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Management of Mal de Debarquement Syndrome as Vestibular Migraines

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Abstract

Objective—Mal de débarquement syndrome (MdDS) is a balance disorder which typically starts after an extended exposure to passive motion, such as a boat or plane ride. Management is typically supportive (e.g. physical therapy), and symptoms that persist beyond six months have been described as unlikely to remit. This study was conducted to evaluate the response of patients with MdDS to management with migraine prophylaxis, including lifestyle changes and medical therapy.

Study Design—Prospective review

Setting—Ambulatory setting at a tertiary care medical center

Methods—Clinical history, detailed questionnaires, and audiograms were used to diagnose patients with MdDS. Those patients with the diagnosis of the MdDS were placed on our institutional vestibular migraine management protocol.

Results—Fifteen patients were diagnosed with MdDS with a predominance of females (73%), with a mean age of 50 ± 13 years. Eleven patients (73%) responded well to management with a vestibular migraine protocol, which included lifestyle changes, as well as pharmacotherapy with verapamil, nortriptyline, topiramate, or a combination thereof.

Conclusions—Management of MdDS as vestibular migraine yields successful results in improving patients' symptoms and increasing the quality of life. Nearly all the patients suffering from MdDS had a personal or family history of migraine headaches or had signs or symptoms suggestive of atypical migraine.

Keywords

MdDS; Mal de débarquement syndrome; vestibular migraine; quality of life

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Introduction

Mal de débarquement syndrome (MdDS), also known as rocking dizziness or “sea legs”, was first described by Brown and Baloh in 1987.¹ It is a subjective sense of motion after being exposed to passive motion and, in most cases, occurs after sea travel²; however, it has been reported to occur after air or land travel as well.³ The pathogenesis of MdDS is still unclear.⁴⁻⁶ The distinction between the transient and persistent MdDS is very important. Persistent MdDS is considered pathologic; however, the transient variation is a common disorder which is most frequently observed in naval personnel.⁷

Patients usually feel a rocking, bobbing, or swaying sensation which is often accompanied by unsteadiness and disequilibrium that occurs persistently after cessation of the exposed passive motion stimulus.⁸ Previous studies indicate a high association of MdDS and headache⁹ with migraine, especially in patients with spontaneous mal de débarquement (MdD) episodes.¹⁰ This association of MdDS and migraines might help to better understand the pathophysiology of MdDS. Modification of lifestyle, diet, and sleep hygiene has been useful in treatment and improvement of patients with migraine disorder and vestibular migraine.¹¹ Due to the significant overlap between migraine and vestibular disorders,¹² we sought to evaluate whether migraine treatment modalities may also be applicable in patients with MdDS and improve their quality of life (QOL). This study was designed to prospectively evaluate and measure the changes in the QOL in patients with MdDS treated with migraine prophylactic medications.

Methods and Materials

All patients with signs and symptoms of dizziness presenting to our tertiary neurotology clinic were asked to fill out a questionnaire to further explore their dizziness, headaches (if any), and other migraine related symptoms. Clinical history and MdDS criteria¹³ were used to diagnose patients with MdDS [Table 1]. MRI of the brain, audiogram and vestibular testing were used to exclude other causes of vertigo or dizziness. If a patient's diagnosis remained uncertain, or if they had the signs or symptoms of transient MdD, they were excluded from the cohort. Approval was obtained from the Institutional Review Board.

A group of 15 patients presenting with MdDS from 2013 to 2015 were treated with our migraine protocol [Table 2]. A historical control group of 17 patients diagnosed with MdDS between 2010 and 2012 were additionally retrospectively reviewed. All patients in the control group were treated with physical therapy and vestibular rehabilitation (VR). Meclizine 25 mg every 6 hours or diazepam 2 mg every 8 hours as needed was used for symptomatic relief in the control group. Four of the control group patients had been treated with a hydrochlorothiazide/triamterene combination by other physicians prior to their presentation to our center.

