European Archives of Oto-Rhino-Laryngology
https://doi.org/10.1007/s00405-022-07604-3

OTOLOGY

Oral splint therapy in patients with Menière's disease and temporomandibular disorder: a long-term, controlled study

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Received: 23 May 2022 / Accepted: 8 August 2022

Abstract

Purpose To assess the effect of oral splint therapy on audio-vestibular symptoms in patients with Menière's disease (MD) and temporomandibular disorder (TMD).

Methods Retrospective case–control study. Treatment group: 37 patients with MD and TMD who received gnatological treatment. Control group: 26 patients with MD and TMD who had never received gnatological treatment. The number of vertigo spells in 6 months (primary endpoint), pure-tone audiometry average (PTA), MD stage, functional level, Dizziness handicap Index (DHI), Tinnitus handicap Index (THI) and Aural Fullness Scale (AFS) were compared at baseline and after 24 months according to groups. Analysis of Covariance was used to determine the treatment effect.

Results Groups were comparable for demographic, clinical data, baseline PTAs and the number of vertigo spells. Analysis of covariance showed a significant effect of gnathological treatment on number of vertigo spells ($\eta_p^2 = 0.258$, $p < 0.001$), PTA ($\eta_p^2 = 0.201$, $p < 0.001$), MD stage ($\eta_p^2 = 0.224$, $p < 0.001$), functional level ($\eta_p^2 = 0.424$, $p < 0.001$), DHI ($\eta_p^2 = 0.421$, $p < 0.001$), THI ($\eta_p^2 = 0.183$, $p < 0.001$), but not for AFS ($\eta_p^2 = 0.005$, $p = 0.582$). The treatment group showed vertigo control of class A in 86.5% and class B in 13.5% of patients. In the control group, vertigo control was of class A in 19.2% of patients and class B in 11.5%, class C in 30.8%, class D in 11.5%, class E in 19.2% and class F in 7.7%. Classes of vertigo control differed significantly (X^2 test, $p < 0.001$).

Conclusions Oral splint therapy could represent a viable treatment in patients with TMD and uncontrolled MD disease. The effects are maintained at least after 2 years.

Keywords Meniere disease · Vertigo · Temporomandibular disorders · Temporomandibular joint dysfunction syndrome · Temporomandibular joint

Introduction

Menière's Disease (MD) is characterized by recurrent episodes of spontaneous vertigo, sensorineural hearing loss, tinnitus, and a feeling of fullness or pressure in the affected ear. The diagnosis is clinical when other causes for deafness and vertigo are excluded [1]. Although the condition has been described for more than 100 years and despite the efforts of the scientific community, the etiopathogenesis is still uncertain; hypothesized etiologies include genetic, immune, and vascular factors, with a necessary but not sufficient contribution of endolymphatic hydrops in causing the typical attacks [2]. Commonly administered treatments are conservative therapies and ablative procedures as a second-line choice, with the first showing only partial

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Published online: 26 August 2022

evidence of effectiveness and the latter yielding adjunctive morbidity [3].

Temporomandibular disorder (TMD) is a broad term encompassing pain and/or dysfunction of the masticatory musculature and the temporomandibular joint (TMJ). The most important feature is pain, followed by restricted or limited jaw movement, and joint noises during jaw movement [4]. Etiology is complex and multifactorial, including major and minor traumatic events, malocclusion, psychosocial factors, and central sensitivity syndrome [5]. Diagnosis is based on patient symptoms and clinical findings, that define two main categories: pain-related TMD (when pain related to TMJ movements represents the main symptom) and intra-articular TMD (when mechanical dysfunction of the TMJ appears to be the principal disorder) [4]. Therapeutic options include topical and systemic anti-inflammatories during acute pain onset, oral appliance treatment, meditation/relaxation strategies, education about sleep hygiene, psychotherapy, and in some cases TMJ surgery. Among others, oral appliance therapy has shown durable evidence-based effectiveness in reducing pain, improvement of mouth opening, and disappearance of TMJ sounds in patients suffering from TMD [5].

A relationship between TMD and audio-vestibular symptoms was first observed by Monson and Wright in 1920 [6]. Since then, extensive reports have linked TMD to otological complaints, such as deafness, tinnitus, and vertigo. Several pathogenetic models have been proposed, based on interrelated mandibular and auricular embryological development, anatomical connections, and common peripheral and central neural pathways involved in auditory and somatosensory processing [6]. Improvement of otologic symptoms in patients with TMD after conservative therapies has been largely reported [7]; however, case–control studies on audio-vestibular symptoms in patients with MD after TMD treatment are currently lacking.

To clarify this latter aspect, we assessed the effects of gnathological treatment on otovestibular symptoms in patients with MD and TMD compared to patients who received only conventional conservative therapies. The hypothesis is that restoring the correct function of TMJ could avoid the direct and indirect damage to the audio-vestibular system, preventing peripheral and central pathologic pathways that contribute to precipitating MD symptoms.

Materials and methods

Patients

Patients referred to the Dental Clinics of Rome and Vicenza between 2014 June 1st and 2020 January 1st with a diagnosis of definite MD [1] and TMD [4] treated with oral splint were included in the treatment group.

The control group consisted of patients referred to the Audio-Vestibology Unit of the Otorhinolaryngology Department, Cattinara University Hospital in the same period with a diagnosis of definite MD [1] and TMD [4] who did not receive any orthognathic treatment in the study period.

Inclusion criteria were a diagnosis of unilateral or bilateral definite MD (2015 Barany Society criteria [1]) and TMD (Research Diagnostic Criteria for Temporomandibular Disorders consortium network and orofacial pain special interest group [4]) and a minimum follow-up length of 24 months.

Patients were excluded from this study if other otologic and neuro-otologic diagnoses were made before or after the study period, if they had received ablative treatments for MD or otologic procedures before or during the study period, if they had received maxillofacial procedures before or during the study period, if they abandoned the prescribed oral splint therapy before 24 months of follow-up, in case of inability to complete the outcome measures (e.g., incapacitating cognitive impairment).

This retrospective study was approved by the Trieste University Ethics Committee (date 2022/04/26, number 121). Each participant signed informed consent for data publication at the first examination. All procedures were conducted in accordance with the latest version of the declaration of Helsinki.

Orthognathic evaluation

On recruitment, patients underwent orthognathic assessment and clinical inspection of mandibular posture in the three spatial planes (sagittal, horizontal, and frontal) to detect possible jaw deviation from normal occlusion: deep bite, retruded mandible, and cross-bite.

