Vestibular drop attacks in Ménière's disease

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Abstract

The aim of the present study was to evaluate the severity of vestibular drop attacks (VDA) in Ménière's disease (MD). In addition, association between VDA severity and various complaints of MD were examined. The study used a cross-sectional survey design and included 602 people with MD belonging to Finnish Ménière Federation (FMF). The mean age and mean duration of MD of participants was 56.7 years and 12.4 years, respectively. 79.2% of participants were females. The data was gathered using a 38-item electronic questionnaire. The VDA was classified into four classes based on its severity for further analysis. VDA occurred in 305 (50.7%) of the 602 patients. Of these, 133 (22%), 80 (13%), and 92 (15%) patients experienced mild (i.e., VDA associated to tripping over), moderate (i.e., VDA associated with threatening fall unless they had been able to grab support), and severe (i.e., patients fell to the ground as in classical Tumarkin attack) degrees of VDA, respectively. There was no association between occurrence of VDA and duration of MD. In 70% of participants, VDA occurred less than once a week. Duration of VDA was few seconds in 90% of participants. 87% had single attacks whereas 13% had VDA in clusters. VDA was associated with visual auras, reduced quality of life, poor postural control and fatigue. Approximately half of the people with MD experience VDA in variable degree of severity. If VDA causes to falls or near falls, the attacks should be adequately treated.

Key Words

Ménière's disease, Vestibular drop attacks, Tumarkin attacks, Vestibular migraine, Migraine, Headache

Introduction

The Ménière's disease (MD) is an inner ear disorder consisting by definition of episodic vertigo, fluctuant hearing loss, tinnitus, and aural fullness [1]. The essential element of the illness is accumulation of endolymph in the inner ear causing the so called endolymphatic hydrops that can be visualized in MRI [2]. In this complex disorder, much less attention has been paid on the ailment of the otolith system and the association of the vestibular system with the cognitive [3] and autonomic nervous system [4]. In MD, the ailment of the vestibule of the ear containing the otolith system is frequently observed in MRI [5] and can be recorded with specially tailored tests as visual vertical recordings, cervical Vestibular Evoked Myogenic Potential (cVEMP) and ocular Vestibular Evoked Myogenic Potential (oVEMP) [6]. In the otolith system, the utriculus has the force vector directing to horizontal direction and in this way control the linear movements of the head. The sacculus is lying vertically and reacts to linear acceleration against gravity. Tumarkin was the first who reported sudden vestibular drop attacks (VDA) in that a male patients with MD suddenly slumped to the ground without vertigo and without losing consciousness [7]. These attacks leading to a fall in MD were named after him as "Tumarkin attacks" and were associated with the ailment of the otolith system. The patients often describe the VDA as a sudden alteration of lower extremity muscle tone or usually a violent sense of being pushed [8]. Jansen and Russel [8] describes Tumarkin attacks as "*the most distressing aspect of the attacks to the patients was the lack of warning and suddenness with which they occurred.*" Other complaints in MD associated to the otolith system are postural instability and gait problems [9]. Recent evidence indicates that patients with VDA can lose their consciousness for a short period of time [10].

Only a few studies have examined the prevalence and characteristics of VDA in patients with MD. A study by Morales, Angulo and Teran [11] showed that 33% of MD patients developed VDA in which the VDA diagnostic criteria included patients fell to the ground. However, other studies have reported lower prevalence numbers ranging from 3.3% to 14% [8,12-15]. With a broader definition of VDA (consisting of attacks not leading to fall and those leading to fall). Kentala et al. [16] reported VDA among 72% among 243 patients with MD visiting the tertiary referee center. While Tumarkin attacks focus on the fall to the ground, it is obvious that in milder forms of the VDA the patients can get support from the surrounding and prevent from falling. Therefore, the modern concept of otolith problems should contain different severity degrees of VDA, thus consisting of milder attacks with tripping over to those when falling down to lying position. In the severe attacks, they may suffer from injuries [17]. The more recent estimation indicates that VDA occur in variable severity among 50 to72% of MD patients [17,18].

