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Original Article

The Clinical Benefit of Device Therapy for Meniere's Disease in Adults: Systematic Review and Meta-Analysis

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OBJECTIVES: This study aimed to assess the clinical benefit of device therapy on controlling the symptoms of Meniere's disease (MD).

MATERIALS AND METHODS: We searched PubMed, Embase, the Cochrane Library, China National Knowledge Internet, and Wanfang Data before January 13, 2018. We selected randomized controlled clinical trials, case-controlled studies, and cohort studies that dealt with outcomes of device therapy for the treatment of MD.

RESULTS: Sixteen trials met our inclusion criteria. The use of device therapy resulted in improved vertigo control, which was described as a reduction in the number of vertigo days by month (weighted mean difference [WMD]: 3.15, 95% confidence interval [CI]: 2.00-4.31), in the number of vertigo episodes by month (WMD: 7.37, 95% CI: 2.40-12.35), and in the vertigo visual analog score (WMD: 41.51, 95% CI: 34.68-48.34). In addition, the overall complete vertigo control (class A) rate was 50% (95% CI: 37%-64%). The device therapy also reduced the number of sick days by month (WMD: 4.56, 95% CI: 2.15-6.97), and the functional level improved (WMD: 2.66, 95% CI: 2.15-3.17). The electrocochleographic parameters decreased. The device therapy proved beneficial for hearing changes (WMD: 3.19, 95% CI: 0.66-5.71). No publication bias was found in the funnel plot and the results of Egger's test.

CONCLUSION: This study showed that the device therapy might reduce vertigo attacks and sick days in patients with MD. Additionally, the function level and hearing level may improve after the device therapy. In addition, the decrease in electrocochleographic parameters showed that inner ear electrophysiology improved after device therapy.

KEYWORDS: Meniere's disease, device therapy, vertigo control, function level, hearing level, inner ear electrophysiology, meta-analysis

INTRODUCTION

Meniere's disease (MD) [1, 2] is a chronic inner ear disorder that was first reported by French physician Prosper Meniere in 1861. The etiology of MD is still unclear, and abnormal microcirculation in the inner ear has been considered to be an important histopathological feature of the syndrome linked to MD [3]. In 1995, a consensus for the diagnostic guidelines of MD was reached by the American Academy-Head and Neck Surgery (AAO-HNS) [1]. An American study [4] reported that the lower limit of MD prevalence in the United States population was 73 per 100,000. Another study [5] reported that the prevalence of MD in the United Kingdom was 13.1 per 100,000 person-years; more patients were female, and it was rare among children.

MD is a cruel disease whose typical disorder is currently defined as recurrent vertigo, low-frequency hearing loss, tinnitus and sensation of aural fullness [6]. The episodes of symptoms usually start with cochlear symptoms, which soon appear as vertigo, and may last for a few minutes to several hours. The recurring episodes of symptoms [7] indicate that there would never be an end to them throughout the patient's life. Physical dysfunction affects patients with MD, and it causes mental problems that consist of anxiety and depression, making sufferers unable to maintain a normal life.

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Since MD was first reported, a variety of different treatments [8, 9], including dietary management (a low-salt diet) and typical medical treatments (betahistine or diuretics), surgery and invasive procedures (intra-tympanic injections of steroids orgentamycin), have been used to treat or control the symptoms. However, some patients fail to respond to medical treatment, [10] and they are not eligible for surgery [11]. None of the current medical or surgical treatments can be expected to reduce symptoms for these patients [10]. There is lack of a specific method to control the symptoms of these patients with MD. Effective and minimally invasive treatments are awaited.

Device treatment, including the Meniett device (acting on the middle ear through an implanted tympanic ventilation tube) and other devices have been widely used for recalcitrant MD. We wondered whether the device treatment is beneficial in controlling the symptoms of MD. To assess the effect of the device treatment on reducing the frequency and severity of vertigo, as well as on quality of life of patients affected by MD, we performed a meta-analysis to examine the effect of device treatment for MD in clinical studies.

MATERIALS AND METHODS

Search Strategy and Inclusion Criteria

We identified the relevant studies by systematically searching electronic databases, including PubMed, Embase, the Cochrane Library, China National Knowledge Internet, and Wanfang Data, to the last search entry on January 13, 2018. The keywords we used were MD, Meniere's vertigo, aural vertigo, otogenic vertigo, auditory vertigo, transtympanic micropressure treatment, Meniett pressure, overpressure, and the device treatment. The search strategy is described in Supplementary Method 1. There was no limit to the year of publication or language. Two authors independently checked the titles and abstracts to select eligible studies identified with the search strategy. When studies appeared to meet the inclusion criteria or the title and abstract of the studies were insufficient to make a clear decision for their inclusion, we obtained the full articles. Articles that did not meet the inclusion criteria were excluded, and the reasons were noted. We settled any disagreements between the two review authors about study inclusion by discussion with the third author. The inclusion criteria were as follows:

1) The studies were randomized controlled trials (RCTs), case-controlled studies, and cohort studies.
2) All patients definitely had Meniere's disease according to the 1995 AAO–HNS criteria.[1]
3) All patients were adults over 18 years old.
4) The device treatment, including Meniett device (Medtronic Xomed, Jacksonville, Florida, USA) and TinniTool device (Dismark@, Maur, Switzerland), was used as the main treatment method.
5) The number of included patients per study was more than 10.
6) The outcomes of the study included the primary outcome (vertigo control) and the secondary outcomes (hearing change, sick days, functional level, electrocochleograph parameters or recording).

The exclusion criteria were as follows:1) Patients who had undergone surgical intervention;
2) Patients with endolymphatic hydrops who did not meet MD criteria;
3) Studies that were meta-analyses, reviews, or letters.

Data Extraction

A standard data extraction form, including the data of publication year, study design, device type, and outcomes, was designed by one author. Two authors independently extracted data, and the third author checked the data. We contacted the authors of studies to provide missing data when possible.

Statistical Analysis

All statistical analyses were conducted using the weighted mean difference (WMD) or standardized mean difference (SMD), and 95% confidence interval (CI) as the metrics of effect size when outcomes were measured in the same way. We performed a chi-squared test and the Higgins I^2 test to assess the heterogeneity of the included studies, and results were considered statistically significant for the values of $p<0.05$.[12] We used a random-effects models if $I^2 \geq 50\%$; otherwise, we used a fixed-effects model.[13] To further discuss the clinical significance and sources of heterogeneity, the number of vertigo days by month, the number of vertigo episodes by month, and electrocochleography (ECoG) recording parameters were employed for subgroup analysis. When the eligible studies were equal to or more than 10, the publication bias was evaluated with a funnel plot. Finally, Egger's test was employed to address a quantitative detection bias. The R 3.1.1 software was employed for statistical analyses. The ethics committee approval and informed consent were not required.

