



# Positive pressure device treatment for Menière's disease: an overview of the current evidence and a meta-analysis

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Received: 14 December 2018 / Accepted: 22 February 2019 / Published online: 27 February 2019  
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## Abstract

**Objective** The objective was to critically assess the current evidence investigating the efficacy of using a positive pressure device in patients with definite or probable Menière's disease.

**Methods** We performed a systematic literature search in MEDLINE, EMBASE and PsycINFO up to February 2018. We included both systematic reviews and primary literature [randomized controlled trials (RCTs)] investigating positive pressure treatment, in patients ( $\geq 18$  years of age), with Menière's disease. We assessed the internal validity of systematic reviews using the AMSTAR tool and risk of bias of primary studies using the Cochrane Risk of bias tool. We performed a meta-analysis for each outcome based on the identified studies. The overall certainty of evidence for the outcomes was assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE).

**Results** The search for systematic reviews identified four relevant reviews. These all included the same four RCTs. An updated search identified one additional RCT. In total, five RCTs were included in the data synthesis. Our data synthesis showed no effect of positive pressure treatment on primary nor secondary outcomes. No serious adverse events were reported. The overall certainty of evidence ranged from very low to low, due to the serious risk of bias and imprecision.

**Conclusion** The current available evidence does not support positive pressure device treatment in patients with Menière's disease. However, the limitations of the current literature hinder the possibility of any solid conclusion. There remains a need for randomized controlled trials of high quality to fully assess the utility of this treatment.

**Keywords** Low-pressure device · Meniere's disease · Meniett device · Positive pressure therapy · Vertigo

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**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s00405-019-05359-y>) contains supplementary material, which is available to authorized users.

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## Introduction

Menière's disease is a chronic syndrome characterized by spontaneous episodes of vertigo combined with fluctuating low-frequency sensorineural hearing loss, tinnitus and aural fullness. The hearing loss and vestibular deficits generally progress over time regardless of the treatments provided [1].

There are a broad variety of treatment options including low-salt diet, diuretics, intratympanic installation of steroids or gentamicin, betahistine, surgical treatment modalities as endolymphatic sac surgery, vestibular neurectomy or labyrinthectomy [2]. In addition, an international consensus paper on the treatment of Menière's disease has been published in 2018 recommending positive pressure treatment as one of the first steps of treatment [3]. The concept of using positive pressure treatment for Menière's disease was proposed over 30 years ago [4]. This led to the development of portable devices for local application of positive pressure air pulses. Endolymphatic hydrops is considered a hallmark in Menière's disease and a recent randomized study suggested a normalization of the endolymphatic hydrops in patients that had benefitted from positive pressure treatment [1]. The intermittent positive pressure pulses are delivered via the tympanostomy tube and the middle ear to the membrane of the round window which displaces the perilymph. A hypothesis is that the perilymph displacements alters the endolymphatic pressure through displacement of Reissner's membrane and this is believed to reduce Menière symptoms [5].

Evaluation of any kind of treatment for Menière's disease should consider the natural history with a usually spontaneous improvement with time, the fluctuation of symptoms over time and the well-known placebo effect with Menière's disease. Thus, high-quality placebo-controlled studies are desirable. Previous reviews concerning the effect of positive pressure treatment for Meniere's disease have been published in 2015 and 2016 but with contradicting conclusions.

The objective for this review was to update our current knowledge through systematically identifying and critically assessing the current evidence from randomized controlled studies (RCT), concerning the usage of positive pressure devices in patients ( $\geq 18$  years of age) with definite or probable Menière's. Specifically, we sought to evaluate the effect of positive pressure treatment on vertigo with respect to frequency, severity and duration as well as any serious adverse events, the effect on quality of life, impact on daily life, tinnitus and hearing loss.

## Methods

We conducted this systematic review, based on the principles described in the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach [6] and in accordance with the guidelines of the Cochrane Collaboration and PRISMA [7]. The study protocol was registered in PROSPERO (CRD42018104113) and structured in accordance to the Population, Intervention, Comparison and Outcome (PICO) framework [8], from which literature was selected. This review is a part of a larger guideline on Menière's disease published by the Danish Health Authority in 2018 [9].

### Literature search

We conducted an electronic literature search on December 7th, 2017 and February 6th, 2018. This literature search for published studies was performed in MEDLINE, EMBASE and PsycINFO databases. We performed the search into steps: first, a search for systematic reviews was conducted; second, the search date for primary studies was based on the latest search date from the included systematic reviews. In both steps of the search, the aim was to identify eligible randomized controlled trials (RCT). We conducted the search strategy using medical subject heading (MeSH) and text words related to population, intervention, and outcome. Language was restricted to English, Danish, Swedish and Norwegian. A detailed search description is found in the supplementary information.