The aim of the present study was to evaluate the severity of VDA in MD. In addition, association between VDA severity and various complaints of MD were examined.

Method

Study Design and Participants

The study used a cross-sectional survey design. Permission was obtained from the Finnish Ménière Federation (FMF; Suomen Meniere-liitto) to analyse the registry data that the FMF had collected from their members. The data was based on extensive questionnaire on symptoms related to MD. According to Finnish law this kind of study conducted in association with patient organization, which involved anonymous data does not require ethical approval. The FMF has 1,453 individual members. The e-mail address was missing among 501 members. Hence, the FMF sent the electronic survey to 952 members. Four email reminders were sent for those who did not respond to initial request to complete the survey. In total, 602 persons responded (i.e., 63.2% response rate) to the survey. The mean age of the study participants was 56.7 years (range 25 to 75 years). The mean duration of the disease was 12.4 years (range 0.5 to 35 years). The respondents included 477 (79.2%) females and 125 (20.8%) males representing the gender distribution of FMF. In order to characterize the diagnosis of MD among FMF members, we have previously evaluated the diagnostic accuracy in a group of members (n=706) with expert program and compared with the 1995 American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) criteria. In AAO-HNS criteria 97.0% of the persons had definite MD and 2.7% probable MD [19].

Data Collection

The data was gathered using a 38-item electronic questionnaire. 12 FMF board members provided input to the development and refinement of the questionnaire [20]. The questions focused on impact, social economic aspects and complaints of MD, specifically related to VDA. In this study, the *VDA was defined as a short attack of sudden perturbation of postural stability that was not associated with head movement.* We classified the VDA *as mild VDA* when the patient experienced sudden feeling of instability associated to tripping over, in *moderate VDA* the subjects could search for support with hands and prevent from falling to the ground. In *severe form of VDA* they fell to the ground. When questioning about transient loss of consciousness (T-LoC) in connection with VDA, we asked whether it was eye witnessed [20]. In addition, there were 6 disease and impact specific assessment using a mixture of open-ended and closed questions. In structured (i.e., closed) questions, the impact of the VDA was rated on four-point scale from no impact to severe impact. The diagnosis of migraine was based on previous medical diagnosis mostly carried out by neurologist, and headache was queered with 4 questions [21]. Also, three questions focused on presence of visual aura experiences. Finally, we adopted the visual analogue scale (VAS) instrument from EQ-5D-3L EuroQol to measure impact of current situation on general health-related quality of life [22,23].

Data Analysis

Descriptive statistics were used to explore the data. For continuous variables, the differences were examined using the analysis of variance (ANOVA) when data was normally distributed and non-parametric Kruskal-Wallis H test was used when data was not normally distributed to study differences between groups. Chi square test and Fisher's exact test was used to examine the association among groups for categorical variables. A *p*-value of 0.05 was used for interpretation of statistical significance.

Results

Association between demographic variables and VDA

VDA was experienced by 305 (50.7%) of the 602 patients. VDA associated to tripping over (i.e., mild VDA) was experienced by 133 (20.7%). VDA associated with threatening fall unless they had been able to search for support (i.e., moderate VDA) was experienced by 80 (13.3%) patients. Remaining 92 (15.3%) patients reported having fallen to the ground (i.e., severe VDA).

The ANOVA suggested no difference between the VDA groups for variables age and duration of MD. Also, no statistically significant differences were noted in the gender distribution in different VDA groups (see Table 1).

Table 1: Age, duration of MD and gender distribution classified by severity of the VDA. Mean and SD are given.