RESULTS

Search Results

Our initial search returned 1865 studies. We identified 68 studies as potentially relevant by title and abstract screening. We read the full article, and finally identified 16 articles [14-29] that were included in our study. The process of trial selection is described in Figure 1. Of these, 16 studies with 395 patients were included to analyze the efficacy of the device treatment on controlling the symptoms of MD, and the reasons for exclusion of studies were described in Supplementary Method 2.

Characteristics of the Included Studies

Of 16 studies, 6 studies [15, 18, 19, 22, 24, 29] were RCTs, 2 studies [20, 21] were cross-sectional studies, and 8 studies [14, 16, 17, 23, 25-27] were before-after studies. The characteristics of included studies are listed in Table 1. In 16 studies, 385 patients in the device group used the Meniett device [14-22, 24-29]. All the patients had a ventilation tube inserted 2 weeks to 2 months before using the device. One received low-level laser therapy by the TinniTool device with a headset. This totaled 10 in the device group [23].

Vertigo was defined as the primary outcome, and the included studies described the effect of vertigo controlled in different ways. We analyzed the data of the studies together; and used the number of vertigo days by month, the number of vertigo episodes by month, vertigo visual analog score (VAS), and overall complete vertigo control to describe the vertigo outcomes. The secondary outcomes included the number of sick days by month, pure-tone audiometry (PTA) hearing changes, electrocochleographic parameters, and functional levels from 16 studies.

Meta-analysis Results

All meta-analyses were performed by comparing the reported pre-treatment and post-treatment data in the device group. We com-

bined the data of the same outcomes, which were measured in the same way in different studies. Vertigo, which was described as the frequency of vertigo days by month, the number of vertigo episodes by month, VAS of vertigo, and the overall completed vertigo control, was considered as the primary outcome. The secondary outcomes were defined as hearing changes, the number of sick days by month, ECoG recording, and functional level.

Primary Outcome: Vertigo Control

The number of vertigo days by month

One study [19] reported the frequency of vertigo days by month. We compared the reported data before treatment and those receiving treatment at 1/2/3/4 months in device group (Meniett device). The subgroup analysis was performed according to different months. The subgroup analysis results showed WMD: 2.70 (95% CI: 0.40-5.00) in 1 month, WMD: 3.30 (95% CI: 1.07-5.53) in 2 months, WMD: 3.60 (95% CI: 1.29-5.91) in 3 months, and WMD: 3.00 (95% CI: 0.62-5.38) in 4 months. The meta-analysis results showed significant improvement in the number of vertigo days by month (WMD: 3.15, 95% CI: 2.00-4.31) (Figure 2). There was no evidence of heterogeneity between studies (p=0.96, I^2=0).

The number of vertigo episodes by month

Five studies [20, 22-25] reported the number of vertigo episodes by month in 1/2/3/6/12/24 months. We combined the data that described the same month from different studies. The subgroup analysis was performed according to different months. The subgroup analysis results showed WMD: 7.50 (95% CI: 3.71-11.29) in 1 month, WMD: 6.36 (95% CI: -1.02-13.93) in 2 months, WMD: 2.70 (95% CI: -1.75-7.15) in 3 months, WMD: 4.70 (95% CI: 0.37-9.03) in 6 months, WMD: 11.98 (95% CI: 9.99-13.97) in 12 months, and WMD: 12.43 (95% CI: 10.52-14.34) in 24 months. The meta-analysis results showed a significant benefit in decreasing the number of vertigo episodes by month after the device treatment (WMD: 7.37, 95% CI: 2.40-12.35) (Figure 3). There was significant heterogeneity (P<0.0001, I^2=98.2%, and a random-effects model was used to analyze this outcome.

