Paroxysmal symptoms among Iraqi patients with multiple sclerosis at Dr. Saad Al Witri Neurosciences Hospital

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Abstract

Background: Paroxysmal symptoms are brief (lasting seconds to minutes) stereotyped symptoms occurring suddenly and many times a day, for days up to a few months. ***Objective:*** to study the prevalence of paroxysmal symptoms in multiple sclerosis patients and their correlation with the demographic data of the patient, type of MS, duration of the illness, severity of the disease, radiological findings and disease modifying therapies. ***Method:*** A cross-sectional survey enrolled (100) patients with multiple sclerosis, conducted in the Multiple Sclerosis Clinic in Dr. Saad Al-Witri Neurosciences Hospital - Baghdad during June 2019 - December 2019. ***Results:*** (29%) of the participants had reported paroxysmal attacks of various types. Betaferon® and Rebif® were found to be significantly correlated with absence of PS. Patients with paroxysmal attacks had longer duration of disease. Patients with PS had significantly lower EDSS score. Highest proportion of patients had paroxysmal paresthesia (34.48%). ***Conclusions:*** Paroxysmal symptoms are common presentations in multiple sclerosis initially or during the course of the disease, with paroxysmal paresthesia being the most common among them. Betaferon® or Rebif® might be a good choice for patients who are experiencing paroxysmal symptoms. Paroxysmal symptoms tend to occur with the least disabled MS patients and longer disease duration.

Keywords: Multiple sclerosis, Paroxysmal symptoms

Introduction

Paroxysmal symptoms (PS) are brief (lasting seconds to minutes) symptoms occurring suddenly and many times a day. They are often stereotyped and continue in clusters with great intensity for days up to a few months. While their pathophysiology is well characterized, they are among the most frequently misinterpreted manifestations of MS. Since the latest revision of the definition of MS relapse, PS (historical or current) are now accepted as relapses as long as they consist of multiple episodes occurring over not less than 24 hours[1]. The loss of the myelin sheath leads to disruption of nerve conduction in patients with MS. Some of these disorders are due to conduction blocking of the passage of nerve impulses related to available channels in the plasma membrane of axons and / or increasing the refractory period of demyelinated axons. Another type of neuro-conduction disorders seems to originate from the non-coupling synaptic electrical activity between axons of the

same nerve fiber, a process known as transmission or ephaptic coupling. The ephaptic transmission occurs when voltage changes induce firing of a new action potential in a neighboring nerve fiber during the action potential of the axon[2]. Transient neurological disturbances mostly come on spontaneously but may be precipitated by exercise, hot baths, smoking and emotion (anxiety), neck flexion, eye movements and hyperventilation[3]. Mostly, reported paroxysmal attacks are paroxysmal dysarthria and ataxia, paroxysmal paraesthesia, paroxysmal diplopia, and paroxysmal hemiparesis. Others are trigeminal neuralgia and Lhermitte's sign. These are typically different from other transient symptoms by their brevity, frequency (from 1 ± 2 times per day up to a few hundred times per day), stereotyped fashion and response to carbamazepine[4].

Methodology

1. *Study design and setting*

This study is a cross-sectional survey conducted in the Multiple Sclerosis Clinic in Dr. Saad Al-Witri Neurosciences Hospital - Baghdad during the period from June 2019 through December 2019.

2. *Study Population*

The study included information about patients with multiple sclerosis who were defined according to the accepted international diagnostic criteria used at the time of conducting the study (McDonald's criteria) at all ages. All patients diagnosed with MS who had paroxysmal symptoms (epilepsy, trigeminal neuralgia, Lhermitte's sign, paroxysmal tonic spasm, paroxysmal dysarthria/ataxia, paroxysmal vertigo and paroxysmal paresthesia) due to demyelinating process, as well as cases of MS without paroxysmal symptoms were included in this study. All the conditions that cause the previous parameters other than demyelinating process confirmed by laboratory, electrophysiology and imaging modalities were excluded.

3. *Data collection tools*

Patients' data was collected retrospectively from clinical records and during their follow-up clinic visits with a sample size of 100 patients. The patients were labeled as clinically definite MS or clinically isolated syndrome according to McDonald criteria 2010. Variables include age at onset, gender, duration of the disease, clinical details of the attack, line and type of DMT, radiological findings and Expanded Disability Status Scale Score

4. *Statistical analysis*

Correlations between variables were assessed using Student's t-test for numerical variables and using Chi-square test and Fisher exact test for categorical variables. P-value of < 0.05 was considered statistically significant.

Results

This study included a total of (100) patient with multiple sclerosis for the evaluation of paroxysmal attacks among them. Twenty-nine patients (29%) of them had reported positive paroxysmal attacks of various types, while the remaining (71%) reported no paroxysmal attacks (figure 1).