	No VDA (n=297)	**Mild VDA (n=133)**	**Moderate VDA (n=80)**	**Severe VDA (n=92)**	**All (n=602)**	**Statistical test outcome**
Age in years	57.6 (±12.6)	55.4 (±12.0)	56.1 (±11.7)	56.3 (±12.7)	56.7 (± 12.4)	F=1.385, *p*=0.246
Duration in years	12.3 (±19.6)	11.9 (±10.1)	12.4 (±10.7	13.5 (±10.4)	12.4 (±19.5	F=0.471, *p*=0.702
Gender: Female	237 (79.8%)	106 (79.6%)	61 (76.2%)	73 (79.3%)	477 (79.2%)	Gender difference with severity of VDA F=0.509, *p*=0.917
Gender: Male	60 (20.2%)	27 (20.4%)	19 (23.8%)	19 (20.1%)	125 (20.8%)	

Occurrence and impact of VDA among patients with MD

The most common duration of VDA lasted few seconds (90%), but in some patients, it lasted for a minute or more (see Table 2). The attacks occurred most commonly less than once a week (i.e., 71%), while some patients experienced VDA weekly or daily. Although, the VDA usually occurred in single occasion (87%), some patient experienced a cluster from attacks (13%). We further explored the occurrence of VDA in clusters as it has been clinically associated with benign recurrent vertigo and migraine. VDA in clusters was prevalent in subjects with *falls or near falls* (X^2*=8.918, p=0.012).* VDA in clusters also caused *social limitations*, *restricted work ability*, *restriction of life*, and *anxiety*. Cluster attacks in VDA was not associated with *migraine* (X^2*=0.001, p=0.976*) and *headache* was also less frequent (X^2*=3.913, p*=0.048). T-LOC was reported in 15% of participants with VDA, 7% reported T-LOC as own experience whereas 8% had outside eyewitness confirming this.

Table 2: Duration, frequency, clustering of attacks and transient loss of consciousness in VDA. Number of subjects and percentages are shown.

Group	Item	Number of subjects	Percent based on all patients (n=602)	Percent based on VDA patients (n=305)
No VDA		297	49.3%	
VDA		305	50.7%	
Duration of VDA	Few seconds	274	45.5%	89.9%
	A minute or longer	31	5.2%	10.1%
Frequency of VDA	Less than once a week	215	35.7%	70.5%
	Weekly	67	11.1%	22.0%
	Daily	23	3.9%	7.5%
Clustering of VDA	Single attack	266	44.2%	87.2%
	Cluster attacks	39	6.5%	12.8%
Transient loss of consciousness (T-LOC)	No T-LOC	229	38.0%	75.1%
	Do not know	31	5.2%	10.1%
	T-LOC own report	21	3.5%	6.9%
	T-LOC outsider confirmed	24	4.0%	7.9%