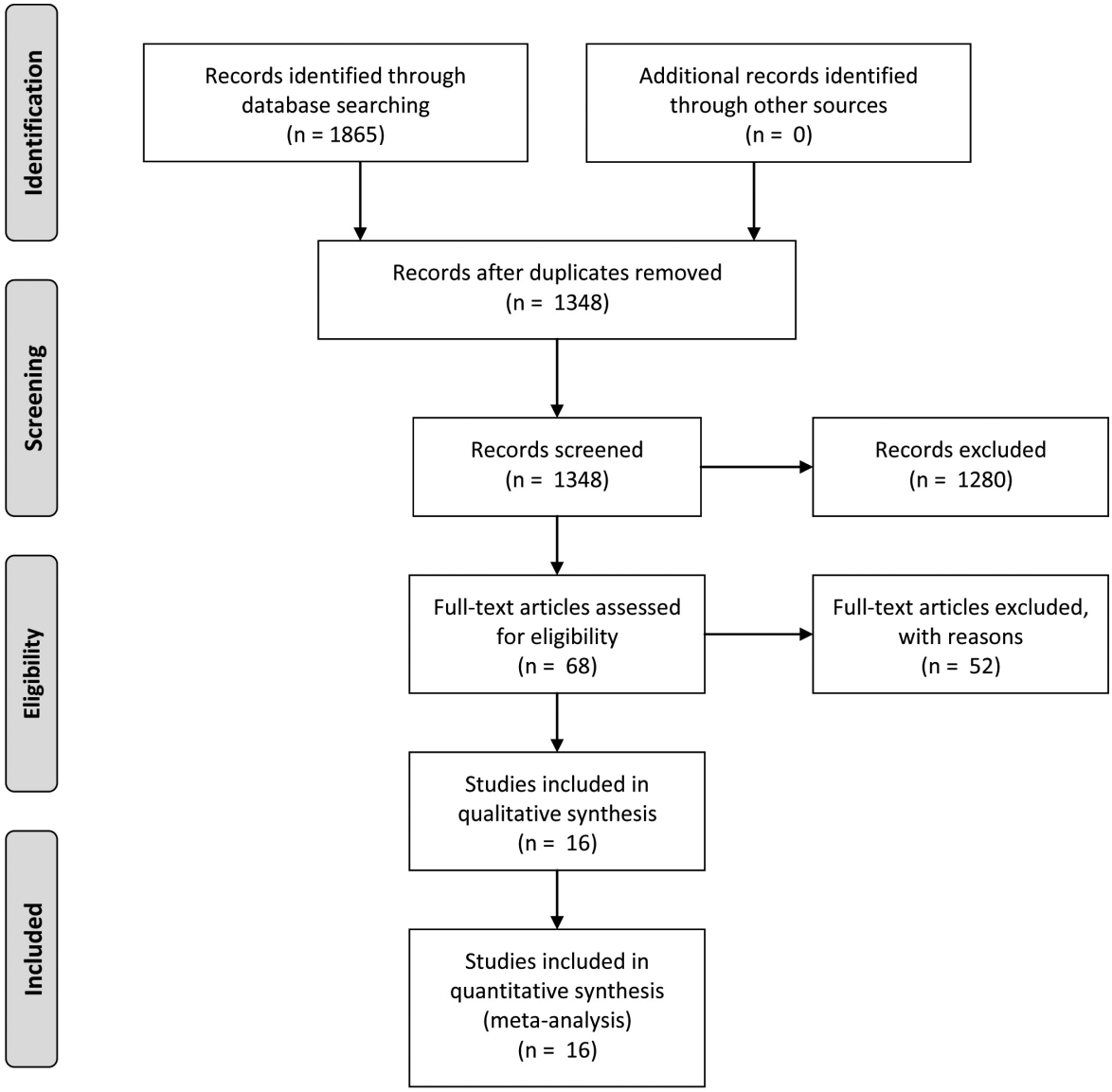

Figure 1. Summary of trial identification and selection.

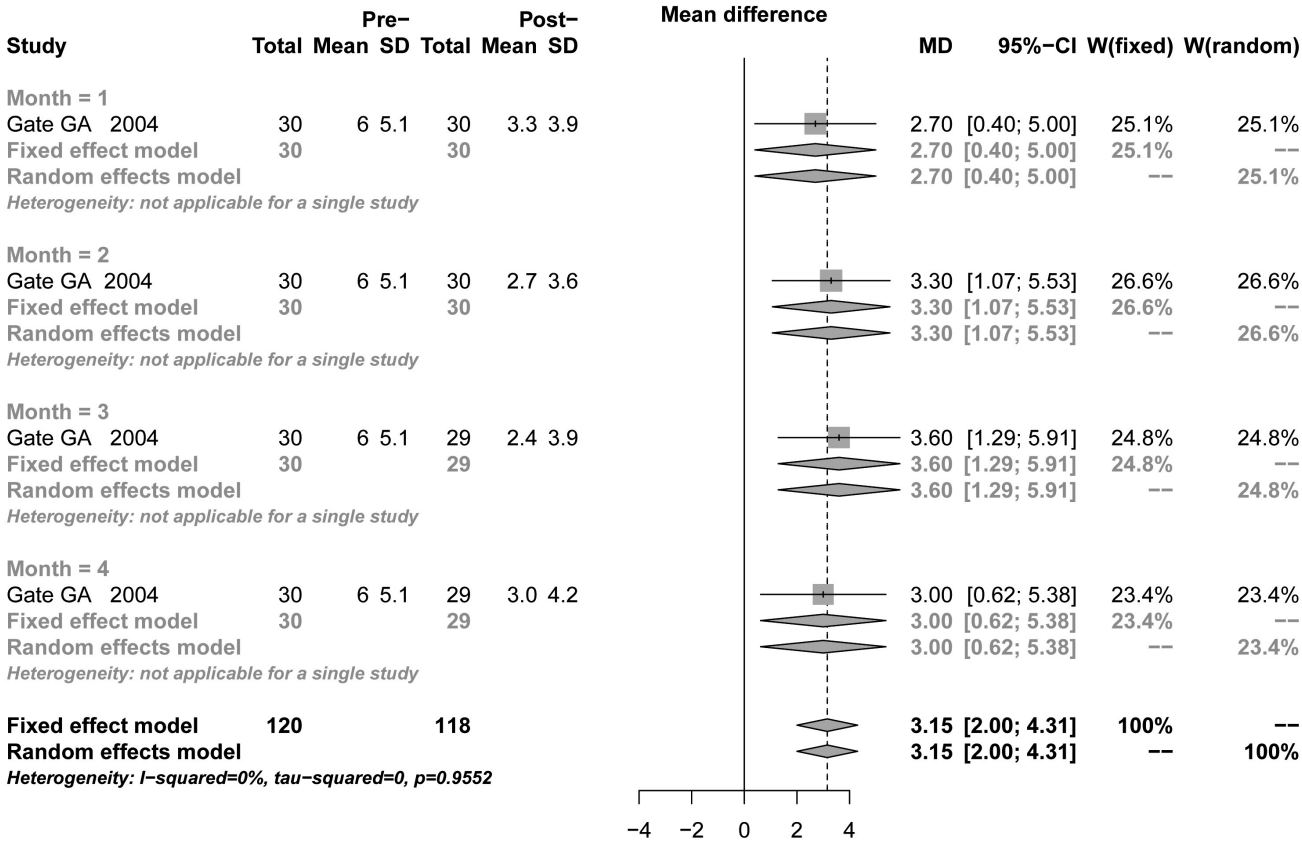

Figure 2. Forest plot of the number of vertigo days by month.

Table 1. The characteristics of each individual study

Study	Year	Country	Study design	Age (Years)	Gender (Male/Female)	Interventions	Follow-up (Months)
Barbara M	2001	Italy	Before-after study	30-64	11/13	Meniett device	1.3
Barbara M	2007	Italy	Before-after study	52.2±11.1	17/19	Meniett device	36
Barbara M	2010	Italy	Before-after study	56.6±12.5	NR	Meniett device	24
Densert B	1997	Sweden	Randomized controlled trial	NR	21/18	Meniett device	NR
Densert B	2001	Sweden	Before-after study	NR	NR	Meniett device	24
Dornhoffer JL	2008	USA	Before-after study	57.5±10.5	NR	Meniett device	48
Gates GA	2002	USA	Randomized controlled trial	53.5±15.2	5/5	Meniett device	8
Gates GA	2004	USA	Randomized controlled trial	48.8	NR	Meniett device	4
Gates GA	2006	USA	Randomized controlled trial	48.9±9.3	20/38	Meniett device	24
Huang W	2009	China	Cross-sectional study	45.5±11.4	9/9	Meniett device	28
Mattox DE	2008	USA	Before-after study	NR	NR	Meniett device	36
Rajan GP	2005	Australia	Cross-sectional study	46.7±25.5	9/9	Meniett device	18
Russo FY	2017	Italy	Randomized controlled trial	50±1.9	43/54	Meniett device	3
Teggi R	2008	Italy	Before-after study	42.5±12.3	11/9	TinniTool device	6
Thomsen J	2005	Multinational	Randomized controlled trial	20-65	NR	Meniett device	2
Yang HD	2007	China	Before-after study	40.9±8.52	4/6	Meniett device	3

NR: None reported.