To evaluate the contact relationship of the occlusal surfaces of the upper and lower teeth and to obtain information to prepare a personalized oral appliance, an alginate impression was taken of the dental arches, as previously described [9]. Dental stone models were made from impressions of the teeth and were transferred in an articulator in a relationship individually determined for each of the three spatial shifts connected with the mandible repositioning. The relationship was chosen by our team's orthodontist, through the registration of a wax check bite directly in the patient's mouth. The same clinician determined the interocclusal relationship for each of the three spatial shifts connected with the mandible repositioning. The vertical shift is aimed at obtaining 1 mm overbite between the antagonist central incisors; the sagittal shift

is aimed at obtaining 1–2 mm overjet; the lateral shift is aimed at lining up the upper and lower median labial frenulum. Any possible dental misplacement was considered when determining the above-mentioned parameters.

The clinical gnathological examination included assessment of clicking on mouth opening, TMJ crepitus, limitation of articular motility, pain evoked on masticatory muscle palpation, spontaneous otalgia, and otalgia evoked on endoauricular palpation.

Orthognathic treatment

An individualized acrylic oral splint was realized by the same senior author (EB) and applied to each patient. The device was equipped with orthodontic clamps which fixed it to the teeth of the lower dental arch. It consists of an occlusal bite plane set between the two antagonist dental arcades, which modifies the vertical dimension, and of a repositioning wall that works over the vestibular surfaces of the canines. This repositioning wall modifies both the sagittal and the lateral relationship between the maxilla and the mandible. The pressure exerted by the mandibular condyle over the external auditory canal is reduced after wearing the oral splint, as verified by endaural palpation. Patients were required to wear the appliance continuously, except at mealtimes.

A 6-month treatment was established for each patient, with monthly assessment by the orthodontist to monitor device functioning. During the monthly assessments, tolerance was evaluated by the orthodontic specialist who asked patients about the difficulty in using the oral appliance as prescribed. After this period, patients could continue with the oral splint treatment or stabilize the new occlusal configuration with orthodontic treatment.

Outcome measures

Primary and secondary outcomes were defined and analyzed according to American Academy of Otolaryngology–Head and Neck Surgery Society (AAO–HNS) guidelines [8]. Data for this study were collected at baseline (T1: start of the gnathological treatment or of the traditional conservative treatment, according to groups) and after 24 months (T2).

The primary outcome was variation in the number of vertigo episodes. The number of attacks in the 6 months before T1 and in the 6 months before T2 was compared. The rate of vertigo control was calculated as numerical value [(number of vertigo in the 6 months before T1/number of vertigo in the 6 months before T2) × 100] and then grouped into 6 classes (A–F, with A = complete control of vertigo and F = start of secondary treatment due to disability from vertigo) according to AAO–HNS recommendations [8]. The number of vertigo spells was recorded during a face-to-face appointment at the first evaluation and follow-up.

Secondary outcomes were hearing levels measured with pure tone audiometry, MD stage, and self-report measures of audio-vestibular symptoms, assessed in the 6 months before T1 compared with the 6 months before T2.

Pure tone audiometries were contralesional and ipsilesional air conduction thresholds at 0.25–0.5–1–2–3–4–8 kHz and bone conduction at 0.5–1–2–3–4 kHz. In line with the AAO–HNS recommendations for reporting hearing loss in MD, the mean ipsilesional pure-tone low-frequency threshold across 0.5–1–2–3 kHz (pure tone average, PTA) was included in the analyses. In the case of multiple audiograms, the worst audiograms within the selected 6-month intervals were taken for comparison. In case of bilateral MD, the worst ear was taken for comparison. Menière's disease stage was defined in 4 categories (1 = PTA ≤ 25 dB, to 4 = PTA > 70 dB) from PTA levels, according to the AAO–HNS recommendations for reporting outcomes in MD treatments [8].

To measure the symptom-related quality of life, patients completed the Dizziness Hearing Inventory (DHI; 0–100 scale, with physical, emotional and functional subscales) [10], the Functional Level Scale (FLS; 6-point Likert scale to assess the burden of vertigo on daily activities) [8], the Tinnitus Handicap Inventory (THI; 0–100 scale, with functional, emotional and catastrophic response subscales) [11], and Aural Fullness Scale (AFS; 0–10 analog scale) [12] at baseline and follow-up. Scores obtained at T1 and T2 were compared.

Statistical analysis

Continuous variables are expressed as mean value (MV) ± standard deviation (SD), while categorical variables as count and percentage. Continuous variables were compared with the Student *t* test. Categorical variables were compared using the Fisher's exact when binomial and the X^2 test when polynomial.

Analysis of Covariance (ANCOVA) assessed group differences in primary and secondary outcomes across timepoints. Outcomes were compared at T2, with T1 of each measure included as a covariate. As the *first step* for each analysis, the presence of Group × Pre-test interactions was examined. These interactions were not significant for the number of vertigo spells, FLS, DHI, and THI but resulted to be significant for PTA, MD stage, and AFS. As a *second step*, the analyses were re-run without Group x Covariate interactions for the number of vertigo spells, FLS, DHI, and THI, while the interaction was kept in the model for PTA, MD stage, and AFS.

Partial eta-squared (η_p^2) is reported for each main effect and interaction effect, where $\eta_p^2 = 0.01$, 0.06, and 0.14 constitute small, medium, and large effect sizes, respectively. We considered a significance level of $p < 0.05$ for all outcome measures. We did not adjust for multiple testing given the a-priori definition of a single primary outcome [13].

Statistical significance was assumed with p values < 0.05. Data were analyzed using IBM SPSS, Version 28.0 (IBM Corp., Armonk, NY, US).

Data preparation

The final data set was composed of the data of 63 patients, who completed the entire assessment at both timepoints.

The ANCOVA assumptions of linearity and homogeneity of variance were fully met for PTA, MD stage, THI, and AFS. On the other hand, the number of vertigo spells only partially met the assumption of linearity. The assumption of normal distribution of residuals was not met, with all the outcomes residuals presenting minor skewness ($-2 <$ skewness $< +2$) and kurtosis (kurtosis < 5) [14]. The data were not transformed, nor outlier scores substituted, given that ANCOVA is robust against the violation of normal distribution of residuals when conducted with appropriate sample size and groups of equal size [15].