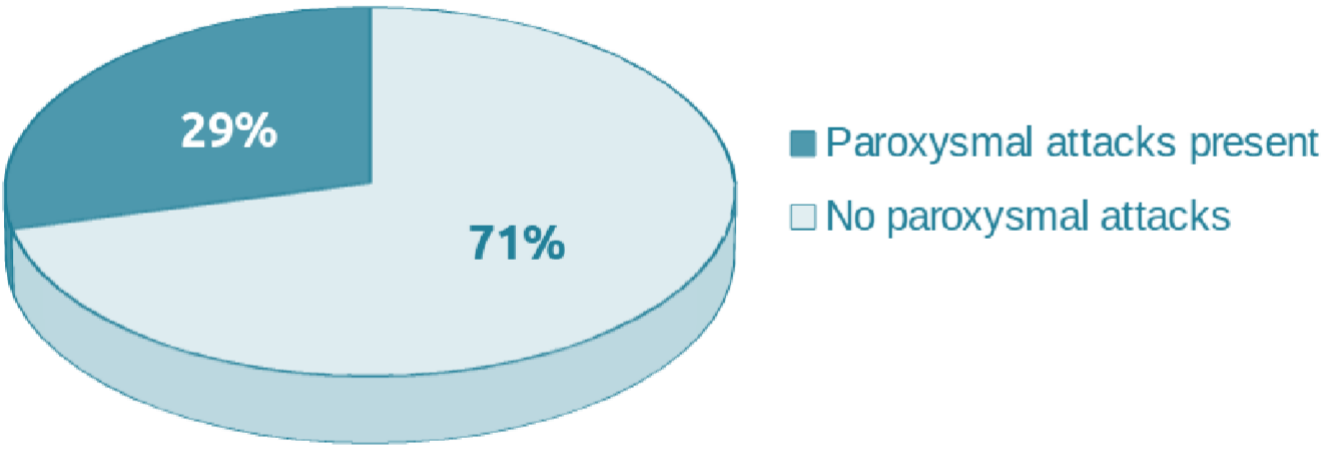

Figure (1): Proportion of paroxysmal symptoms among multiple sclerosis patients with paroxysmal attacks, P-value of 0.027.

No significant difference in age was observed among those with paroxysmal attacks (35.93 ± 12.50) and those without (38.11 ± 10.19), Student's t-test = 0.91, P-value = 0.366. Higher proportion of study participants were females, forming (66%) of total patients with paroxysmal attacks, while males comprised the remaining (34%). No relationship was observed between gender and the presence of paroxysmal attacks, chi-square = 0.99, P-value = 0.319. The commonest disease type among study participants was relapsing/remitting (RR), with a proportion of (94%). Among patients with paroxysmal attacks, disease type was relapsing/remitting (RR) in (89.66%), followed by clinically isolated syndrome (CIS) in (6.90%) and primary progressive (PP) in (3.45%). There was significant correlation between Betaferon® and paroxysmal attacks, with P-value of 0.047. Paroxysmal attacks were present in (38.0%) of patients who used Betaferon®, while the remaining (62.0%) did not have paroxysmal attacks. There was another significant correlation between Rebif® and Paroxysmal attacks were present in only (9.5%) of patients who used Rebif®, while the majority (90.5%) did not have paroxysmal attacks. The mean duration of disease among study participants was (3.73 ± 3.38) years, ranging from (2 months) up to (20 years). There was significant difference in duration of disease among patients with paroxysmal attacks (5.34 ± 5.38) and those without (3.08 ± 1.74) with P-value of 0.034. Patients with paroxysmal attacks had longer duration of disease with a mean difference of (2.26) years. Expanded Disability Status Code (EDSS) of study participants ranged from (0 – 7) with a median of (2.5). Patients with paroxysmal attacks had significantly lower EDSS score (median = 2) compared to patients without paroxysmal attacks (median = 3), Mann-Whitney U test = 754.50, P-value = 0.035. Regarding the type of the paroxysmal attack, highest proportion of patients had paroxysmal paresthesia (34.48%), followed by paroxysmal dysarthria/ataxia in (27.59%). Table (1) provides the details.

Table (1): Types of paroxysmal symptoms

Type of Paroxysmal Attacks	No.	Gender No. (%)		Out of the total (%) (n=100)	Out of those with PS (%) (n=29)	P-value (Fisher exact test)
		Male (n=12)	Female (n=17)			
Paroxysmal paresthesia	10	6 (50.00%)	4 (23.53%)	(10%)	(34.48%)	0.236
Paroxysmal dysarthria/ataxia	8	2 (16.67%)	6 (35.29%)	(8%)	(27.59%)	0.408
Lhermitte's sign	5	3 (25.00%)	2 (11.76%)	(5%)	(17.24%)	0.622
Paroxysmal vertigo	5	2 (16.67%)	3 (17.65%)	(5%)	(17.24%)	1.000
Trigeminal neuralgia	2	-	2 (11.76%)	(2%)	(6.90%)	0.497
Paroxysmal tonic spasm	1	-	1 (5.88%)	(1%)	(3.44%)	1.000

Majority of patients (75.86%) had the onset of the attack during the course of disease, and it lasted for a few seconds (less than 5 seconds) in (79.31%). Aggravating factors were present in 22 patients, forming three-quarters of the patients (75.86%), with hotness being the commonest factor among them (40.91%). Regarding MRI findings among patients with paroxysmal attacks, peri-ventricular lesion was the commonest, accounting for (86.20%) of multiple sclerosis patients with paroxysmal attacks, followed by spinal cord lesions in (55.17%).