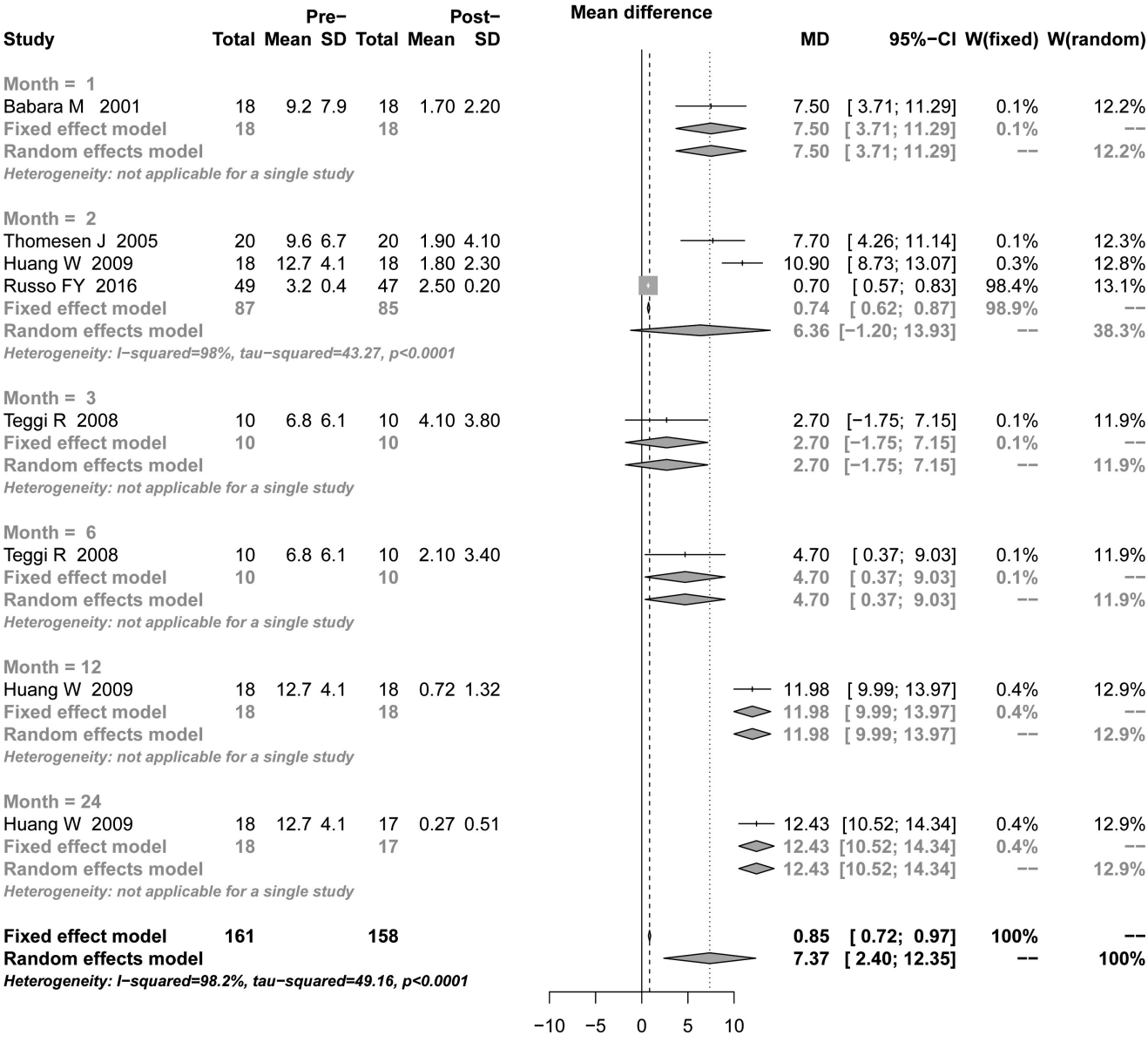

Figure 3. Forest plot of the number of vertigo episodes by month.

The VAS of vertigo

Two studies [21, 24] reported the VAS of vertigo. The meta-analysis showed a significant benefit in decreasing the VAS of vertigo after device treatment (WMD: 41.51, 95% CI: 34.68-48.34) (Figure 4). There was no significant heterogeneity (p=1.0, I^2=0).

The overall complete vertigo control

Nine studies [16-18, 20, 25-29] reported the data of complete (class A) vertigo control after the device treatment. The rate of complete vertigo control was 50% (95% CI: 37%-64%), as shown in Figure 5.

Secondary Outcomes

Hearing change

Nine studies [14, 16-21, 23, 26] reported hearing changes, and these studies all used pure-tone audiometry (PTA) to measure the changes in average low frequencies (0.25, 0.5, 1kHz) of hearing thresholds. Figure 6 shows a statistical difference between pre-treatment and post-treatment in the device group (WMD: 3.19, 95% CI: 0.66-5.71).

Sick days

Two studies [19, 20] reported the data of sick days before treatment and had received treatment in 1/2/3/4 months. The meta-analysis results showed the benefit of decreasing sick days (WMD: 4.56, 95% CI: 2.15-6.97) in Figure 7. There was significant heterogeneity (p<0.0001, I^2=97.1%), and a random-effects model was used to analyze this outcome.

The ECoG parameter recording

One study [15] reported the change in ECoG parameters before and after using the Meniett device. For the parameters of ECoG, we could not combine the data because of differences in the way that the data were measured. Therefore, we used SMD and 95% CI to perform the

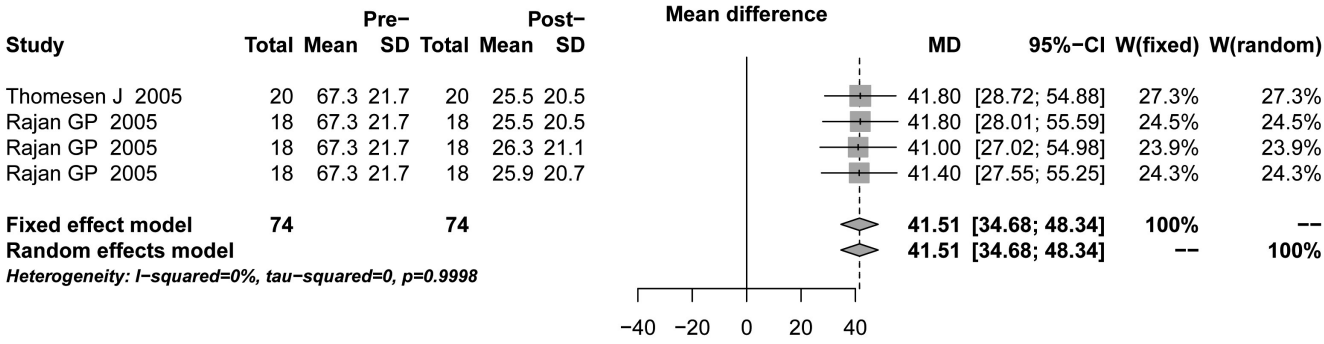

Figure 4. Forest plot of the visual analog score of vertigo.