### Study selection

One reviewer (LD) independently assessed title and abstract of all search hits (including the search for systematic review and primary studies). Subsequently, three authors (L.D., D.D.H and F.L.G.) screened and evaluated the full text of potential studies according to the eligibility criteria for both the systematic review and RCTs. The eligibility criteria included all systematic reviews and RCTs, matching the defined population, intervention and comparison as described below. If a systematic review was considered relevant in relation to our research question, eligible RCTs within the reviews were identified. Disagreement was resolved through discussion and, if needed, by including an additional author (H.E.C).

### Population

Inclusion criteria consisted of studies investigating patients aged 18 years and above with definite or probably Menière's

disease as defined by Bárány Society 2015 [10] or the American Academy of Otolaryngology–Head and Neck Surgery (AAO–HNS) criteria from 1995 [11]. Exclusion criteria consisted of studies that investigated patients with a diagnosis of vertigo other than Menière’s disease and studies including patients with Menière’s syndrome that did not use the appropriate diagnostic criteria.

### Intervention and comparison

The intervention included positive pressure therapy in conjunction with a tympanostomy tube. Patients using a placebo device served as a control group.

### Outcome

The primary outcomes for the data synthesis included the frequency of vertiginous episodes and number of patients with serious adverse events assessed at a minimum of 1 month following initial treatment. Secondary outcomes included: duration and severity of vertigo episodes as well as the proportion of patients with a reduction in tinnitus assessed minimum 1 month following initial treatment. Frequency of vertigo, hearing loss, quality of life and impact on daily life were assessed at longest follow-up (minimum 1 year following initial treatment).

### Critical appraisal

We assessed the internal validity of the systematic reviews using the AMSTAR tool [12]. All included RCTs, either found independently or in systematic reviews, were assessed for risk of bias using the Cochrane Risk of Bias tool [13] by evaluating the risk of inadequate patient allocation and concealment, blinding of patients, personnel and outcome assessors, attrition of data, selective outcome reporting and other types of bias.

### Data extraction from randomized controlled trials

Data concerning the pre-specified outcomes, the demographic characteristics (age and gender), the inclusion/exclusion criteria of the study and description of the intervention were extracted in the software Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia) [14]. Two authors (L.D and H.E.C) independently performed the data extraction. Any discrepancies were resolved through discussion among all authors. Only data available in the respective studies were used. Authors of the included studies were not contacted for further information.

### Data synthesis

Dichotomous outcomes were analyzed by calculating the relative risk (RR). For continuous outcomes, the effect size was assessed as mean difference if data were reported using the same measurement scale. If different measurement scales were used, the effect size was calculated using standardized mean difference (SMD). A 95% confidence interval was estimated for both dichotomous and continuous outcomes. Where applicable, data for each outcome was combined and statistical heterogeneity (inconsistency) was quantified using  $I^2$  statistics [15].

Either fixed-effects or random-effects model was applied, depending on the level of heterogeneity for the given outcome [16, 17]. The analyses and forest plots were produced in the Review Manager Software (version 5.2) (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) [18].

### Overall certainty of evidence using GRADE

The certainty of evidence for each outcome was evaluated using the GRADE approach, by which each outcome was assessed for factors that potentially could affect the reliability of the given effect estimate. These included risk of bias, inconsistency, indirectness, imprecision and publication bias. The overall quality of evidence could range from high, moderate, low and very low [6]. All findings were summarized in a summary of findings table [19].

## Results

### Literature search

In the search for systematic reviews, we identified 156 records. Following a check for duplicates and none-relevant references, we identified eight systematic reviews that we obtained in full and read thoroughly. Of these, four systematic reviews matched the population, intervention and control group of interest. From the Cochrane review we identified four relevant RCTs that matched the inclusion criteria of our review [20]. The remaining three reviews [21–23] did not contribute with any further studies. A search for primary studies was conducted from the date of search used in the Cochrane review (in this case June 6th 2014) to February 6th 2018. Here, 113 records were identified. Following title and abstract screening, the number of studies was reduced to one additional RCT that matched the inclusion criteria [24]. Thus, in total we included five RCT studies, comprising a total number of 504 patients [5, 24–27]. A flowchart including the reason for exclusion is provided in the supplementary information.

## Study characteristics of the primary studies

The population in the included RCTs consisted of patients aged 19–74 years. Thomsen et al. [5], Gürkov et al. [25], and Russo et al. [24], all included patients diagnosed with definite Menière's disease fulfilling the diagnostic criteria from AAO-HNS 1995. Gates et al. [26] and Ödkvist et al. [27] did not disclose what diagnostic criteria were used, yet the description of the included patients matched the diagnosis of definite Menière's disease, in accordance to the criteria of the Bárány Society 2015 [10]. In all studies, the intervention was treatment with positive pressure therapy using a Meniett device compared to a placebo device. A detailed description of the individual RCTs can be found in the supplementary material.