An ANCOVA power calculation performed with G*Power (groups = 2; covariates = 1; numerator df = 1) showed that a total sample of at least 60 participants would be needed to detect medium–large effect sizes ($\eta_p^2 = 0.12$), considering 80% power and 0.05 alpha error. Since the final sample consisted of 63 participants, the study was adequately powered.

Results

Patient selection and characteristics

Treatment group a total of 79 patients referred to the Dental Clinic for TMD between 2010 September 1st and 2020 January 1st had a previous diagnosis of MD. Of these, 21 refused to be treated for TMD with an oral appliance, 13 did not fulfill the latest criteria for definite MD, 3 did not tolerate the oral appliance and abandoned it earlier than 24 months, and 5 were lost at follow-up. The remaining 37 patients who completed the assessment at all timepoints were included in the statistical analysis. No adverse effects attributable to oral appliances have been observed during the study.

Control group a total of 82 patients with a diagnosis of definite MD were referred to the Audiology and Vestibology Unit of the Otorhinolaryngology and Head and Neck Surgery Department of Cattinara University Hospital between 2014 January 1st and 2020 January 1st. Of these, only 43 had a diagnosis of TMD at the time of the first evaluation. Of these, 7 had undergone previous gnathological conservative or surgical intervention for TMD or malocclusion, 5 received ablative treatment for MD before T2, and 5 were lost at follow-up. The remaining 26 patients who completed the assessment at all timepoints were included in the statistical analysis.

Patient characteristics and comparisons between the treatment group and the control group are reported in Table 1. No statistically significant differences between groups were found for comorbidities, precedent or actual therapies, nor for MD and TMD characteristics.

Comparison between groups at baseline and post-treatment

Baseline, post-treatment and post-observation data with comparisons between the treatment and control groups are reported in Table 2.

Some group differences were observed at baseline assessments for Functional level, DHI, and THI, with worse scores for the treatment group. No statistically significant differences were observed at baseline assessments for the number of vertigo spells (primary outcome), nor for the PTA and the MD stage.

Post-treatment comparisons revealed a statistically significant lower number of vertigo spells, functional level, DHI, THI (overall and for the emotional subscale) and ear fullness for the treatment group. No statistically significant differences were shown for PTA, MD stage, functional and catastrophic response subscales of the THI.

The treatment group showed a vertigo control of class A in 32/37 (86.5%) and class B in 5/37 (13.5%) patients. In control group, vertigo control was of class A in 5/26 (19.2%) patients, class B in 3/26 (11.5%), class C in 8/26 (30.8%), class D in 3/26 (11.5%), class E in 5/26 (19.2%) and class F in 2/26 (7.7%). Class of vertigo control differed significantly between the 2 groups when compared with the Pearson's X^2 test ($p < 0.001$).

Before/after comparisons

Baseline, post-treatment and post-observation data with before/after comparisons according to the group are reported in Table 3.

In the treatment group, PTA and MD stages did not show significant before/after variations, while a significant reduction was recorded for the number of vertigo spells, functional level, DHI (overall and for each subscale), THI (overall and for each subscale) and AFS.

Table 1 Patient characteristics

Patient characteristics	Treatment group (n = 37)	Control group (n = 26)	*p* value
Age	54.6 (12.8)	59.9 (14.5)	0.128
Male sex	22 (59.5)	11 (42.3)	0.208
BMI	23.9 (3.5)	24.4 (3.7)	0.567
Comorbidities			
Allergy	7 (18.9)	10 (38.5)	0.148
Hypertension	13 (35.1)	9 (34.6)	> 0.999
Type 2 diabetes	3 (8.1)	2 (7.7)	> 0.999
Cardiopathy	4 (10.8)	3 (11.5)	> 0.999
Psychiatric disorder			
Depressive disorder	4 (10.8)	3 (11.5)	0.928
Anxiety disorder	5 (13.5)	5 (19.2)	
Mixed anxiety-depressive disorder	4 (10.8)	3 (11.5)	
Migraine	14 (37.8)	11 (42.3)	0.796
Autoimmune disorder	6 (16.2)	4 (15.4)	> 0.999
Alcohol consumption			
No	19 (51.4)	12 (46.2)	0.799
Moderate	18 (48.6)	14 (53.8)	
Smoke			
Active	10 (27.0)	6 (23.1)	0.938
No	12 (32.4)	9 (34.6)	
Former	15 (40.5)	11 (42.3)	
Coffee (cups/day)	1.6 (1.5)	1.8 (1.7)	0.643
Low salt diet	21 (56.8)	13 (50.0)	0.618
Betahistine			
No	16 (43.2)	11 (42.3)	0.952
During acute attacks	15 (40.5)	10 (38.5)	
Long-term use	6 (16.2)	5 (19.2)	
Cinnarizine			
No	26 (70.3)	18 (69.2)	0.968
During acute attacks	7 (26.9)	10 (27.0)	
Long-term use	1 (2.7)	1 (3.8)	
Diuretic treatment	16 (43.2)	10 (38.5)	0.923
Affected ear			
Right	15 (40.5)	12 (46.2)	0.531
Left	20 (54.1)	11 (42.3)	
Bilateral	3 (11.5)	3 (11.5)	
MD duration before study (months)	102.6 (112.4)	61.7 (54.4)	0.060
TMD			
Pain-related TMD	24 (64.9)	14 (53.8)	0.439
Intra-articular TMD	13 (35.1)	12 (46.2)	

Continuous variables are expressed as mean (standard deviation) and compared with the Student *t* test
Categorical variables are expressed as counts (percentage) and compared with the X^2 and Fisher exact test

In the control group, PTA and MD stages show a statistically significant increase in T2. A significant reduction was observed for AFS and for total THI score, but not for each subscale. No statistically significant difference was noted for the remaining disease-specific characteristics.

Hypothesis testing

Detailed results of the ANCOVA are reported in Table 4.

