic hydrops by middle ear ventilation. *Eur Arch Otorhinolaryngol* 1997;254:213–218.
- Hornibrook J, Kalin C, Lin E, O'Beirne GA, Gourley J. Transtympanic electrocochleography for the diagnosis of Meniere's disease. *Int J Otolaryngol* 2012;2012:852714.
- Claes GM, De Valck CF, Van de Heyning P, Wuyts FL. The Meniere's disease index: an objective correlate of Meniere's disease, based on audiometric and electrocochleographic data. *Otol Neurotol* 2011;32:887–892.
- Le CH, Truong AQ, Diaz RC. Novel techniques for the diagnosis of Meniere's disease. *Curr Opin Otolaryngol Head Neck Surg* 2013;21:492–496.
- Bouccara D, Ferrary E, El Garem H, Couloigner V, Coudert C, Sterkers O. Inner ear pressure in Meniere's disease and fluctuating hearing loss determined by tympanic membrane displacement analysis. *Audiology* 1998;37:255–261.
- Sakikawa Y, Kimura RS. Middle ear overpressure treatment of endolymphatic hydrops in guinea pigs. *ORL J Otorhinolaryngol Relat Spec* 1997;59:84–90.
- Densert B, Densert O, Arlinger S, Sass K, Odkvist L. Immediate effects of middle ear pressure changes on the electrocochleographic recordings in patients with Meniere's disease: a clinical placebo-controlled study. *Am J Otol* 1997;18:726–733.
- Mattox DE, Reichert M. Meniett device for Meniere's disease: use and compliance at 3 to 5 years. *Otol Neurotol* 2008;29:29–32.
- Ahsan SF, Standring R, Wang Y. Systematic review and meta-analysis of Meniett therapy for Meniere's disease. *Laryngoscope* 2015;125:203–208.
- Syed MI, Rutka JA, Hendry J, Browning GG. Positive pressure therapy for Meniere's syndrome/disease with a Meniett device: a systematic review of randomised controlled trials. *Clin Otolaryngol* 2015;40:197–207.
- van Sonsbeek S, Pullens B, van Benthem PP. Positive pressure therapy for Meniere's disease or syndrome. *Cochrane Database Syst Rev* 2015;3:CD008419. doi: 10.1002/14651858.CD008419.pub2