## Internal validity of the systematic reviews

We assessed the internal validity of the systematic reviews using the AMSTAR tool. All reviews provided an 'a priori' design, performed a comprehensive literature search and included two independent reviewers to select studies and extract data. The status of grey publication was unclear in two of the reviews [21, 23], yet mentioned in the remaining reviews. A list of studies was only included in two of the reviews [20, 23]. Only one systematic review [21] did not provide any characteristics of the included studies, documented the quality of the studies, or included a conflict of interest. VanSonsbeek et al. 2015 [20] was the only systematic review that provided relevant studies. This review had adequate description of all the necessary domains assessed by AMSTAR. An overview of the internal validity of the reviews can be found in the supplementary material.

## Risk of bias for primary studies

The risk of bias for the RCTs was assessed using the Cochrane risk of bias tool (see supplementary information). Allocation generation and concealment: In Gates et al. 2004 [26] and Russo et al. 2017 [24], there was low risk of bias for allocation sequence generation and concealment, as the method applied is considered adequately. In the remaining studies [5, 25, 27] the random sequence generation and allocation was unclear due to inadequate description. Blinding: In Gates et al. [26], Gürkov et al. [25] and Thomsen et al. [5], blinding of both participants, personnel and outcome assessors were low. In Russo et al. 2017, there was low risk of bias concerning blinding of participants, whereas blinding of outcome assessors was unclear. In Ödkvist et al. [27] blinding was not described. Incomplete data and other biases; In Russo et al. [24], there were no apparent sources of bias in terms of incomplete outcome data, selective reporting or other sources of bias. In Thomsen et al.

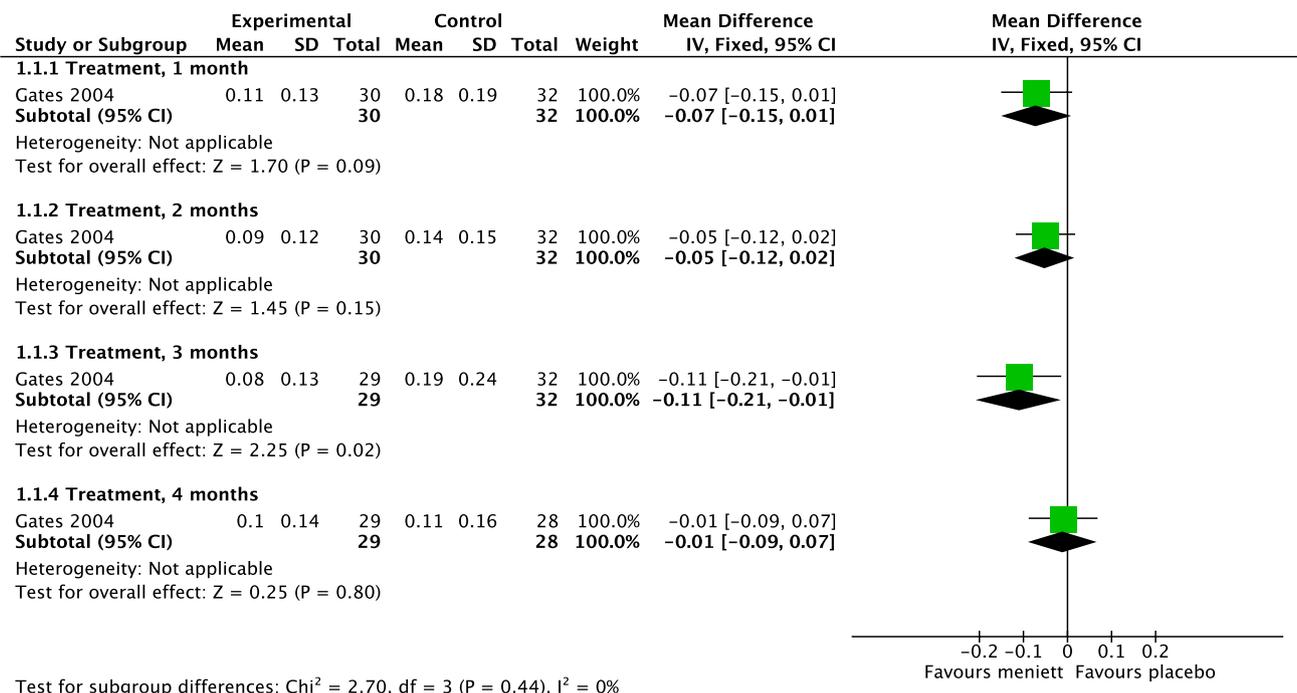
[5], incomplete outcome data and selective reporting were unclear as there was no description of exclusion/dropouts and differences at baseline. There were no other apparent sources of bias. In Gürkov et al. [25], incomplete outcome data was unclear due to inadequate description of dropouts. There was low risk of bias concerning selective reporting and other sources of bias. In Gates et al. [26], the risk of bias for incomplete data was unclear, as failure of treatment was asymmetrical between groups. The dropouts were inadequately described, leading to high risk of bias in terms of selective reporting. There were no apparent sources of additional bias. In Ödkvist et al. [27], incomplete outcome data and selective reporting were all high risk of bias due to no description of flowchart, dropout or baseline characteristics and very unclear presentation of data.