The patients with the diagnosis of MdDS were treated with migraine prophylactic medications even in the absence of a migraine headache diagnosis. The patients were most commonly prescribed nortriptyline 25 mg qhs with gradual escalation of 25 mg every 3 weeks up to 75 mg if the symptoms had not improved. Nortriptyline was given to patients

who had difficulty sleeping, had interrupted sleep, or admitted to significant stress or anxiety. To avoid confounding, patients who were on antidepressant medications prior to presentation were excluded. In cases where the patient's blood pressure was elevated at the time of the visit, Verapamil SR 24 hr 120 mg qhs was used with escalation to 180 mg and then 240 mg every 2 weeks if symptoms were not improved. If the patient's symptoms had not improved after the initial medication, the second medication (either nortriptyline or verapamil) was added. If the combination was not effective, acetazolamide 125 mg qam with gradual escalation weekly to 500 mg bid at the highest dose or topiramate 25 mg qhs with weekly escalation of 25 mg up to 150 mg qhs was given [Table 2]. The patient was instructed to not increase the dose if the symptoms were under control. If the patient was experiencing bouts of vertigo, they were instructed to report back and increase the medication as scheduled. All of the patients in the treatment group had previously been treated with some degree of physical therapy and/or VR prior to presenting to our center.

Assessment of QOL

We used a modified version of a QOL questionnaire originally developed by Kato et al. for the QOL implications of Meniere's disease (MD).¹⁴ We chose this questionnaire because there are several similarities between MdDS and MD. Vertigo and dizziness attacks are common between these two disorders. We omitted the questions related to hearing loss and tinnitus which are mostly seen in patients with MD. Also we rephrased some sentences and changed the MD to MdDS, similar to the study by Macke et al.¹⁵ This questionnaire was validated by our study team.

This MD QOL Questionnaire is an internally validated tool with 17 multiple-choice questions to determine QOL after treatment of MdDS in 3 different categories (physical, emotional and social well-being). There were 34 paired items for pre- and post treatment conditions, slightly modified to meet the treatment instituted here. Numerical values from 0 to 4 are assigned to the answers, with 0 corresponding to the answer indicating the poorest QOL and 4 given to the answer indicating the best QOL (Minimum score = 0; Maximum Score = 68). The sum of the answers for the pre-treatment and post-treatment items was calculated. Each one of these values is then divided by the maximum possible scores to determine the “pre-treatment QOL score” and “post-treatment QOL score”, respectively.

$$\text{Pre-treatment QOL score} = \frac{\text{sum of Pre-treatment question scores}}{\text{Maximum possible pre-treatment scores}} \times 100$$

$$\text{Post-treatment QOL score} = \frac{\text{sum of Post-treatment question scores}}{\text{Maximum possible post-treatment scores}} \times 100$$

The questionnaire was given to the patients before starting the medication to evaluate their QOL. After taking medications and initiating lifestyle modifications for an average time of 3, 6, and 12 months, patients were visited again at the clinic. They were asked to fill out the

questionnaire which was evaluating their quality of life after treatment. Pre-treatment and post-treatment scores were compared.

Also, the Visual Analog Scale (VAS) was used to determine the severity of symptoms described by the patients before and after treatment [Table 3].

Statistical Analysis

Questions on the MdDS-Q were classified into three separate domains: mental, physical, and social. Questions 7, 8, 15, 16, 19, 20, 21, and 22 were used to evaluate mental health; Questions 9, 10, 13, 14, 17, 18, 23, 24, 31, 32, 33, and 34 assessed physical health; and Questions 3, 4, 5, 6, 11, 12, 25, 26, 29, and 30 evaluated social health. Domain-specific QOL scores were determined for each domain, and each domain-specific QOL score showed statistically significant improvement after treatment.

The frequency and percentage of patients with a diagnosis of MdDS was determined, and their rate of response to migraine prophylactic treatment is reported. Paired t-test analysis was performed for comparing the changes in the pre and post treatment scores. Because multiple comparisons were made on the same data, the Bonferroni correction was applied to reduce the occurrence of type I errors. Therefore, a P value of <0.002 was considered as significant. All statistical analyses were performed using PASW 18.0 (SPSS Inc., Chicago, IL).

Results

Forty-two patients were diagnosed with signs and symptoms of Mal de Debarquement Syndrome (MdDS) during 2010 to 2015. These patients had the feeling of being on a boat. Between 2013 and 2015, 15 patients (34%) were diagnosed with persistent MdDS, while 17 patients were diagnosed between 2010 and 2012.