Association of VDA with visual complaints of MD

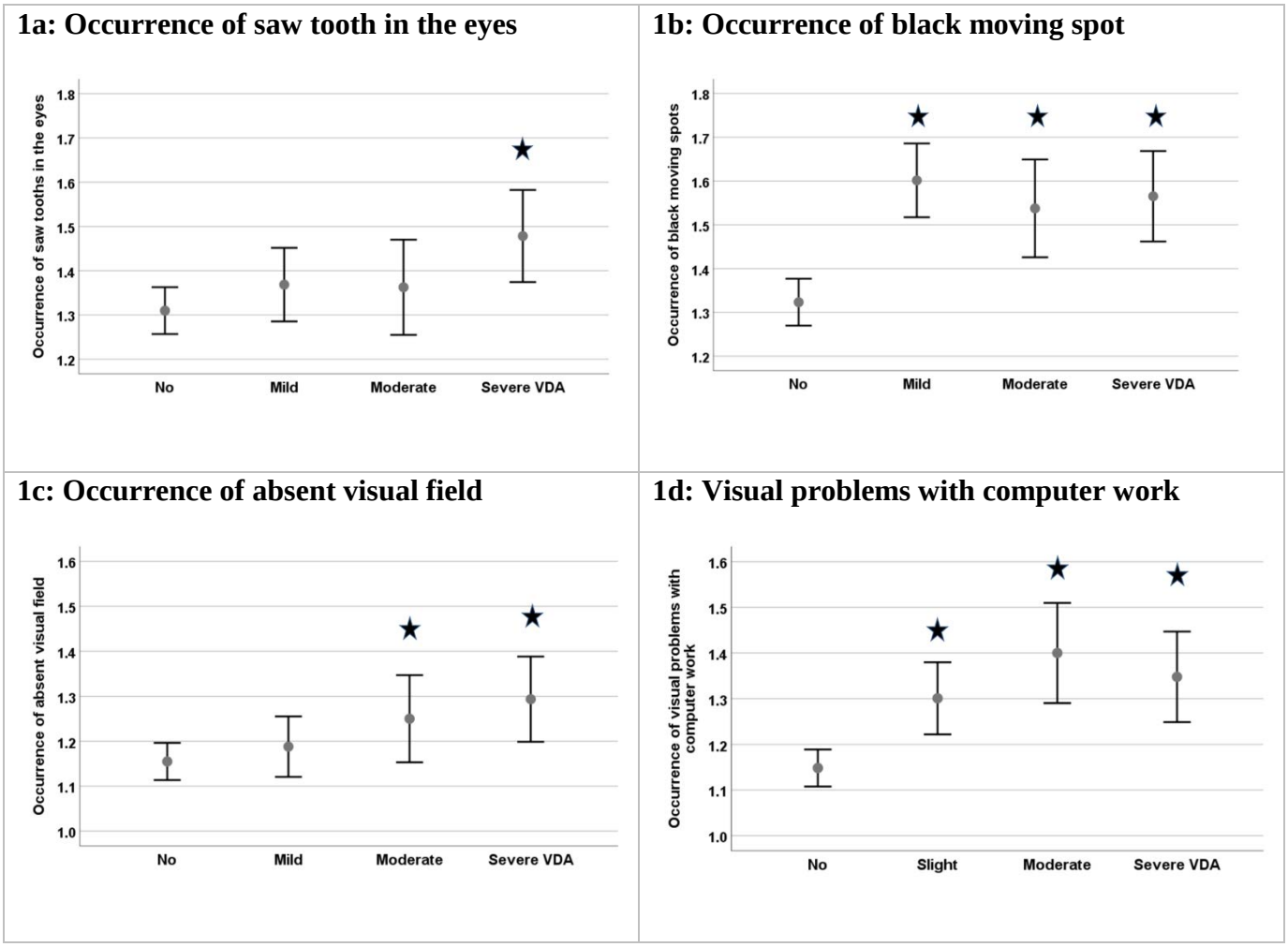
Table 3 presents the Chi square test results which showed that VDA was associated with temporary visual impairments in connection with vertigo as *saw tooth phenomenon*, *occurrence of moving black spots*, *part of the visual field absent*, and *experienced problems in watching the computer*. The visual impairment was increased with severity of VDA (see Figure 1). The patients with VDA had *headache* and *migraine* more often than non-VDA patients (see Table 3).

Table 3: Distribution of visual aura, migraine and headache associated with MD based on severity of VDA. Mean, SD, and Chi square test results are presented.

	No VDA (n=297)	Mild VDA (n=133)	Moderate VDA (n=80)	Severe VDA (n=92)	Chi square test results
Saw tooth in eyes	1.31 (±0.46)	1.38 (±0.50)	1.36 (±0.5)	1.48 (±0.50)	X^2=5.739, p=0.017
Black moving spots	1.32 (±0.47)	1.61 (±0.49)	1.54 (±0.50)	1.57 (±0.50)	X^2=40.522, p<0.001
Absent visual field	1.15 (±0.36)	1.10 (±0.39)	1.25 (±0.44)	1.29 (±0.46)	X^2=7.785, p=0.005
Computer watching problems	1.14 (±0.35)	1.31 (±0.48)	1.40 (±0.49)	1.35 (±0.85)	X^2=31.685, p<0.001
Headache	1.22	1.35	1.39 (±0.49)	1.34	X^2=6.326,

	(±0.41)	(±0.48)		(±0.48)	p=0.013
Migraine	1.24 (±0.43)	1.31 (±0.46)	1.34 (±0.48)	1.33 (±0.47)	X^2=5.443, p=0.020

Figure 1: Occurrence of visual complaints based on VDA severity. (1a) Occurrence of saw tooth in the eyes, (1b) Occurrence of black moving spot, (1c) Occurrence of absent visual field, and (1d) Visual problems with computer work. The y-axis indicate proportion of the population affected with the complaint and x-axis indicates the severity of the VDA. Mean and 95% of CI are shown. (* = p<0.05 between no VDA and VDA groups).