## Data synthesis

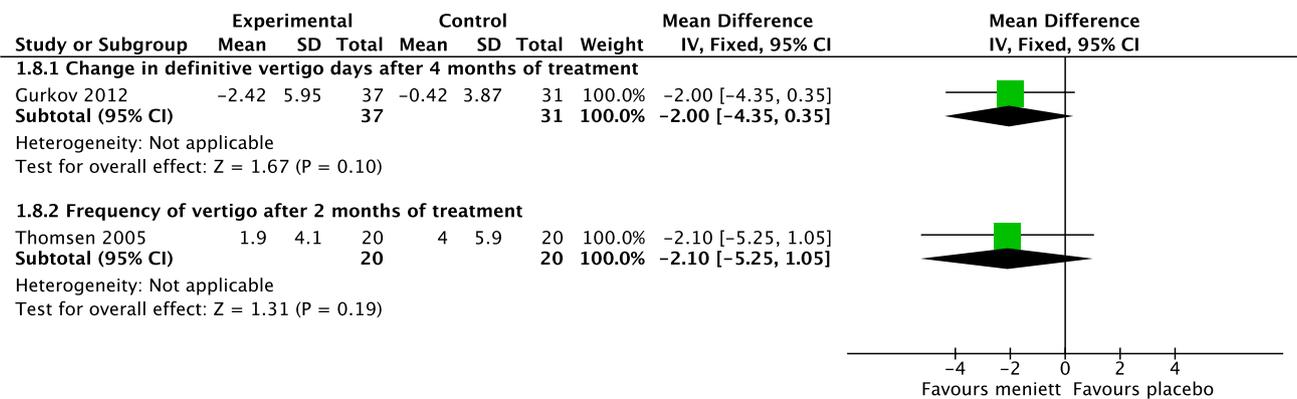
### Primary outcome

**Frequency of vertigo attacks** For the primary outcomes, it was not possible to combine data reporting on the frequency of vertigo attacks from the individual studies due to heterogenic reporting style. Thus, the results from the studies on this outcome will be individually described. Gates et al. [26] investigated the effect of the Meniett device on the proportion of days with definitive vertigo within a month. The effect was assessed 1, 2, 3 and 4 months following initial treatment. Results showed no mean difference (MD) between the two groups at 1 month (MD  $-0.07$ , 95% CI  $-0.15$  to  $0.01$ ) and at 2 months (MD  $-0.05$ , 95% CI  $-0.12$  to  $0.02$ ). At 3 months there was a slight indication of a positive effect following active treatment (MD  $-0.11$ , 95% CI  $-0.21$  to  $0.01$ ), yet this vanished at 4 months (MD  $-0.01$ , 95% CI  $-0.09$  to  $0.07$ ) (Fig. 1). In a similar fashion, Gürkov et al. [25] assessed the change in the mean number of days with definitive vertigo attacks following 4 months of treatment. Analyses showed no significant difference between treatment groups (MD  $-2.00$  95% CI  $-4.35$  to  $0.35$ ) (Fig. 2). Thomsen et al. [5] investigated the frequency of vertigo following a 2-months treatment period. Analyses showed no significant difference between active treatment and placebo device (MD  $-2.10$  95% CI  $-5.25$  to  $1.05$ ) (Fig. 2).

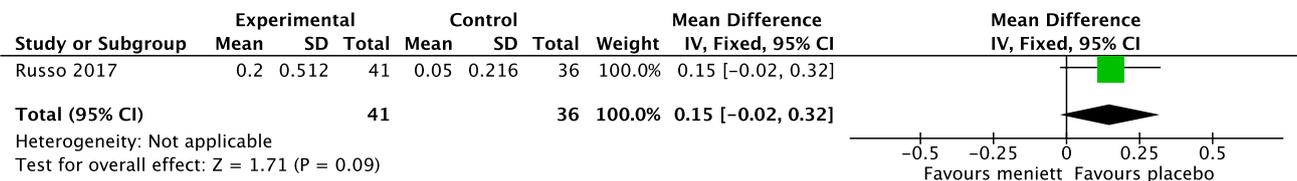
Russo et al. [24] investigated the effect of positive pressure device on vertigo episodes following 6 weeks of treatment. Here, no difference in the number of patients who experienced an improvement in vertigo attacks lasting more than 20 min (RR 1.19, 95% CI 0.82–1.71) (Fig. 3). Ödkvist et al. [27] indicated that there was a decrease in the frequency of vertigo. Yet there were no exact data or variance parameters reported. None of the included studies reported any serious adverse events.