Table 2 Disease-specific symptoms

Characteristic	T1			T2		
	Treatment group	Control group	*p* value	Treatment group	Control group	*p* value
PTA	48.09 (17.01)	40.04 (15.04)	0.057	45.41 (21.47)	55.63 (22.81)	0.129
MD stage	2.57 (0.80)	2.23 (0.86)	0.117	2.41 (1.01)	2.73 (0.78)	0.155
MD stage (%)						
1	5 (13.5)	7 (26.9)	0.375	11 (29.7)	3 (11.5)	0.384
2	8 (21.6)	6 (23.1)		3 (8.1)	3 (11.5)	
3	22 (59.5)	13 (50.0)		20 (54.1)	18 (69.2)	
4	2 (5.4)	0 (0.0)		3 (8.1)	2 (7.7)	
Vertigo spells	15.00 (12.65)	11.19 (18.96)	0.342	0.49 (1.48)	4.73 (5.79)	0.001*
Functional level	4.22 (0.82)	3.04 (1.18)	< 0.001*	1.05 (0.23)	2.54 (1.27)	< 0.001*
Functional level (%)						
1	0 (0.0)	1 (3.8)	< 0.001*	35 (94.6)	6 (23.1)	< 0.001*
2	0 (0.0)	9 (34.6)		2 (5.4)	9 (34.6)	
3	9 (24.3)	9 (34.6)		0 (0.0)	4 (15.4)	
4	11 (29.7)	2 (7.7)		0 (0.0)	5 (19.2)	
5	17 (45.9)	5 (19.2)		0 (0.0)	2 (7.7)	
6	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
DHI	70.54 (13.71)	50.54 (19.56)	< 0.001*	17.24 (3.95)	42.46 (20.73)	< 0.001*
Physical	20.22 (4.78)	13.69 (5.56)	< 0.001*	4.59 (1.48)	12.31 (5.90)	< 0.001*
Emotional	25.03 (4.39)	18.62 (7.06)	< 0.001*	6.32 (1.38)	15.00 (7.55)	< 0.001*
Functional	25.30 (4.93)	18.23 (7.10)	< 0.001*	6.23 (1.52)	15.23 (7.63)	< 0.001*
THI	71.62 (21.67)	57.31 (26.01)	0.021*	34.05 (23.62)	47.31 (26.92)	0.043*
Functional	35.78 (10.26)	28.62 (12.70)	0.016*	19.41 (16.72)	28.08 (21.03)	0.074
Emotional	22.76 (7.03)	18.23 (8.47)	0.024*	12.11 (9.10)	17.23 (10.35)	0.042*
Catastrophic response	13.14 (4.75)	10.54 (5.26)	0.045*	7.73 (5.70)	10.85 (6.63)	0.050
AFS	7.14 (2.25)	5.04 (3.59)	0.012*	1.92 (2.31)	4.85 (3.30)	< 0.001*

Continuous variables are expressed as mean (standard deviation) and compared with the Student *t* test. Categorical variables are expressed as count (percentage) and compared with the X^2 test

PTA pure-tone average, *MD* Menière's disease, *DHI* Dizziness Handicap Inventory, *THI* Tinnitus Handicap Inventory, *AFS* Aural Fullness Scale, *T1* baseline, *T2* 24-month follow-up

*p < 0.05

Primary outcome: vertigo spells

The ANCOVA showed a significant main effect of randomised Group ($F[1, 60] = 20.851$, $p < 0.001$, $\eta_p^2 = 0.258$), after controlling for number of vertigo spells at pre-test ($F[1, 60] = 2.504$, $p = 0.119$, $\eta_p^2 = 0.040$). Participants in the experimental condition reported a significant decrease in number of vertigo spells in 6 months at post-test ($M = 0.49$, SD = 1.46), relative to those in the control group ($M = 4.73$, SD = 5.79) (Fig. 1).

Secondary outcomes

The ANCOVA showed a significant main effect of the Group factor for PTA, MD stage, functional level, DHI (overall and for each subscale), and THI (overall and for each subscale). Group did not show a significant effect on AFS (Table 4).

Baseline values had a significant effect for PTA, MD stage, THI (overall and for each subscale), and AFS, while did not show a significant effect for functional level, DHI (overall and for each subscale) (Table 4).

Significant interactions between group x baseline values were observed for PTA and MD stage, while no significant interaction was found for ear fullness (Table 4, Figs. 1, 2, 3 and 4).

Table 3 Before/after comparisons

Characteristic	Treatment group			Control group		
	T1	T2	*p* value	T1	T2	*p* value
PTA	48.09 (17.01)	45.41 (21.47)	0.184	40.04 (15.04)	55.63 (22.81)	0.006*
MD stage	2.57 (0.80)	2.41 (1.01)	0.110	2.23 (0.86)	2.73 (0.78)	0.009*
Vertigo spells (6 months)	15.00 (12.65)	0.49 (1.48)	< 0.001*	11.19 (18.96)	4.73 (5.79)	0.096
Functional level	4.22 (0.82)	1.05 (0.23)	< 0.001*	3.04 (1.18)	2.54 (1.27)	0.114
DHI	70.54 (13.71)	17.24 (3.95)	< 0.001*	50.54 (19.56)	42.46 (20.73)	0.133
Physical	20.22 (4.78)	4.59 (1.48)	< 0.001*	13.69 (5.56)	12.31 (5.90)	0.405
Emotional	25.03 (4.39)	6.32 (1.38)	< 0.001*	18.62 (7.06)	15.00 (7.55)	0.051
Functional	25.30 (4.93)	6.23 (1.52)	< 0.001*	18.23 (7.10)	15.23 (7.63)	0.114
THI	71.62 (21.67)	34.05 (23.62)	< 0.001*	57.31 (26.01)	47.31 (26.92)	0.024*
Functional	35.78 (10.26)	19.41 (16.72)	< 0.001*	28.62 (12.70)	28.08 (21.03)	0.878
Emotional	22.76 (7.03)	12.11 (9.10)	< 0.001*	18.23 (8.47)	17.23 (10.35)	0.565
Catastrophic response	13.14 (4.75)	7.73 (5.70)	< 0.001*	10.54 (5.26)	10.85 (6.63)	0.807
Ear fullness	7.14 (2.25)	1.92 (2.31)	< 0.001*	5.04 (3.59)	4.85 (3.30)	0.006*

Continuous variables are expressed as mean (standard deviation) and compared with the paired-sample Student *t* test. Categorical variables are expressed as count (percentage) and compared with the X^2 test

PTA: pure tone average, *MD* Menière's disease, *DHI* Dizziness Handicap Inventory, *THI* Tinnitus Handicap Inventory, *AFS* Aural Fullness Scale, *T1* baseline, *T2* 24-month follow-up

*$p < 0.05$

Discussion

Association between otologic symptoms and TMD has been widely reported in the literature, with tinnitus (6.4–100%), deafness (6.8–80%), dizziness and vertigo (1.6–100%) and ear fullness (5–92.5%) as the most frequent complains [6]. When compared to healthy controls, people affected by TMD show a greater rate of symptoms and hearing loss [16, 17]. When treated with oral appliances to reduce muscular tension, patients affected by TMD report a reduction of otologic symptoms [6]. Further confirmation of a connection between TMJ and the inner ear comes from reports of sensorineural hearing loss and vertigo as a complication during surgical procedures on the TMJ [18, 19]. Despite the largely represented connection between TMD and ear affections, few articles have examined the role of TMJ in MD and the potential role of gnathological treatment in this disease, and none of these works included a control group [20, 21]. In this context, we have explored the effects of TMD treatment on symptom relief in patients with definite MD, in a case–control study.