Association of VDA with complaints of MD

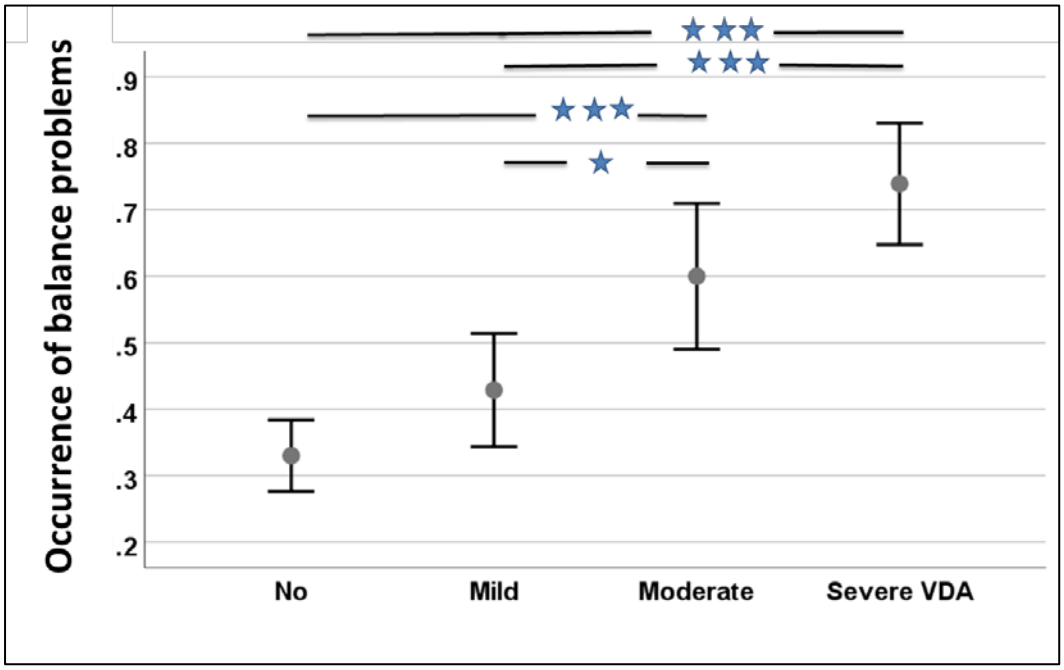
Table 4 presents the Chi square test results which suggests that VDA was associated with complaints as *vertigo spells*, *balance problems*, *fatigue* and *hyperacusis* in MD when compared with those not having VDA. However, no differences between groups was found for *tinnitus* and *hearing problems*. Figure 2 demonstrates the impact of VDA on postural stability. In Chi square test, the balancer problems increased with severity of VDA (X^2*=55.127, p<0.001).* In pairwise comparison using Fisher's exact test, no difference was observed among patients no VDA and mild VDA (p=0.081), but no VDA group differed significantly with moderate (p<0.001) and severe VDA groups (p<0.001). Mild VDA group had significant difference with moderate (p=0.016) and also severe VDA groups (p<0.001).

No significant differences were observed between moderate and sever VDA groups (p=0.072).

Table 4: Distribution of different variables associated with MD based on VDA severity. The severity of VDA was scaled as no VDA, mild VDA, moderate VDA, and severe VDA. Mean and SD, and Chi square test results are presented.