**Fig. 1** Proportion of days with definitive vertigo 1, 2, 3 and 4 months following initial treatment. Results are reported as mean difference (MD) with a 95% confidence interval (CI). The direction of the effect is shown on the right, as either favoring Meniett or the placebo device



**Fig. 2** Change of mean number of days with definitive vertigo attacks following 4 months of treatment and frequency of vertigo following 2 months of treatment. Results are reported as mean difference (MD) with a 95% confidence interval (CI). The direction of the effect is shown on the right, as either favoring Meniett or the placebo device



**Fig. 3** Improvement in vertigo attacks lasting more than 20 min. Results are reported as risk ratio (RR) with a 95% confidence interval (CI). The direction of the effect is shown on the right, as either favoring Meniett or the placebo device

**Secondary outcome**

**Severity of vertigo** For the secondary outcome, the severity of vertigo attacks was reported in Gürkov et al. [25] who found that the cumulative vertigo scores (as assessed daily by the patients using a four-point Likert scale) significantly decreased in the treatment group as compared to placebo treatment. Yet, our analysis of the mean difference between changes in vertigo score showed that the difference between groups was non-significant (MD 5.31 95% CI –2.40 to 13.02) (Fig. 4). The exact data and standard deviations regarding the vertigo scores are not available in the article, which hinders further investigations into this discrepancy.

**Impact on daily life** The impact on daily life following completion of intended treatment was assessed by four studies [5, 24, 25, 27]. Gürkov et al. [25] assessed the impact of the Meniett device on the cumulative activity score, as assessed by the patients themselves who daily scored the activity level using a four-point Likert scale. In the study of Thomsen et al. [5], the effect on functionality profile was assessed using the AAO-HNS criteria, and Russo et al. [24] reported on impact of vertigo on daily life using the AAO-HNS scale. Odkvist et al. [27] assessed functionality profile using a questionnaire designed for the particular study to gather information on the patient’s abilities in daily life and work. Odkvist et al. reports that Meniett device led to an improvement in this outcome, yet there are no exact data

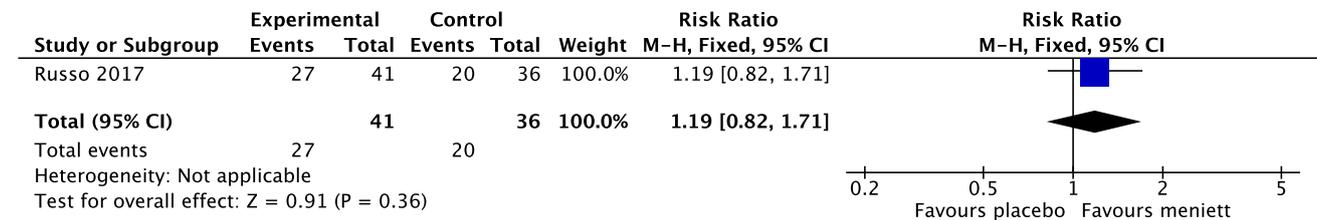
or variance parameters provided, which hindered further analyses. Thus, only three of the studies allowed for conducting a pooled analysis using a SMD estimate. Our pooled analyses of the three studies showed no effect on the impact on daily life after 6 weeks to 6 months of treatment (SMD –0.38 95% CI –0.87 to 0.10,  $I^2 = 63%$ ) (Fig. 5).

**Tinnitus and hearing** Odkvist et al. [27] reported an improvement in tinnitus using the visual analogue scale (VAS) following active treatment, yet there were no exact data or variance parameters available and thus it was not possible to conduct any analyses. Thomsen et al. [5] indicated that they had investigated the treatment effect on the perception of tinnitus and hearing in both cases as measured using the VAS scale, yet no data were provided.

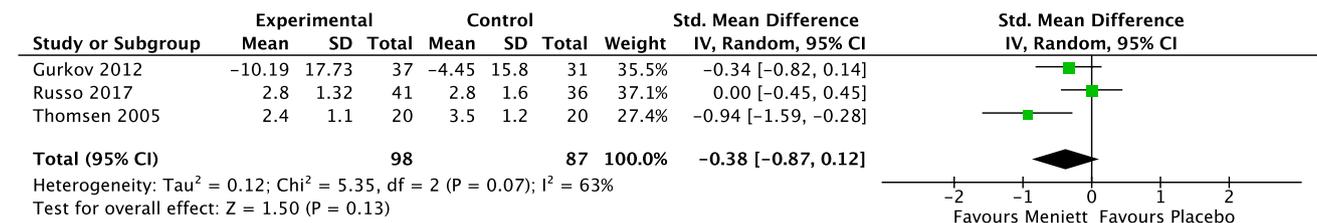
None of the included studies reported on changes in duration of vertigo attacks following initial treatment. In addition, none of the studies reported on vertigo with respect to frequency, hearing loss, quality of life or impact on daily life at longest follow-up (minimum 1 year after initiating treatment).