Our 2 groups resulted comparable both in demographic and clinical characteristics. Clinical confounders that could be involved in MD pathogenesis or precipitating attacks, such as allergies, autoimmune and psychiatric disorders, appeared similarly distributed [2]. In particular, no significant differences were noted in stage and duration of MD, type of TMD and previous or current therapies. The number of vertigo attacks at baseline was found comparable between groups, reducing the risk of biases despite the retrospective nature of this study. Differences in baseline values of some of the secondary endpoints have been easily overcome by including the baseline values as covariates in the hypothesis testing with the ANCOVA.

The gold standard for assessing the success or failure of treatment for MD is vertigo control [8]. Tinnitus, hearing loss, aural fullness, and quality of life are related to the frequency and severity of vertigo spells [22]. In our work, we found a significant effect of gnathological treatment in the reduction of vertigo attacks at the ANCOVA analysis, when controlled for the pre-treatment values. This reduction reflects in a better control rate class in the treatment group, with a greater percentage of classes A and B compared to the control group, and an improvement in vertigo-related quality of life, namely, Functional level and DHI. This is coherent with the study of Bjorne and Agerberg, which reported a linear reduction of symptoms during the 3-year follow-up [20]. Our findings are also supported by the results of Monzani et al., who found a significant reduction of vertigo spells, an improvement in the Situational Vertigo Questionnaire outcomes and an amelioration of stabilometric parameters in closed eyes conditions after a 6-month treatment of TMD with an occlusal splint [21].

A significant effect of the treatment on PTA emerged from the ANCOVA analysis. In addition, the baseline PTA value and its interaction with the treatment effect appeared to be relevant to the final outcome. Analogue effects are observed in changes of MD stages. Conversely, only the

Table 4 Results of the ANCOVA

Endpoint	Factor	F	*p* value	η_p^2
Vertigo spells (primary)	Group	(1, 60) = 20.851	< 0.001*	0.258
	Baseline value	(1, 60) = 2.504	0.119	0.040
PTA	Group	(1, 59) = 14.830	< 0.001*	0.201
	Baseline value	(1, 59) = 23.766	< 0.001*	0.287
	Group × baseline value	(1, 59) = 8.116	0.006*	0.121
MD stage	Group	(1, 59) = 17.028	< 0.001*	0.224
	Baseline value	(1, 59) = 44.445	< 0.001*	0.430
	Group × baseline value	(1, 59) = 10.339	0.002*	0.149
Functional level	Group	(1, 60) = 44.205	< 0.001*	0.424
	Baseline value	(1, 60) = 1.583	0.213	0.026
DHI (overall)	Group	(1, 60) = 43.704	< 0.001*	0.421
	Baseline value	(1, 60) = 1.583	0.213	0.026
Physical	Group	(1, 60) = 39.725	< 0.001*	0.398
	Baseline value	(1, 60) = 0.027	0.869	< 0.001
Emotional	Group	(1, 60) = 46.154	< 0.001*	0.435
	Baseline value	(1, 60) = 2.428	0.124	0.039
Functional	Group	(1, 60) = 44.205	< 0.001*	0.424
	Baseline value	(1, 60) = 1.583	0.213	0.026
THI (overall)	Group	(1, 60) = 13.455	0.001*	0.183
	Baseline value	(1, 60) = 22.167	< 0.001*	0.270
Functional	Group	(1, 60) = 8.840	0.004*	0.128
	Baseline value	(1, 60) = 12.735	0.001*	0.175
Emotional	Group	(1, 60) = 12.005	0.001*	0.167
	Baseline value	(1, 60) = 18.182	< 0.001*	0.233
Catastrophic response	Group	(1,60) = 8.384	0.005*	0.123
	Baseline value	(1, 60) = 10.457	0.002*	0.148
AFS	Group	(1, 59) = 0.306	0.582	0.005
	Baseline value	(1, 59) = 4.535	0.037*	0.071
	Group × baseline value	(1, 59) = 1.917	0.171	0.031

Interactions between group × baseline values were included in the final model when significant at the first step analysis. $\eta_p^2 = 0.01$, 0.06, and 0.14 constitute small, medium, and large effect sizes, respectively

PTA pure tone average, *MD* Menière's disease, *DHI* Dizziness Handicap Inventory, *THI* Tinnitus Handicap Inventory, *AFS* Aural Fullness Scale

*p < 0.05

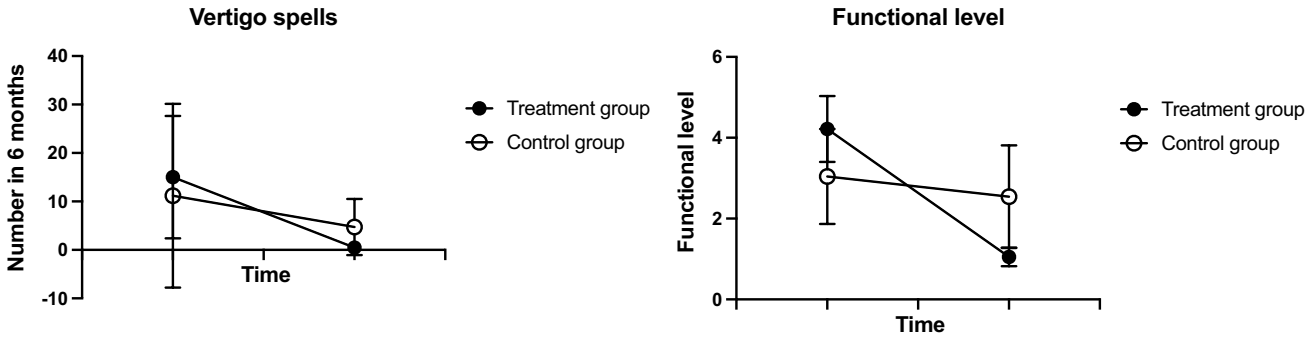

Fig. 1 Changes in vertigo spells and functional level after treatment or observation