All but one of the patients in the treatment group had developed their symptoms after a cruise ship, with the exception of one patient who had been on a 15 hour flight. In the treatment group, there was a predominance of females (11/15; 73%) and a mean age of 50 ± 13 years. Ten of these patient (67%) fulfilled the International Headache Society criteria for migraine headaches. Chronic “sinus headaches” were present in 13 (87%) of these patients. The average VAS score in the treatment group improved from 7.6 to 1.8. Eleven patients (73%) had a greater than 6 point improvement on a visual analog scale (VAS) of 0 to 10, two patients had some improvement (3 points improvement), and two patients had no improvement [Table 3].

In the control group, 12 of the 17 patients with MdDS were females (12/17; 71%), with a mean age of 46 ± 9 years. All of the control group patients developed symptoms after a ride on a ship. In the control group, the average VAS score changed from 7.4 to 6.8. Two patients (12%) had a greater than 5 point improvement. There was no significant improvement in the remaining 15 patients.

Pre- and post-treatment QOL showed statistically significant correlation in some domains among patients in the treatment group [Table 4]. In comparison, the historical control group

showed no statistically significant change in the VAS but showed a statistically significant improvement in 2 similar items of QOL [Tables 3 & 4]. The data on the prevalence of motion sickness, visual motion sensitivity, family history of migraine, etc. is depicted in Table 5.

Discussion

In this study, we found that 73% of patients with persistent MdDS had improvement of their QOL and symptom intensity when treated with migraine lifestyle changes and prophylactic therapy. In our experience, MdDS patients who were treated with physical therapy or vestibular rehabilitation did not have a significant improvement in their symptomatology or their QOL.

The pathophysiology of MdDS has not been clarified yet. Many patients are diagnosed years after the initial onset of symptoms using clinical criteria based on subjective symptoms. There has not been any conclusive objective testing for detecting or diagnosing MdDS. However, recent neuroimaging studies have demonstrated some promising insight into the detection of this debilitating disorder. A study by Cha and colleagues on MdDS patients found a correlation between metabolic activity and functional connectivity of the entorhinal cortex (EC) and amygdala (16). Moreover, positron emission tomography revealed a hypermetabolic state in EC and amygdala, while there was a diffusively spread hypometabolic condition in the cortical and subcortical regions. Functional MRI data showed an increased functional activity between EC/amygdala regions and the visual and vestibular areas of the brain.¹⁶ Interestingly, abnormal activity in these regions of the brain in MdDS patients has also been described in those with chronic migraine.^{17, 18} In another recent study by Cha and colleagues, the investigators described alterations in gray matter in the visual-vestibular processing areas of the brain of the patients with MdDS.¹⁹ There appears to be considerable overlap in results of functional imaging studies of MdDS patients with those of patients with chronic migraine headaches.

MdDS is a debilitating disorder and has impact on the socio-economic status and psychosocial behavior of the patient. There is usually a long period between the onset of symptoms and the time of diagnosis, and oftentimes patients will be subject to numerous care provider visits and diagnostic procedures, which can take up to months or years.¹⁰ This long time period can be frustrating and debilitating for patients and can also lead to psychological and psychiatric consequences, including depression and anxiety.¹⁰ A study by Macke et al showed that the cost to obtain a diagnosis of MdDS was approximately \$3,000 with an average of 19 physician visits for each patient. The total annual cost of the disorder ranged from an average of \$11,500 to \$13,561 per patient based on the employment status prior to developing MdDS.¹⁵ The negative impact of the MdDS on QOL of these patients was also noted in their study results.

MdDS has been reported to be associated with other vestibular disorders, such as motion sickness and migraine, more frequently than the population baseline.¹⁰ The condition can be precipitated by stressful conditions and hormonal changes. It is more common in females^{10, 20} and can also be comorbid in patients with migraine headaches.^{21, 22} Our study showed

a predominance of females (11/15, 73%) and a strong association between MdDS and migraine headaches as defined by IHS criteria (11/15, 73%). We also found an association between MdDS and chronic sinus headaches (13/15, 87%). The review of questionnaires, history and physical exams for the MdDS patients enrolled in this treatment group indicated that they had signs and symptoms that were highly suggestive for a migraine background, but did not fulfill the criteria for migraine headaches and/or vestibular migraines. Our previous experience had noted that treating these patients with migraine prophylactic therapy, which includes dietary and lifestyle modifications, along with medication adjuncts, yields excellent outcomes. Through this analysis, we were able to ascertain these findings, and found that patient quality of life improved in 73% of the MdDS patients (n = 11/15). The QOL score did not change significantly in three of the patients and in another patient the score slightly worsened following treatment. We have found that patients who do not respond to medical therapy are those in whom triggering factors such as poor sleep habits, sleep apnea, or dietary modifications had not been eliminated by the patients.