	No VDA (n=297)	**Mild VDA (n=133)**	**Moderate VDA (n=80)**	**Severe VDA (n=92)**	**Chi square test results**
Hearing problems	1.53 (±0.50)	1.55 (±0.50)	1.45 (±0.47)	1.67 (±0.47)	X^2=0.354, p=0.552
Vertigo spells	1.49 (±0.50)	1.50 (±0.50)	1.75 (±0.44)	1.78 (±0.42)	X^2=14.000, p<0.001
Balance problems	1.33 (±0.57)	1.60 (±0.49)	1.60 (±0.49)	1.74 (±0.44)	X^2=*55.127*, p<0.001
Fatigue	1.44 (±0.50)	1.48 (±0.50)	1.70 (±0.46)	1.67 (±0.50)	X^2=13.559, p<0.001
Tinnitus	1.58 (±0.48)	1.65 (±0.48)	1.61 (±0.49)	1.57 (±0.50)	X^2=0.922, p=0.337
Hyperacusis	1.45 (±0.50)	1.60 (±0.49)	1.61 (±0.49)	1.63 (±0.49)	X^2=14.857, p<0.001

Figure 2: Occurrence of balance problems based on severity of VDA. Mean and 95% of CI are shown (* = p<0.05; *** = p<0.001).

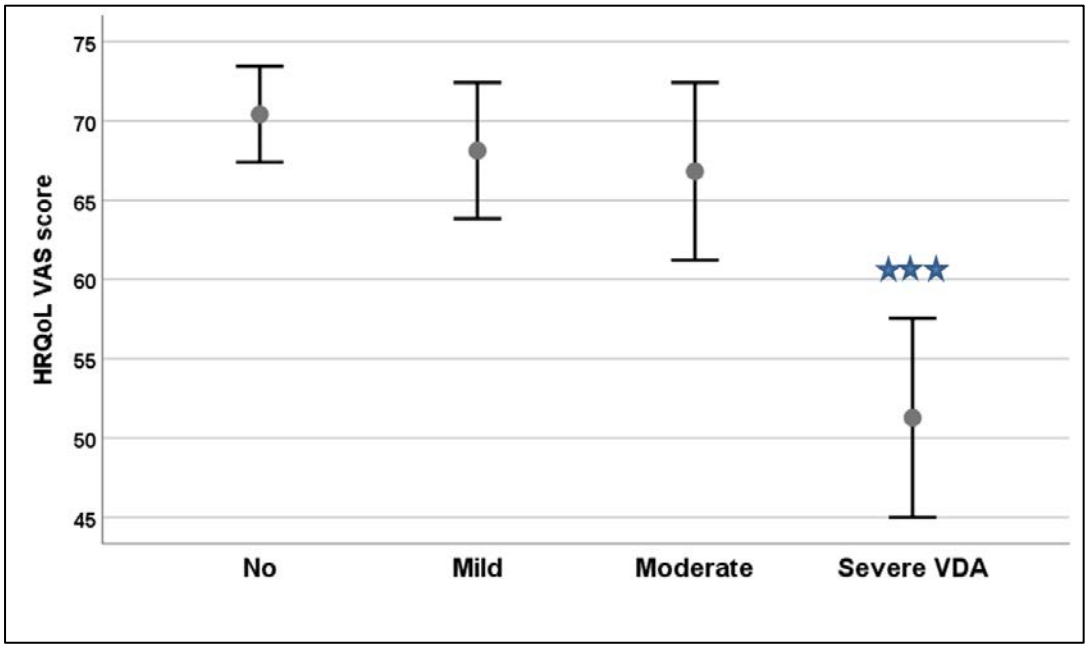


Impact of VDA on health-related quality of life

When examining the impact of VDA on health-related quality of life using the ANOVA, VAS instrument with ratings ranging from 0-100 was used as dependent variable and VDA severity was used as independent variable. There was a statistically significant difference in

health related quality of life was noted between the groups (F=12.4, $p<0.001$) and more severe VDA groups showing worsened health-related quality of life. Bonferroni post-hoc tests showed that only the severe VDA group (i.e., patients who had fallen) differed from other groups ($p<0.001$), but no differences was observed among no VDA, mild VDA and severe VDA groups (see Figure 3).