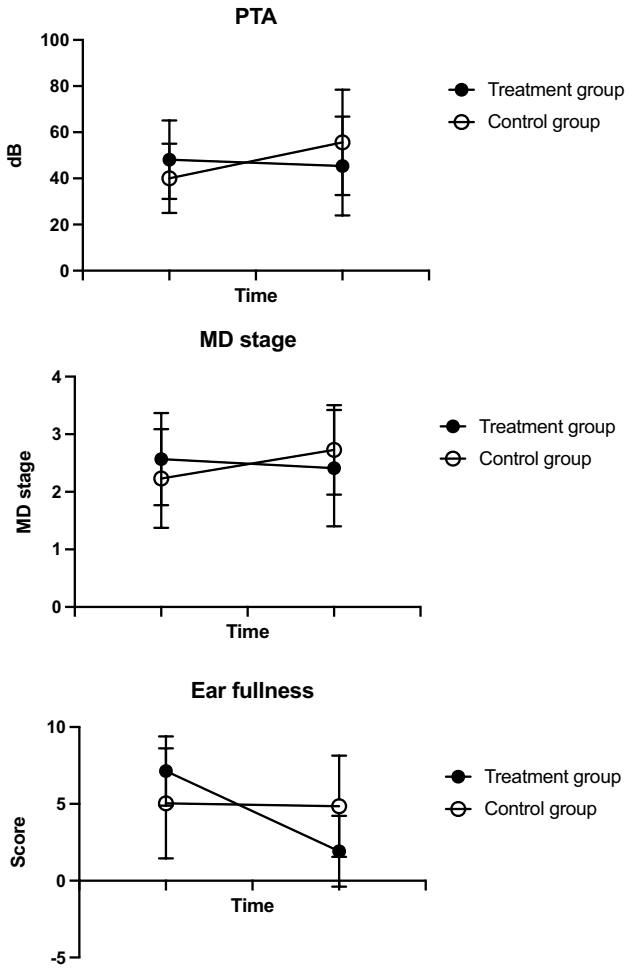

Fig. 2 Changes in pure tone average, Menière's disease stage and ear fullness after treatment or observation. *PTA* pure-tone average, *MD* Menière's disease

baseline value effect seemed to be relevant for ear fullness outcome.

Our results agree with those of Monzani et al., which did not find significant variations in PTA before and after gnathological treatment [21]. In fact, before/after comparisons did not show significant variations in PTA and MD stage in the treatment group, while a worsening of audiological function was seen in the controls. In other terms, the splint therapy seemed to prevent hearing damage.

We hypothesize that the treatment could have protected the inner ear from cumulative insults, such as micromechanical and vascular injuries, extensively discussed below. For what concerns the lack of effect on ear fullness, it could be argued that this symptom is the subjective representation of hearing loss: the fact that in best cases hearing levels remained the same and did not improve could explain the failure in ameliorating subjective fullness.

A significant effect of the gnathological treatment was found in the ANCOVA analysis on the THI outcomes, both overall and for each subscale. The total score and each subscale also were affected by the values at baseline. Treatment and baseline effect did not show any significant interaction. The possible role of TMJ dysfunction and its treatment on tinnitus is widely known since the first works of Costen [16] and gained recent popularity in the concept of somatosensory tinnitus, which implies that stimulation of craniomandibular trigger points and movements of these structures could elicit or worsen tinnitus [23]. The improvement of tinnitus in our population is coherent with this pathophysiologic model, which is furtherly discussed below. Our findings agree with those of Bjorne and Agerberg [20], and partially correspond to the results of Monzani et al. [21]. These latter authors recorded an amelioration in THI overall score and functional and emotional subscales as we did, while the catastrophic response subscale did not significantly vary. This difference could be explained by the different follow-up lengths of the two studies (24 months for our study vs 6 months for Monzani et al.), which could imply that a longer period is required for changing pathologic adaptation responses.

Many pathophysiologic mechanisms have been suggested to explain the coexisting TMJ dysfunction and ear symptoms. The current main hypotheses have been remarkably summarized in a topic review by Ramirez, Ballesteros and Sandoval [6].

The close anatomical and functional relationship between the TMJ and the ear begins during the embryological phase: the mandible is formed from the ventral part of Meckel's cartilage; the ossicles are formed from the dorsal part of Meckel's cartilage and Reichert's cartilage [6].

The middle ear and the mandible keep their anatomical connection with the anterior malleolar and the disco-malleolar ligaments through the petrotympanic fissure, which also contains the chorda tympani, the anterior tympanic artery, and vein [24]. The medial pterygoid muscle and the tensor tympani (TT) muscle both develop from the temporal blastema. These structures along with the tensor veli palatini (TVP) are innervated by V3 through the otic ganglion, which innervates the masticatory muscles coming from the mesoderm of the first branchial arch [25]. The fibers of the most external TVP muscle area and the TT fibers have a common origin in the malleus manubrium [26]. Further anatomical connections between the mandible and the ear are represented by the spheno-mandibular ligament, the deep auricular arteries and veins, and the auriculotemporal nerve [27].

Due to these anatomical relations, muscular hyper-contraction and ligamental stretching could exert a positive pressure via the ossicles on the inner ear fluids of the scala media, creating a hydrostatic condition similar to that in endolymphatic hydrops or worsening a concomitant one.