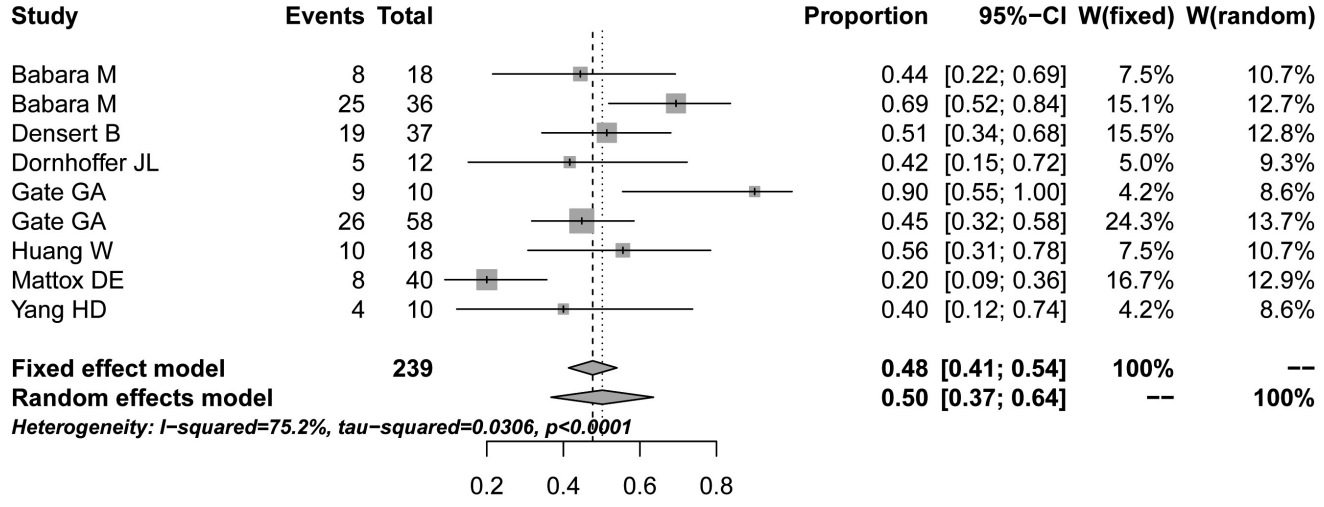

Figure 5. Forest plot of overall complete vertigo control (class A) rate.

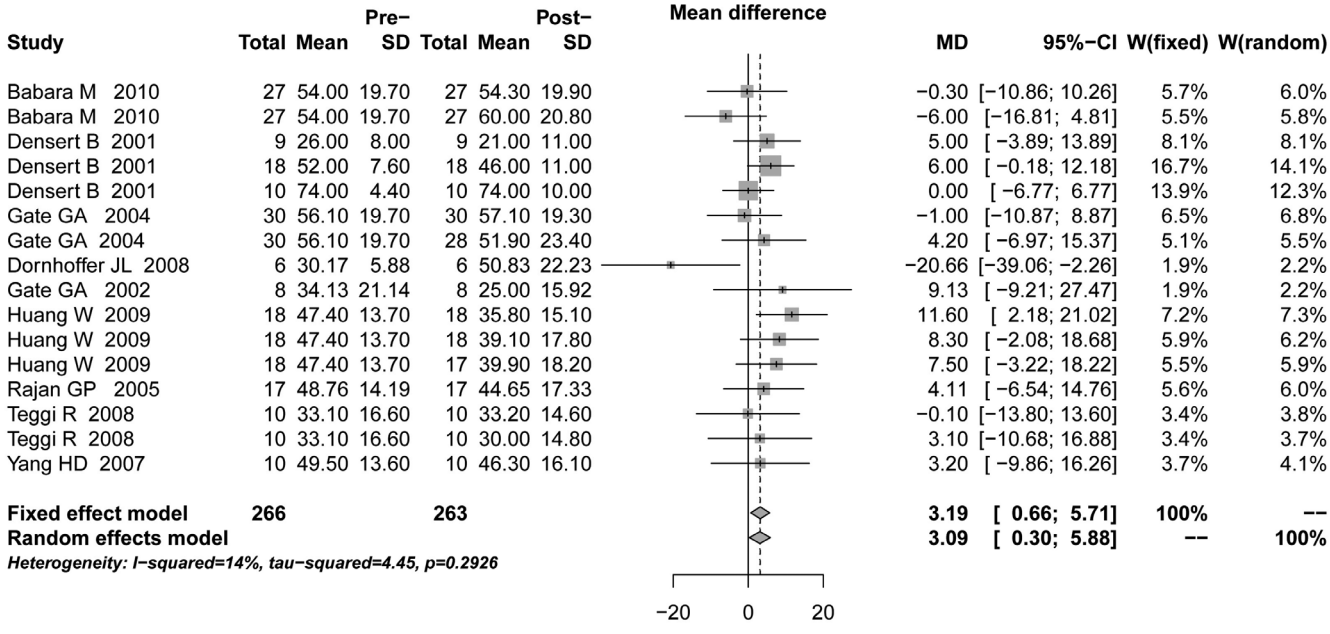

Figure 6. Forest plot of hearing change.