As the exact pathophysiology of the disorder is not well understood, treatment of the MdDS patients has been difficult.²³ Pharmacological treatment of the patients has been successful in some cases using benzodiazepines such as clonazepam and diazepam.^{13, 20} Hain et al²⁰ performed a survey analysis of 27 patients with MdDS and noted that benzodiazepines were of most benefit in symptom reduction. Prophylactic medical therapies have been found to be highly effective in the management of migraines, including tricyclic antidepressants (e.g. nortriptyline), anticonvulsants (e.g. topiramate), and calcium channel blockers (e.g. verapamil). Although some studies indicate that calcium channel blockers are not beneficial in improvement of the symptoms in MdDS patients.^{13, 20} Our study revealed that verapamil, along with lifestyle modification and stress reduction, can be useful in alleviating symptoms in these patients and can improve their QOL. We also noticed that combined nortriptyline and topiramate therapy can also be used safely in some MdDS patients and has promising effects in improvement of the QOL. While as physicians we would ideally like to have one drug at one dose work for all patients, treatment of patients suffering from a migraine-related condition is often much more complicated. We have found that these patients are very sensitive to medications and the dosage of these medications has to be gradually escalated to find a therapeutic dose. Often, combination of drugs at various doses is necessary to achieve substantial improvement in their condition as some patients are able to tolerate higher doses than others. The administered medication is also limited by other medications the patient uses, such as antidepressants, anti-hypertensives, and narcotic medications. If only verapamil at a dose of 120 mg, for example, is studied for this condition, only 2 of the 15 patients would have improved their symptoms in our study. This would have resulted in a negative result for the use of verapamil. However, when the dose is escalated or verapamil is combined with other medications, 7 of the 15 patients had improvement. Therefore, a greater degree of medication management is necessary when treating these patients than most neurologists are accustomed to doing.

Medication management must be accompanied by dietary and lifestyle modification, stress reduction, and proper sleep hygiene. This requires some education to patients and can often be accomplished using a comprehensive handout. We believe that MdDS is likely part of the migraine spectrum and occurs in patients who are carriers of the yet to be identified

migraine gene(s). The condition tends to occur more commonly in females around menopause time and is triggered by excessive motion. Treatment with migraine prophylaxis seems to be much more successful than physical therapy and should be tried in all patients with persistent MdDS.

This study is limited by the small patient cohort which is due to the uncommon nature of this condition. In addition, a historical control group was used rather than a randomized clinical trial. When we first realized that there may be a connection between MdDS and migraine and had good initial results treating our MdDS patients with migraine prophylaxis, we chose to do a prospective study with this group of patients and compare to our historical group. Future studies should involve a randomized controlled clinical trial to confirm the efficacy of migraine prophylaxis in the management of MdDS.

Conclusion

Results from this prospective study indicate that a majority (73%) of patients diagnosed with MdDS respond significantly to migraine diet and lifestyle changes when combined with migraine prophylaxis therapy. Nearly all the patients suffering from MdDS had a personal or family history of migraine headaches or had signs or symptoms suggestive of atypical migraine.

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Table 1
Inclusion criteria for MdDS (13)

<p>a. Chronic perception of rocking dizziness (e.g., rocking, bobbing, swaying) that started after passive motion such as sea, air and land traveler exposure to virtual reality</p> <p>b. Symptoms lasting at least 1 month</p> <p>c. Normal inner ear function or non-related abnormalities as seen by ENG/VNG and audiological tests</p> <p>d. Normal structural brain imaging or non-specific alterations with a non-contrast MRI scan (when no additional more advanced analyses were carried out)</p> <p>e. Symptoms not better accounted for by another diagnosis made by a physician</p>

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Table 2
Medications used to treat patients with MdDS and doses of medication at last follow up