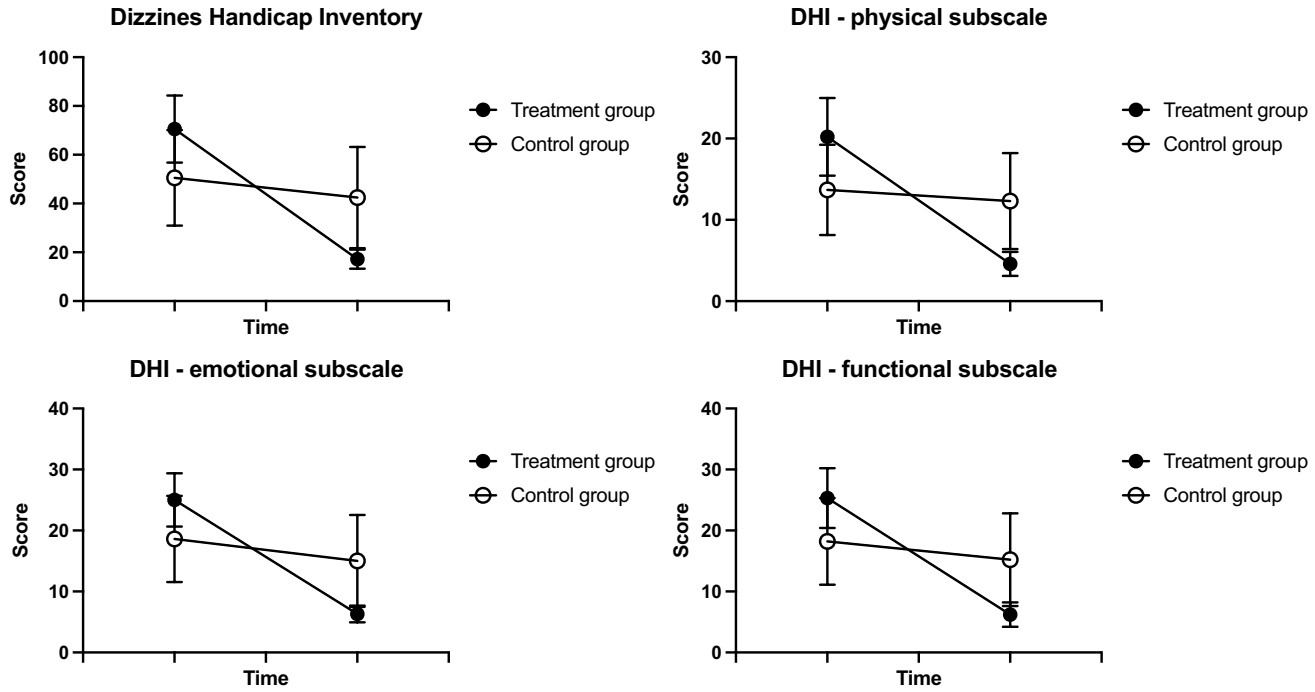

Fig. 3 Changes in the Dizziness Handicap Inventory, overall and for each subscale. *DHI* Dizziness Handicap Inventory

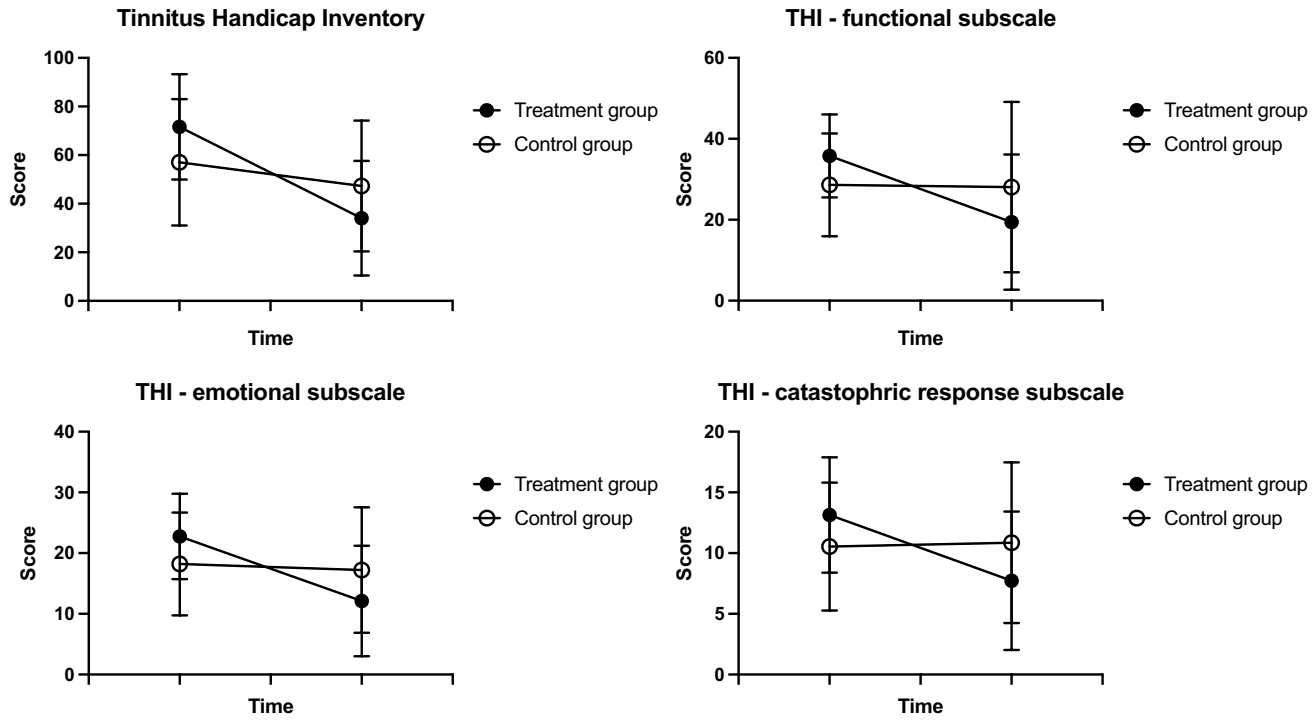

Fig. 4 Changes in the Tinnitus Handicap Inventory, overall and for each subscale. *THI* Tinnitus Handicap Inventory

Temporomandibular disorders may produce constant or episodic contraction and tension in the TVP and TT muscles during a state of fatigue. If masticatory muscles are hypertonic because of a TMD, the TVP and TT muscles may be hypertonic due to equal innervation by V3 [6]. Normal excursion of the disc and condyle during mandibular

movement may not provoke malleus mobility and altered tympanic membrane tension; however, functional or inflammatory joint disorders such as disc luxation or secondary edema may produce ossicular chain tension by ligament traction. In a cadaveric study, Sencimen et al. have described the anatomical relations between the mandible and the malleus; in their case series, they have shown that when the anterior malleolar ligament was overstretched, a movement of the malleus was observed in 11/15 cadavers (73%) [27]. A study of patients with unilateral TMD assessed by multiple frequency tympanometry reported significant alterations in the resonance frequency for the affected ear compared with the normal contralateral ear [28]. These changes indicate that TMD could cause subtle alterations in middle-ear biomechanics, with the variation of tension of the malleus altering the position of the stapes. The latter could cause a pressure change in inner-ear fluids and alter the polarization state of cochlear and vestibular hair cells [28]. Further hints supporting this model come from the recent work by Miehe et al., where MD patients showed a significantly lower absorbance at tympanic peak pressure on wideband tympanometry compared to healthy control [29]. This micromechanical concept could also explain the reported effectiveness of tenotomy of the middle ear muscles in patients with MD: in this case, the therapeutic effect is attributed to increasing the compliance of the ossicular chain to hydropic fluctuations by sectioning the ligaments of the TT and stapedial muscles [30].