**Certainty of evidence (GRADE)**

For both the primary and secondary outcomes, the quality of evidence ranged from low to very low, due to serious risk of bias and very serious imprecision. In accordance to GRADE, the overall quality of evidence is based on the



**Fig. 4** The effect on severity of vertigo. Results are obtained as mean difference (MD) and the accompanying 95% confidence interval (CI). The direction of the effect is shown on the right, as either favoring Meniett or the placebo device



**Fig. 5** The effect on impact on daily life reported by three studies, using different assessment scales. Results are obtained as the standardized mean difference (SMD) and the accompanying 95% confi-

dence interval (CI). The direction of the effect is shown on the right, as either favoring Meniett or the placebo device

primary outcome, in which the overall quality was very low. A summary of findings can be found in Table 1.

## Discussion

Our objective was to obtain an overview and critically assess the evidence investigating the usage of positive pressure therapy in Menieres disease. Based on the collective evidence from the five identified randomized placebo-controlled trials, there are no indications that positive pressure therapy has a positive effect on the symptomatology found Menière's disease.

During our search, we identified four systematic reviews that investigated the effect of positive pressure therapy in Menière's disease [20–23], that all included the same RCTs. Our updated search identified one additional RCT. We included the results from the identified five RCTs, in an overall data synthesis. The primary outcome was the frequency of vertiginous episodes. However, due to the inconsistency between the studies on how to collect and report outcome data, it was not possible to conduct any pooled analysis for this outcome. Odkvist et al. [27] was the only study that reported a positive effect on the frequency of vertigo following active treatment, however, the lack of sufficient data in the respective study prevented further validation of these results. The remaining studies found no effect of positive pressure therapy on vertigo frequency at the end of the respective trials. The quality of evidence for the primary outcome was low to very low due to the risk of bias and imprecision. Thus, there is no substantial evidence for the effectiveness of positive pressure treatment on vertigo frequency. This non-significant finding is similar to what was found in the Cochrane review from 2015 [20] which analyzed the same outcome from Gürkov et al. [25] and Gates et al. [26]. Impact on daily life, tinnitus and severity of vertigo attacks were predefined as secondary outcomes for this review. Three of the RCTs provided data, measured impact on daily life by three different scales (AAO-NHS; self-reported Likert scale; self-constructed scale), enabling the only pooled analysis in this review. Results showed a non-significant effect on the impact on daily life. Two of the studies [5, 27] indicated that positive pressure therapy might reduce the severity of vertigo attacks as well as tinnitus, yet there were no data available in the two studies to support this finding. In combination with the low quality of evidence, the positive effects on vertigo severity and tinnitus should be interpreted with uttermost caution. Gürkov and Gates also assessed the impact on vertigo severity, yet no numerical data or variance parameters are provided, and therefore it was not possible to include these findings in an analysis. The authors of these two papers, however, report that application of the Meniett device, significantly decreases the severity

of vertigo attacks over the course of the 4-month treatment period, with the effect being most prominent during the first 3 months. Furthermore, our assessment of the evidence showed that no studies have investigated the predefined outcome at longest follow-up (minimum 1 year), thus the long-term effects of positive pressure therapy are unknown.

In contrast to our findings, the systematic reviews from Zhang et al. [22] and Ahsan et al. [21] both found a positive effect on the frequency of vertigo following treatment with the Meniett device. They did not confine their study-design to RCT studies, but also included prospective, retrospective and cross-sectional studies, which might explain the opposing conclusions. The fluctuation of symptoms and the natural spontaneous remission observed for this disease, obstructs the possibility of differentiating between treatment effect and spontaneous improvement, thus making these other study-designs less desirable. As assessed by AMSTAR, these two reviews, furthermore, had flaws in their reporting, thus decreasing the internal validity of these reviews. Similar to our review, Syed et al. [23] and the Cochrane review [20] only included RCT studies, with the results being identical to ours. The investigated outcomes were largely the same, however as opposed to Syed et al. [23], we wished to assess the effect observed both shortly after initial treatment (minimum 1 month after) as well as at the longest follow-up after initial treatment (minimum 1 year). We included one additional study by Russo et al. [24] that has been published since the two previous reviews, However, the conclusion remains the same, that there is no solid evidence in the favor of positive pressure treatment.

The reporting of outcome data hindered the making of high quality meta-analysis at this time. In 1995 the AAOH tried to standardize the reporting of data and recommended the functional level scale, a score for definitive vertigo spells per months 6 months prior to treatment and a follow-up of 18 to 24 months following or during treatment [11]. However, as it is clearly demonstrated in these 5 RCT trials, there is no consensus on how to report one of the main complaints from the patients, the frequency and severity of vertigo episodes. To move forward, it is essential that future research hold a common ground on which outcomes are to be included when assessing treatment modalities in Menière's disease and a uniform reporting of the results. Furthermore, none of the five RTC-studies included a large number of patients, which diminishes the precision and power of the estimates. Research on the treatment modalities for Menière's disease has been challenged by the lack of consensus on and, over time, changing the diagnostic criteria for the disease. This may have had an impact on the low amount of relevant literature that was found during the systematic search for this particular review. Surely, this may prove less problematic in future research due to the consensus criteria from the Barany society [10].