Medication	Dose	Number of patients	Total number of Patients	Percent Total (%)
Nortriptyline	25 mg	3	5	33
	50 mg	2		
	75 mg	0		
Verapamil	120 mg	2	4	26
	180 mg	1		
	240 mg	1 (not better)		
Nortriptyline + Verapamil	10 + 240 mg	1	3	20
	50 + 120 mg	1		
	75+120 mg	1 (mildly better)*		
Topiramate	150 mg	1	1	7
Nortriptyline + Topiramate	50 + 150	1 (not better)	1	7
Nortriptyline + Verapamil + Topiramate	50+240+100	1 (mildly better)*	1	7

* mildly better means clinically they showed improvements; however statistically there was no significant change.

Table 3
Descriptive characteristics of patients with MdDS completing the QOL survey (means \pm SD) and Visual Analog Scale (VAS)

Characteristic	Patients group	Control group
Participants (n)	15	17
Female gender, n (%)	11 (73%)	12 (71%)
Age at which symptoms started (years, mean \pm SD)	45 \pm 14	42 \pm 10
Age at which patients presented to clinic (years, mean \pm SD)	50 \pm 13	46 \pm 9
Duration of symptoms (months, mean \pm SD)	48 \pm 41	42 \pm 32
Duration of follow up after treatment (months, mean \pm SD)	16 \pm 11	14 \pm 8
VAS before treatment (mean \pm SD)	7.6 \pm 0.9	7.4 \pm 1.1
VAS after treatment (mean \pm SD)	1.8 \pm 2.6	6.8 \pm 1.6

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Table 4

Summary of domain-specific QOL score changes

Groups	Domain	Average Pre Treatment Score	Average Post Treatment Score	Score change	P - value
Treated with migraine prophylactic medication	Mental	7	15	+8	0.003
	Physical	9	17	+9	0.000
	Social	8	18	+10	0.000
Treated with physical therapy and vestibular rehabilitation	Mental	6	16	+10	0.01
	Physical	7	11	+4	0.07
	Social	6	12	+6	0.05

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Table 5
Prevalence of symptoms and clinical features related to migraine among patients with MdDS after treatment with migraine prophylactic medications and comparing with patients with MdDS treated with physical therapy and VR

Clinical Feature	All patients with MdDS		Patients treated with Migraine prophylactic medications		Patients treated with physical therapy & VR		Treatment vs. Control P value*
	Frequency, N=32	%	Frequency, N=15	%	Frequency, N=17	%	
Sensitivity							
Visual Motion Sensitivity	16	50%	9	60%	7	41.2%	0.48
Light Sensitivity	15	46.9%	7	47%	8	47.1%	0.85
Sound Sensitivity	13	40.7%	7	47%	6	35.3%	0.87
Head Motion Sensitivity	20	62.5%	10	67%	10	58.8%	0.79
Smells Sensitivity	10	31.3%	4	27%	6	35.3%	0.43
Weather Change Sensitivity	7	21.9%	2	13%	5	29.4%	0.49
Medication Sensitivity	5	15.6%	2	13%	3	17.6%	0.63
Motion sickness	23	71.9%	10	67%	13	76.5%	0.35
Mental Confusion (Head Fog)	17	53.1%	9	60%	8	47.1%	0.12
Family History							
Family History of Migraine	8	25%	3	20%	5	29.4%	0.56
Family History of Meniere's Disease	0	0	0	0	0	0	0.92
Family History of Motion Sickness	1	3.1%	1	6.7%	0	0	0.05
History of Using Medication for Migraine	7	21.9%	3	20%	4	23.5%	0.73
Sinus Pain, Facial Pressure, or Headache When exposed to Wind or Air Conditioner	23	71.9%	13	86.7%	10	58.8%	0.01
Pain in Scalp or Face from touching	5	15.6%	1	6.7%	4	23.5%	0.03
History of Getting Headache When Eating Ice Cream	18	56.3%	9	60%	9	52.9%	0.81
History of Sinus Headaches	23	71.9%	13	86.7%	10	58.8%	0.04
Neck Stiffness	12	37.5%	8	53.3%	4	23.5%	0.06
Fulfilled IHS Criteria for Migraine Headache	23	72%	11	73.3%	12	71%	0.9