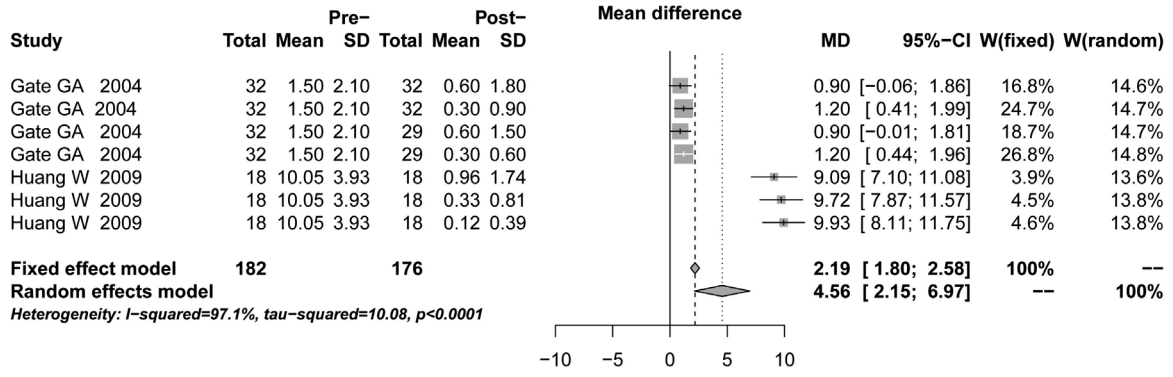

Figure 7. Forest plot of the sick days by month.

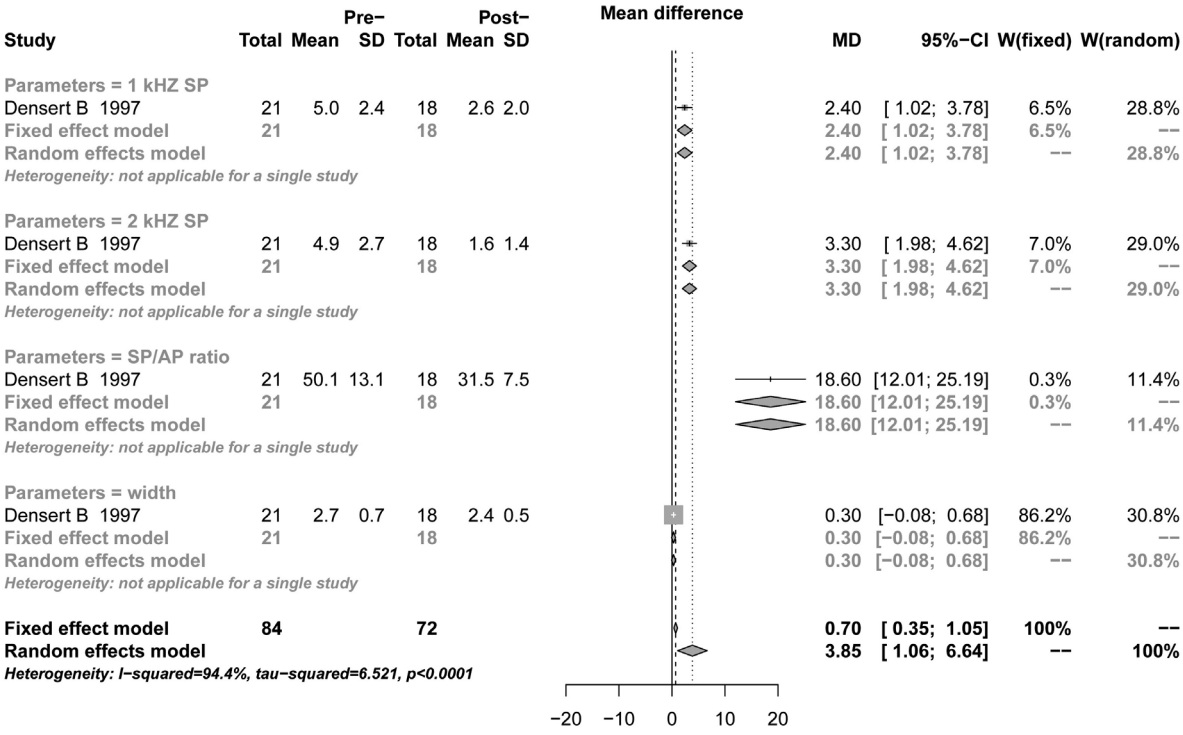

Figure 8. Forest plot of electrocochleograph parameters recording.

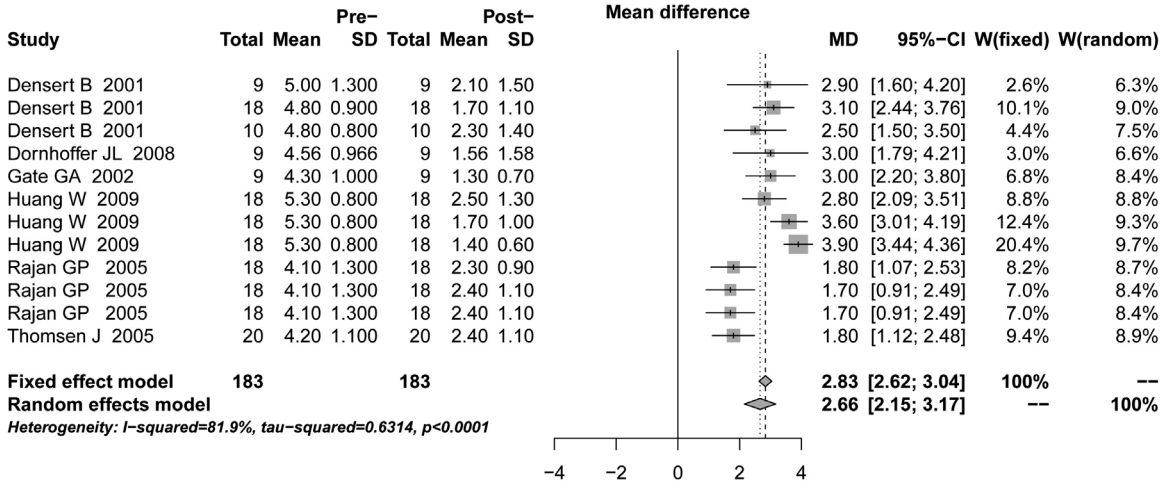

Figure 9. Forest plot of functional level.

analysis. The results of subgroup analysis for parameter 1 kHZ was SMD: 2.40 (95% CI: 2.15-6.97), 2 kHZ was SMD: 3.30 (95% CI: 1.98-4.62), summating potential/action potential (SP/AP) radio was SMD: 18.60 (95% CI: 12.01-25.19), and width was SMD: 0.30 (95% CI: -0.08-0.68, as shown in Figure 8. The meta-analysis results showed a significant decrease in the ECoG parameters.

Functional level

Six studies [16-18, 20, 21, 24] reported the data of functional levels. The meta-analysis results showed significant improvement in the pre-treatment compared with the post-treatment (WMD: 2.66, 95% CI: 2.15-3.17), as shown in Figure 9.