**Table 1** Summary of finding and quality of evidence tabel

Outcome Time frame	Results and scales	Effect estimates		Certainty of evidence	Summary
		Placebo device	Meniett device		
Number of patients with improvement in no. of vertigo attacks lasting > 20 min After 1 month of treatment Primary outcome	Relative risk: 1.19 (95% CI 0.82–1.71) Based on data from 77 patients in 1 study	556 per 1.000 Difference: 106 more per 1.000 (95% CI 100 fewer – 395 more)	662 per 1.000 662 per 1.000 (95% CI 100)	Low Due to very serious imprecision <sup>2</sup>	Meniett device may have little or no difference on number of patients with improvement in vertigo attacks lasting > 20 min
Proportion of days with definitive vertigo attacks After 4 months of treatment Primary outcome	Based on data from 57 patients in 1 study	Difference: MD 0.01 lower (95% CI 0.09 lower – 0.07 higher)	0.09 lower (95% CI 0.09 lower)	Very low Due to serious risk of bias, Due to very serious imprecision <sup>4</sup>	Meniett device may have little or no difference on proportion of days with definitive vertigo attacks
Change in definitive vertigo days After 4 months of treatment Primary outcome	Based on data from 68 patients in 1 study	Difference: MD 2 higher (95% CI 0.35 lower – 4.35 higher)	0.35 lower (95% CI 0.35 lower)	Low Due to very serious imprecision <sup>6</sup>	Meniett device may have little or no difference on change in definitive vertigo days
Frequency of vertigo After 2 months of treatment Primary outcome	Based on data from 40 patients in 1 study <sup>7</sup>	Difference: MD 2.10 lower (95% CI 1.05 higher – 1.05 higher)	2.10 lower (95% CI 5.25 lower)	Low Due to serious risk of bias, Due to serious imprecision <sup>8</sup>	Meniett device may have little or no difference on frequency of vertigo
Mean no. vertigo attacks lasting < 20 min After 6 weeks of treatment Primary outcome	Based on data from 77 patients in 1 study <sup>9</sup>	Difference: MD 0.15 higher (95% CI 0.02 lower – 0.32 higher)	0.15 higher (95% CI 0.02 lower)	Low Due to very serious imprecision <sup>10</sup>	Meniett device may have little or no difference on mean number of vertigo attacks lasting < 20 min
Impact on the activities of daily life After 6 weeks–6 months of treatment Secondary outcome	Based on data from 185 patients in 3 studies <sup>11</sup>	Difference: SMD 0.38 lower (95% CI 0.87 lower – 0.12 higher)	0.38 lower (95% CI 0.87 lower)	Low Due to serious risk of bias, Due to serious inconsistency <sup>12</sup>	Meniett device may have little or no difference on impact on the activities of daily life
Vertigo score After 4 months of treatment Secondary outcome	Based on data from 66 patients in 1 studies <sup>13</sup>	Difference: MD 5.31 higher (95% CI – 2.40 lower to 13.02 higher)	5.31 higher (95% CI – 2.40 lower to 13.02 higher)	Low Due to serious risk of bias, Due to serious inconsistency <sup>14</sup>	Meniett device may have little or no difference on impact on the activities of daily life

**Table 1** (continued)

Summary of findings including an overview of the primary and secondary outcomes and their respective time frames. The studies included and the number of patients is given as well as the effect estimates, reported as either continuous or binary data. The overall quality of evidence for each outcome is provided, with a description of the GRADE assessment given in the footnotes. A narrative summary description regarding the effect for each outcome is provided

Population: Patients with definite or probably Menière disease, aged 18 or above

Intervention: Meniett device

Comparison: Placebo device

<sup>1</sup>Russo 2017

<sup>2</sup>Imprecise effect estimate: Very serious. Only data from one study, Low number of patients

<sup>3</sup>Gates 2004

<sup>4</sup>Risk of bias: Serious. Incomplete data and/or large loss to follow up, Selective outcome reporting, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Imprecise effect estimate: Very serious. Low number of patients, Only data from one study

<sup>5</sup>Gurkov 2012

<sup>6</sup>Imprecise effect estimate: Very serious. Low number of patients, Wide confidence intervals, Only data from one study

<sup>7</sup>Thomsen 2005

<sup>8</sup>Risk of bias: Serious. Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Incomplete data and/or large loss to follow up, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; Imprecise effect estimate: Serious. Only data from one study, Low number of patients

<sup>9</sup>Russo 2017

<sup>10</sup>Imprecise effect estimate: Very serious. Low number of patients, Only data from one study

<sup>11</sup>Thomsen 2005, Russo 2017, Gurkov 2012

<sup>12</sup>Risk of bias: Serious. Incomplete data and/or large loss to follow up, Selective outcome reporting, Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias; Inconsistent results: Serious. The magnitude of statistical heterogeneity was high, with  $I^2$ : 63%

<sup>13</sup>Gurkov 2012

<sup>14</sup>Imprecise effect estimate: Very serious. Low number of patients, Wide confidence intervals, Only data from one study

## Strengths and limitations related to this systematic review

Our systematic review and meta-analyses were performed using transparent methods and a priori defined criteria in accordance with the guidelines of the Cochrane Collaboration and PRISMA, including protocol registration, comprehensive search and duplicate study selection, data extraction and quality assessment. Limitations included a restricted search in language and study design. The Authors of the included studies were not contacted for further information and thus the results are solely based on the published data.