Discussion

This is the second survey conducted in Iraq that studies the prevalence of paroxysmal symptoms among patients with multiple sclerosis. Our study showed that (29%) of MS patients reported PS of various types. It is lower than the result shown by Hawass[5] which was (62%), and this could be explained by the exclusion of paroxysmal diplopia, paroxysmal itching, ice-pick headache and facial myokymia in our study and its inclusion in the aforementioned study. In comparison with Magdalena *et al.* [6] which showed (4.5%) of patients experienced PS, our study showed higher proportion, mostly because we included paroxysmal tonic spasms and Lhermitte's sign which were excluded in Magdalena[6]. Tüzün *et al.* [7] showed that (3.6%) of patients had PS which is lower than our study. This could be explained by the fact that the above research studied paroxysmal tonic spasms, paroxysmal diplopia and paroxysmal ataxia/dysarthria only. Also we should take in consideration the environmental factors that could increase the triggering of PS in our patients than in patients in other climates. Females had the largest quantity of PS which reflects the higher proportion of MS among

them than in males. There was no correlation between gender and age with the presence of paroxysmal symptoms, (P-value = 0.319 and 0.366) respectively. Regarding the effect of the disease modifying therapy (DMT), Betaferon® and Rebif® have a good correlation with a reduced PS frequency (P-value = 0.047, 0.027 respectively). The difference in the P-value among them attributed to the wider use of Betaferon® over Rebif®. The significance of Rebif® in our study was comparable to that shown by Hawass[5] (P-value = 0.018). It is found that the more duration of the disease, the more incidence of PS (P-value = 0.034) which is corroborative by the higher proportion of occurrence of PS during the disease course (75.86%).Therewasan inverse relationship between the presence of PS and the increment in EDSS scaling (median = 2, P-value = 0.035) which is identical to Tüzün[7] (median = 2). These are possibly explained by the decay in ephaptic transmission in the advanced conditions of the disease. This study showed that paroxysmal paresthesia had the highest proportion among PS (34.48%) closely similar to Twomey[3] (35.71%). Paroxysmal dysarthria/ataxia in the present study was (27.59%) among PS, which was compatible with Twomey[3] (28.57%) and to a lesser extent with Osterman[8] (31.81%). Lhermitte's sign settled in the third sequence with (5%) from the total sample, which is comparable to Solaro *et al.* [9] (9%) but lower than Al-Araji[10] (41%), and this could be due to the larger sample size and the different method used in data collection. Paroxysmal vertigo also had a prevalence of (5%) of the total sample, which is compatible with the percentage shown in Hawass[5] (5.3%). Trigeminal neuralgia was estimated to be (2%) in our study, closely similar to the finding by Solaro *et al.* [9] (2.2%). Paroxysmal tonic spasm was reported by one patient only who represents (1%) of the total sample, identical with that shown in Bsteh *et al.* [1] (1%). Among aggravating factors, hotness was the commonest one with (40.91%), which can be explained by the long duration of hot months in our country and even sitting in close proximity to heaters in the coldmonths. Periventricular lesions were the most frequent lesions among PS reflecting its commonness and characteristicness in MS patients as a whole[11,12]. Cerebellar lesions were frequent among patients with paroxysmal dysarthria/ ataxia as Gorard[39] states in his paper along with brainstem area as Tüzün[4] concluded and spinal cord lesions that result in sensory ataxia. The MRI lesions of paroxysmal tonic spasm in our study distributed along the corticospinal tract area as that mentioned in Spissu[13] and Tüzün[4]. Spinal cord lesions recorded a high percentage among patients with Lhermitte's sign comparable to Al-Araji[10]. Trigeminal neuralgia is correlated with plaques in the brainstem similar to that mentioned in Stefano[14]. Paroxysmal vertigo seems to result from the lesion at the cerebellum as Sasaki[15] conducted in his case report. Finally, paroxysmal paresthesia associated with lesions distributed from juxtacortical area to the spinal cord (i.e. spinothalamic tract). The limitations that we faced in this study were the constriction to one MS center, the small sample size and the short duration of the study.

Conclusions

This study elucidated that paroxysmal symptoms are common presentations in multiple sclerosis initially or during the course of the disease, with paroxysmal paresthesia being the most common among

them. Betaferon® or Rebif® might be a good choice as a DMT for MS patients who are experiencing PS. PS tend to occur with the least disabled MS patients and longer disease duration.

Recommendations

To conduct further studies with a larger sample size, a longer duration and at various MS centers and especially for the effect of DMT on the PS. Not to ignore the importance of PS in the early diagnosis of suspected cases of MS nor the seriousness of these attacks during the course of the definite cases when considering a relapse. To raise the awareness of the patients about the aggravating factors of PS and to seek for relieving agents.

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