Publication bias

We used a funnel plot to investigate the publication bias. The rough symmetry suggested that there was no publication bias. Furthermore, the results of Egger's test indicated no significant difference in the primary outcomes of hearing change (bias=-1.03, 95% CI: -3.079-1.016, p=0.298) or functional level (bias=-4.240, 95% CI: -9.498-1.018, p=0.103).

DISCUSSION

Medical treatment, such as betahistine or diuretics, is used to treat the majority of patients with MD. However, some people still fail to respond to conservative medical treatment, and some patients may choose surgical or chemical ablation [6]. It should be observed that surgical procedures to treat patients with MD are associated with facial paralysis, intracranial complications, and hearing loss, although these complications are uncommon. The risks of chemical ablation [30] such as chemically induced ablation with gentamicin include potential loss of residual hearing and reduction of vertigo control rates. Therefore, complementary treatment should be developed for some patients with MD, and device treatment may be a good choice for them [31]. The Meniett device and the TinniTool device were included in our analysis. The Meniett device [31] is a portable device that delivers low-pressure pulses to the vestibular system of the inner ear. It requires an implanted tympanic ventilation tube to transmit pressure pulses into the middle ear. The TinniTool device [23] is a diode laser that can deliver continuous-wave laser light in a specifically designed headset. A wavelength of the laser is 650 nm, and the complete power output is 5 mW. It is easy for the laser to be positioned in the auditory system, and it is easy to transmit the energy of the laser to the inner ear because of the specifically designed headset. Both the Meniett and the TinniTool were non-destructive treatments in patients with MD.

In our study, we used internal controls (i.e., compared the before treatment data with the after treatment data in the device group) to evaluate the effect of the treatment, and did not compare it with the placebo group. Among the included 16 studies, 15 studies used the Meniett device, and one study used the TinniTool device. In patients with MD, the primary disability, vertigo, is usually accompanied by vomiting, which makes it difficult to maintain a normal life [2]. The patients were most affected by vertigo considering all the symptoms of MD, which therefore was defined as the main outcome. We described the primary outcome, vertigo, as the number of vertigo days by month, the number of vertigo episodes by month, and VAS of vertigo. The overall complete vertigo control (class A) rate after treatment was also used to evaluate the effect of the device treatment in vertigo control.

According to the result of vertigo control, the device treatment can reduce the duration of vertigo attack and relieve the frequency of vertigo. The result of the VAS of vertigo showed patients has significant improvement after the treatment, which suggests, to an extent, the device treatment has an effect of controlling the vertigo strength. Our subgroup based on the number of vertigo episodes by month suggested that the vertigo control effectiveness was related to the duration of the devices used. The device treatment significantly relieved the frequency of the vertigo episodes in the early period (1 month), and it showed no effectiveness in the medium period (2/3/6 month). While in the 12/24 months, there was significant effectiveness of the device treatment in relieving the vertigo episodes. These observations indicated a possible cumulative benefit with the device treatment in controlling the frequencies of vertigo, with the long-term treatment duration. The effects may be underrated if the duration of the follow-up time was less than 12 months.

There was a trend toward improvement of hearing after device treatment. However, the efficacy was limited. A previous meta-analysis [32] also found a favorable effect on hearing. The results also suggested that the device treatment had a significant effect on improving functional levels. The severity of symptoms reducing and the life quality improving may be the reasons for that. We did not find such improvement of symptoms in the placebo group. All studies reported the treatment is safe, and there were no identified adverse outcomes linked to the device group.

To our knowledge, this is not the first-time evidence for the device treatment in controlling the symptoms of MD was found. The effect of the Meniett device on MD was systemically reviewed by several meta-analyses with different results. Syed et al. [32] and van Sonsbeek et al. [33] only included RCTs and compared the effect of the Meniett device against a placebo device. They found no evidence to justify the Menitt device in patients with MD. Ahsan et al. [34] and Su et al. [35] used internal controls and found effective treatment for MD to some extent. Our study included the TinniTool device, which was different from previous meta-analyses [32-35]. No previous meta-analysis considering other device therapy for patients with MD was identified.

Within this analysis, we developed specific eligibility criteria using the Participants, Intervention, Comparison, Outcome Study framework. In our analysis, internal control was used to assess outcomes. The determination of outcome measures were strictly in accordance with the recommended AAO-HSN guidelines [1]. To assess the effect of the device therapy for patients with MD comprehensively, we listed more outcomes than previous studies.

There are several limitations to our analysis. First, the follow-up time of 6 studies (37.5%) in 16 included studies is 4-6 months, which was shorter than the AAO–HNS 1995 guidelines that recommend a follow-up time of 2 years. Longer follow-up time studies may be required in this regard. Second, the number of patients that received the TinniTool device treatment is small, and most of the patients included in the analysis were treated with the Meniett device. More studies on different kinds of devices are needed. Third, we only used

the data of the device group to report the results, which may be a potential source of bias.

CONCLUSION

Overall, the current evidence suggests that device treatment can reduce symptoms of vertigo in patients with MD. It also has a favorable effect on hearing, reducing the number of sick days, and improving functional levels. In addition, the treatment can decrease the ECoG parameters. Additional long-term follow-up studies are needed in this area to explore the benefit of device treatment with MD.

Ethics Committee Approval: This study was approved by the Ethics Committee of Taihe Hospital, Hubei University of Medicine.

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.Z., J,L.; Design - C.Z., J,L..; Supervision - C.Z., S.J.W.; Resource – H.Y., Y.Y.Y.; Materials - S.J.W., H.Y.G.; Data Collection and/or Processing - S.J.W., H.Y.G., J.L.; Analysis and/or Interpretation – Y.Y.Y., H.Y.G., L.L.L.; Literature Search - S.J.W., C.Z.; Writing - S.J.W.; Critical Reviews - C.Z., J,L.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Supplementary Method 1. Detailed search strategy.

Supplementary Method 2. Reason from exclusion of literature.

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Supplementary Method 1. Detailed search strategy.

1. Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily, and Versions(R)

#1 Meniere Disease.mp.
#2 Meniere Syndrome.mp.
#3 Aural Vertigo.mp.
#4 Otogenic Vertigo.mp.
#5 Auditory Vertigo.mp.
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 Transtympanic Micropressure Treatment.mp.
#8 Meniett Therapy.mp.
#9 Tympanic Membrane Massage.mp.
#10 Device treatment.ti, ab.
#11 Pressure.mp.
#12 Overpressure.mp.
#13 #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 #6 and #13

2. EMBase + EMBase Classic

#1 'meniere disease'/exp
#2 'meniere syndrome'/exp
#3 'aural vertigo':ti,ab
#4 'otogenic vertigo':ti,ab
#5 'auditory vertigo':ti,ab
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 'transtympanic micropressure treatment':ti,ab
#8 'meniett therapy':ti,ab
#9 'tympanic membrane massage':ti,ab
#10 'device treatment':ti,ab
#11 'pressure':ti,ab
#12 'overpressure':ti,ab
#13 #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 #6 AND #13
#15 #6 AND #13 AND ([embase]/lim OR [embase classic]/lim)

3. CENTRAL, The Cochrane Library

#1 MeSH descriptor: [Meniere Disease] explode all trees
#2 (Meniere syndrome):ti,ab,kw
#3 (Aural vertigo):ti,ab,kw
#4 (Otogenic vertigo):ti,ab,kw
#5 (Auditory vertigo):ti,ab,kw
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 MeSH descriptor: [Transtympanic Micropressure Treatment] explode all trees
#8 (Meniett therapy):ti,ab,kw
#9 (Tympanic membrane massage):ti,ab,kw
#10 (Device treatment):ti,ab,kw
#11 (Pressure):ti,ab,kw
#12 (Overpressure):ti,ab,kw
#13 #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14 #6 AND #13

4. China National Knowledge Internet (CNKI)

#1 梅尼埃病
#2 耳源性眩晕
#3 内耳性眩晕
#4 听觉眩晕
#5 #1 OR #2 OR #3 OR #4
#6 经鼓膜微压治疗
#7 梅尼特
#8 压力治疗
#9 器械疗法
#10 #6 OR #7 OR #8 OR #9
#11 #5 AND #10

5. WanFang Data

#1 梅尼埃病
#2 耳源性眩晕
#3 内耳性眩晕
#4 听觉眩晕
#5 #1 OR #2 OR #3 OR #4
#6 经鼓膜微压治疗
#7 梅尼特
#8 压力治疗
#9 器械疗法
#10 #6 OR #7 OR #8 OR #9
#11 #5 AND #10

Supplementary Method 2. Reason from exclusion of literature

Study	Year	Title	Reasons
Covelli	2017	Delayed Effect of Active Pressure Treatment on Endolymphatic Hydrops	The population didn't meet the inclusion criteria.
Clyde	2017	Current Management Practices in Ménière's Disease	This is a review.
Ahsan	2017	In response to systematic review and meta-analysis of Meniett therapy for Meniere's disease	This is a comment or letter.
Ingvardsen	2015	Antisecretory therapy with no improvement in functional level in Meniere's disease	The inventions didn't meet the inclusion criteria.
Sharon	2015	Treatment of Menière's Disease	This is a review.
Basura	2014	Comparison of second-echelon treatments for Ménière's disease	The inventions didn't meet the inclusion criteria.
Garcia	2013	Vestibular rehabilitation with virtual reality in Ménière's disease	The outcomes didn't meet the inclusion criteria.
Martin-Sanz	2013	The use of electrocochleography to monitor the response of Meniere's disease patients to intratympanic steroids	The inventions didn't meet the inclusion criteria.
Gurkov	2012	Effect of transtympanic low-pressure therapy in patients with unilateral Menière's disease unresponsive to betahistine: a randomised, placebo-controlled, double-blinded, clinical trial	The outcomes didn't meet the inclusion criteria.
Watanabe	2011	Intermittent pressure therapy of intractable Meniere's disease and delayed endolymphatic hydrops using the transtympanic membrane massage device: a preliminary report	The population didn't meet the inclusion criteria.
Stokroos	2006	Functional outcome of treatment of Meniere's disease with the Meniett pressure generator	The outcomes didn't meet the inclusion criteria.
Herráiz	2006	Tinnitus retraining therapy in Ménière disease	The outcomes didn't meet the inclusion criteria.
Thomsen	2006	Local overpressure treatment reduces vestibular symptoms in patients with Menière's disease--secondary publication. A clinically randomised multicenter double-blind placebo-controlled study	This is a duplicate.
Franz	2005	P-100 in the treatment of Meniere's disease: a clinical study	The outcomes didn't meet the inclusion criteria.
Feijen	2005	Treatment of Meniere's Disease with Intermittent Middle Ear Pressure	The outcomes didn't meet the inclusion criteria.
Boudewyns	2005	Meniett therapy: Rescue treatment in severe drug-resistant Ménière's disease?	The inventions didn't meet the inclusion criteria.
Anniko	2004	Local overpressure treatment of Meniere's Disease	The population didn't meet the inclusion criteria.
Odkvist	2004	Pressure treatment in Meniere's disease	The outcomes didn't meet the inclusion criteria.
Wang	2004	Qingkailing acupoints injection combined with electroacupuncture for treating Meniere's disease in 34 cases.	The inventions didn't meet the inclusion criteria
Gates	2003	The effect of transtympanic micropressure treatment in people with unilateral Meniere's disease	This is a duplicate.
Fattori	2002	Alternobaric oxygen therapy in long-term treatment of Meniere's Disease	The inventions didn't meet the inclusion criteria.
James	2002	Menière's disease	The study design didn't meet the inclusion criteria.
Odkvist	2001	Pressure treatment versus gentamicin for Meniere's disease	The inventions didn't meet the inclusion criteria.
Black	2001	Letter to the editor	The study design didn't meet the inclusion criteria.
Odkvist	2000	Effects of Middle Ear Pressure Changes on Clinical Symptoms in Patients with Me´nie`re's Disease—a Clinical Multicentre Placebo-controlled Study	The outcomes didn't meet the inclusion criteria.
Quaranta	1997	Comparison of long-term hearing results after vestibular neurectomy, endolymphatic mastoid shunt, and medical therapy	The outcomes didn't meet the inclusion criteria.
Miura	1994	Ketasregistered trade mark treatment for Meniere's disease	The outcomes didn't meet the inclusion criteria.
Savinkov	1985	Management of acute vestibular disorders in Meniere's disease	The inventions didn't meet the inclusion criteria.
Zhang	1983	The clinical observation on acute attack of Meniere's Disease treated with acupuncture	The inventions didn't meet the inclusion criteria.
Boronoev	1978	Evaluation of the effectiveness of oxygen and carbogen therapy in Menier's disease by clinical and electroencephalographic data	The outcomes didn't meet the inclusion criteria.
Martins	1968	New basis for control of Meniere's Disease	The inventions didn't meet the inclusion criteria.
Elia	1966	Double-blind evaluation of a new treatment for Meniere's syndrome	The inventions didn't meet the inclusion criteria.