## Conclusion

Despite the lack in evidence, there are clinical experiences with individual patients reporting a positive effect on symptoms following positive pressure therapy and since there are no serious adverse events related to its usage, patients are still being offered this treatment. Our findings show that the evidence is of low quality, and does not indicate an effect of positive pressure therapy. However, the limitations of the current literature hinders the possibility of drawing any solid conclusion, as to whether this treatment is effective in improving symptoms found in Menière's disease. Given the high expenses of this treatment, it is essential that more high quality research is performed, to assess if it is worthwhile or whether patients would be better off with other treatment modalities. It seems safe and there are indications that it may provide benefit in some patients but overall its utility is not proven.

**Acknowledgements** The authors would like to thank information specialist Birgitte Holm Pedersen for assistance with the literature search.

**Funding** The study was initiated and financed by the Danish Health Authority.

## Compliance with ethical standards

**Conflict of interest** The Authors declare no financial conflict of interests.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

## References

- Covelli E et al (2017) Delayed effect of active pressure treatment on endolymphatic hydrops. *Audiol Neurootol* 22(1):24–29
- Magnan J et al (2018) European position statement on diagnosis, and treatment of Meniere's disease. *J Int Adv Otol* 14(2):317–321
- Nevoux J et al (2018) International consensus (ICON) on treatment of Meniere's disease. *Eur Ann Otorhinolaryngol Head Neck Dis* 135(1 s):S29–Ss32
- Tjernstrom O (1977) Effects of middle ear pressure on the inner ear. *Acta Otolaryngol* 83(1–2):11–15
- Thomsen J et al (2005) Local overpressure treatment reduces vestibular symptoms in patients with Meniere's disease: a clinical, randomized, multicenter, double-blind, placebo-controlled study. *Otol Neurotol* 26(1):68–73
- Guyatt GH et al (2011) GRADE guidelines: a new series of articles. *J Clin Epidemiol* 64(4):380–382
- Moher D et al (2015) Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 4:1
- Guyatt GH et al (2011) GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 64(4):395–400
- DanishHealthAuthority. National klinisk retningslinje for behandling af Menières (2018) October 9, 2018]; Available from: <https://www.sst.dk/da/udgivelse/2018/nkr-behandling-af-menieres>
- Lopez-Escamez JA et al (2015) Diagnostic criteria for Meniere's disease. *J Vestib Res* 25(1):1–7
- 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(3): 181–5
- Shea BJ et al (2007) Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Med Res Methodol* 7:10
- Higgins JP et al (2011) The cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 343:d5928
- Covidence (Online software). 21.06.2018]; Available from: <https://www.covidence.org/home>
- Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. *Stat Med* 21(11):1539–1558
- DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. *Control Clin Trials* 7(3):177–188
- Mantel N, Haenszel W (1959) Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 22(4):719–748
- Review Manager (RevMan) (Computer program). 2014
- MAGICapp (Online software). 21.06.2018]; Available from: <https://app.magicapp.org/app-/guidelines>
- van Sonsbeek S, Pullens B, van Benthem PP (2015) Positive pressure therapy for Meniere's disease or syndrome. *Cochrane Database Syst Rev* 2015(3):Cd008419
- Ahsan SF, Standring R, Wang Y (2015) Systematic review and meta-analysis of Meniett therapy for Meniere's disease. *Laryngoscope* 125(1):203–208
- Zhang SL et al (2016) Meniett therapy for Meniere's disease: an updated meta-analysis. *Otol Neurotol* 37(3):290–298
- Syed MI et al (2015) Positive pressure therapy for Meniere's syndrome/disease with a Meniett device: a systematic review of randomised controlled trials. *Clin Otolaryngol* 40(3):197–207
- Russo FY et al (2017) Meniett device in meniere disease: Randomized, double-blind, placebo-controlled multicenter trial. *Laryngoscope* 127(2):470–475
- Gurkov R et al (2012) Effect of transtympanic low-pressure therapy in patients with unilateral Meniere's disease unresponsive to betahistine: a randomised, placebo-controlled, double-blinded, clinical trial. *J Laryngol Otol* 126(4):356–362

26. Gates GA et al (2004) The effects of transtympanic micropres-  
sure treatment in people with unilateral Meniere’s disease. *Arch  
Otolaryngol Head Neck Surg* 130(6):718–725
27. Odkvist LM et al (2000) Effects of middle ear pressure changes on  
clinical symptoms in patients with Meniere’s disease—a clinical  
multicentre placebo-controlled study. *Acta Otolaryngol Suppl*  
543:99–101

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