Temporomandibular disorders could indirectly impair hearing and balance by causing or exacerbating cervical spine disorders and interfering with somatosensorial ascending cervico-vestibular pathways. Clinical correlations between TMDs and cervical spine disorders are widely described in the literature [31].

Proprioception is mostly dependent on the deep short intervertebral neck muscles. The neck input participates in perceptual functions and reflex responses—namely, cervicopostural and cervico-ocular reflexes. Neck input modulates body posture and stabilizes the head with respect to the trunk by cervico-collic reflexes, interacting with vestibulo-collic reflexes which stabilize the head in space. The cervical muscular disorder may interfere with the proprioception in the vestibular nucleus and in the cervico-oculo-vestibular muscle reflex controlling the posture of the head [32].

Also, isometric cephalo-cervical exercises can change the loudness, pitch, and location of tinnitus by modulating the somatosensory and acoustic central neural pathway, in tinnitus and non-tinnitus patients [23]. It has been hypothesized that an increased cervical muscular tension may be transmitted to the vertebral artery which feeds the basilar artery and inner ear inflow, exacerbating aural symptoms [33].

Also, a neurogenic hypothesis involving trigeminal connections with the peripheral and central nervous systems has been formulated. Symptoms such as vertigo, tinnitus, and hearing loss can result from a new auditory innervation pattern that involves the trigeminal nerve. In animals, the trigeminal innervation of the vascular system controls the cochlear and the vestibular labyrinth function, mediating vasodilatory responses to metabolic stresses via fibers of the Gasser ganglion to the cochlea through the basilar and anterior inferior cerebellar arteries [34]. The reduction of cochleovestibular blood flow could result from abnormal activity in the trigeminal ganglion due to TMD-related pain.

As reported by Shore et al., the trigeminal ganglion innervates the ventral cochlear nucleus and the superior olivary complex [35]. This can interfere with the auditory pathways which lead to the auditory cortex in the presence of constant peripheral somatic signals from the ophthalmic and mandibular trigeminal peripheral innervation in TMD.

It has been shown from experiments on rats that trigeminal terminals make contact with vestibulospinal neurons in the inferior and lateral vestibular nuclei, proving a trigeminovestibulospinal pathway [36]. Such connections in humans can be hypothesized from indirect evidence. Trigeminal stimuli could interfere with the vestibular ascending pathway that terminates in the insula, where pain-related anterior and posterior cortical areas are constantly represented [37–39]. The anterior cingulate cortex can be activated both by vestibular and noxious stimuli [40]. Finally, it has been shown with functional that occlusal therapy can activate parietal sensorimotor integration areas, which participate in sensory information processing and postural reflexes and gait modulation [41].

In this trigeminal-mediated model, an abnormal intermittent or constant noxious stimulation could activate peripheral vasomotor reflexes and balance and auditory processing central areas, enhancing audio-vestibular symptoms.

The documented clinical amelioration in MD symptoms can, therefore, be attributed to breaking these pathogenic mechanisms by treating TMD. Further benefit could come in the improvement of 2 conditions frequently associated with both MD and TMD, which are Obstructive Sleep Apnea Syndrome (OSAS) and headache.

Headache is a common complaint in 70% of patients with MD. During vertigo spells, patients with MD experienced a headache in 41% and a migraine-type headache in 8.4% [42]. On the other hand, OSAS is seen in approximately 15% of MD patients, and it is thought to worsen audio-vestibular function due to insufficient blood supply via the vertebral basilar artery, which feeds the inner ear. In OSAS this insufficient supply might be exacerbated at night, while patients are sleeping [43].

Both OSAS and headache contemplate gnathological therapy when a malocclusion or a TMD is present [44, 45]. In the hypothesis that TMD would have a key role in patients presenting with MD, OSAS and headache, treating it as the

common denominator of a syndrome could provide an overall benefit for all the aspects.

Treating MD still represents a clinical challenge. Common conservative treatments show partial effectiveness and are not supported by solid evidence of efficacy [3]. Ablative therapies (e.g., intratympanic gentamicin injection, vestibular neurectomy, surgical labyrinthectomy) are usually administered as a second-line treatment once conservative approaches have failed. Despite the good control of the vertigo spells, these treatments have adjunctive risks, such as permanent sensorineural hearing loss as well as morbidity associated with the surgical procedure; furthermore, these side effects are irreversible [3].

Conversely, treatment with oral appliances for TMD is not burdened by adjunctive comorbidity, except for some possible discomfort during the early phases. If the oral appliance is not tolerated, it can be simply removed without permanent effects. In light of current clinical evidence, patients with TMD and uncontrollable symptoms from MD could benefit from oral appliances before being referred to ablative, non-reversible therapies.

This study has several strengths and limitations.

To our knowledge, this is the first *controlled* study to explore the effect of gnathological therapy on MD patients. The main strong points are the presence of a matched control group and adequate sample size. In addition, the long follow-up helps to minimize the confounding placebo effect.

The main limitations are the lack of objective vestibular and craniomandibular measurements. In addition, a possible selection bias resides in the retrospective nature of the study. A prospective, long-term case–control study with objective vestibular and gnathological measures is advocated to resolve these issues.

Conclusions

Treating TMD with oral appliances could improve symptoms in patients with MD. The beneficial effect of gnathological therapy on audio-vestibular epiphenomena is maintained at least after 2 years of treatment. Occlusal splints could represent a safe, conservative option for MD patients refractory to traditional therapies before undergoing vestibular ablation. Further studies are needed to clarify the dynamics underlying the observed beneficial effects and to identify patient characteristics useful to orient the therapeutic approach.

Authors' contributions All authors contributed to the study conception and design. Material preparation and data collection were performed by EB, GB, EC, AD. Analysis was performed by VC and CG. The first draft of the manuscript was written by VC and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding No funding was received for conducting this study.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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