Figure 3: The effect of VDA severity on health related quality of life measured using the VAS scale of EQ-5D-3L instrument. Mean and 95% of CI are shown (*=$p<0.001$)**



Discussion

The current study explored the VDA severity in MD as well as association between VDA severity and MD complaints. The VDA was defined as sudden imbalance without head movement occurring even in sitting position. In this respect, the definition of VDA used in this study covers wider spectra of balance problems and differs from the original definition of "Tumarkin attacks" (i.e., subjects fell to the ground). As the current study included milder cases, the prevalence of VDA in MD was 50.7%, which is much higher than what is reported in the literature [8, 11-15]. Of these two thirds of the cases were mild to moderate VDA and only one third experienced severe VDA in which patients fell to the ground. Also, 13% of patients with VDA experienced T-LoC (6.5% of all subjects with MD) and these numbers are similar to recently published studies [15,24]. In half of the cases, the VDA associated T-LoC was eye witnessed [20]. The VDA attacks varied in terms of frequency and were often associated with visual complaints. Moreover, VDA impacted health related quality of life and it was associated with fatigue, increased balance problems and anxiety. However, it is noteworthy that in the classification recommendation of MD there is no instructions to notify possible involvement of otolith organ in MD [1]. Nevertheless, physicians treating MD patients should be aware and pay attention to VDA that occurs in variable degree of severity

[23]. They should also discuss the possible restrictions and injuries associated with VDA [17]. If VDA causes falls or near falls, the attacks should be adequately treated.

Effect of vestibular problems on autonomic nervous system and related cognitive processes

The specific role of the otoliths is to provide a gravitational reference frame with semicircular canals which to interpret other sensory signals to provide agile mobility, stable vision, and autonomic control of the cardiovascular and other gravity-sensitive systems [25-27]. This, in turn, is critical for the vestibular contribution to cognitive processes such as spatial memory and spatial orientation. Less is known about the autonomic nervous system elements such as fatigue, anxiousness, visual aura and T-LoC [28,29]. Our recent studies have shown that the visual complaints are common in VDA and are in correlation with T-LoC associated with MD [10,22]. The abnormal cardiovascular responses in vestibular patients is mediated by vestibulo-sympathetic reflexes originating from otolith afferents to serve body homeostasis during rapid rise from lying position [30] and failure can produce postural hypotony and cardio-inhibitory reflexes that triggers the T-LoC events [4,10,22].

The vestibular afferents are influencing the visual system in many different ways. The most known effect after vestibular lesion is oscillopsia and changes of visual vertical. We observed visual aura as moving visual spots, saw tooth or a partial loss of the visual field. The vestibular induced visual aura seem to be generated by the stimulation of the otolith afferent [31]. Noteworthy was that the visual aura perceptions in the present study were not associated with migraine [32,33].

Most physical illnesses are associated with fatigue; although it is often viewed as one of the least important symptoms by physicians [34]. It is a key component in many instruments measuring health related quality of life, as in 15D instrument [35] and SF-36 instrument [36]. Fatigue is a subjective sensation of tiredness and lack of energy and is characterized by weariness unrelated to activity levels. The brain mechanism causing fatigue is largely unknown [34]. In a population study among 9,062 repliers on fatigue symptoms, short-term fatigue (< 6 months) was reported by 5%, chronic fatigue by 31% (> 6 months), whereas “chronic fatigue like syndrome” was present only in 1% of the population [37]. In Benign paroxysmal positional vertigo (BPPV), moderate fatigue has been shown in about 30% of the subjects [38]. Levo et al. [39] adopted a fatigue question from 15D instrument and administered among 728 patients with MD. In this study, 70% of the subjects with MD reported fatigue and 30% were moderately or severely exhausted. In the present study, fatigue correlated with severity of the VDA. We observed that 40% of those subjects not having VDA and up to 70% those with falls or near falls reported fatigue. Our findings confirm the outcome of a study of Perez-Fernandez et al. [40] who observed that patients with Tumarkin attack were more disabled and experienced more autonomic nervous symptoms and fatigue. As fatigue is a common complaint even in MD and especially in its severe form, it should be addressed and included in therapeutic procedures [17,39,41].

Balance problems

Balance problems was one of the leading complaints of MD patients with VDA. Igarahsi and Kato [42] made selective lesions in squirrel monkeys vestibular organ and found that a lesion in utriculus lead to most prominent changes in body posture whereas sacculus was not so important. Noteworthy was also that the semicircular canal ablation led to significant balance problems, indicating that the collaboration of the signals from otolith organ and semicircular canal system is needed to execute a normal gait and balance. Layman et al. [6] evaluated with oVEMP and cVEMP the utricular and saccular function, respectively, and related these to gait in 246 subjects participating in the ageing study. They found that saccular function associated with changes in gait. The finding of significant associations between cVEMPs and gait speed is consistent with prior studies demonstrating a greater role for the saccule during locomotion [43,44]. Thus, dysfunction of the saccule could delay information needed for multisensory integration and coordinated gait. The lack of utricular influence on gait may also reflect the anatomy and physiology of the utricle. Ramos et al. [45] electrically stimulated the otoliths with prosthetic implants of two patients with bilateral vestibular function loss. The stimulation resulted in significant improvement in postural control, gait and in associated visual exploratory functions. The maculae utriculus and sacculus are, however, unable to discriminate between translations and tilts because both stimulate the hair cells in a similar way [28].

The disease characteristics of MD could differ depending on unilateral or bilateral occurrence [46], although this was not considered in the current study. A bilateral involvement of the MD could theoretically lead to higher prevalence of VDA as both ears could cause VDA. Endolymphatic hydrops can be symptomatic or asymptomatic, although MD diagnosis is based on symptoms. In MRI we previously indicated that up to 65% of patients with unilateral MD had endolymphatic hydrops also in asymptomatic ear [5]. Huppert et al. [47] analyzed the data of 46 studies (with a total of 7,852 patients). In their study bilaterality of MD increased with increasing duration of the disease (up to 35% within 10 years, up to 47% within 20 years). However, in the present study the duration of the MD nor age did not correlate with VDA, indicating that bilaterality of MD may not explain the occurrence of VDA nor severity of it. This topic, however, deserves to be studied more carefully.

Study Limitations

The current study used a broader definition of VDA than the original Tumarkin definition and demonstrated that VDA severity is associated with various complaints of MD. However, the study has a few limitations. First, the response rate of subjects was 63%. This means that there could be some sampling bias of including more symptomatic patients in the current study. Second, the study did not differentiate unilateral versus bilateral MD patients which could have bearing towards interpretation of study results. Researchers needs to consider and account for these limitations when planning future studies.

Conclusions

We evaluated the character, frequency and severity of VDA among patients with MD. We used a novel classification containing definition of VDA from slips to fall. The results

indicate that VDA, mostly mild, occurs in 50% of the 602 patients who were members of a patient organization in Finland. In all participants with MD the VDA associated to tripping over was experienced by 21%. VDA associated with threatening fall unless they had been able to grab support was experienced by 13% of participants and 15% participants fell to the ground as in classical Tumarkin attack. In 90% of participants, VDA occurred rarely than once a week, and 86% had single attacks whereas 14% had VDA in clusters. In 15% of the participants with VDA the attack was associated with short lasting T-LoC. VDA was associated with visual auras, reduced quality of life, poor postural control, and fatigue. These effects should be recognized by physicians and included in therapeutic procedures of MD patients.

Authorship

IP conceived this study and it was designed by VM. NP collected the data from patients with MD. This manuscript was drafted by IP. All authors critically appraised and approved the manuscript.

Conflict of Interest

None to declare.

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None to declare.

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