

Research Article

Patients with Multiple Sclerosis Present more Chronic and Recurrent Pain than a Control Population

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Abstract

Background and Objective: Multiple sclerosis (MS) is a chronic disease affecting the central nervous system. Although neuropathic pain may be a manifestation of MS, other types of pain can be present.

Method: Interviews were conducted individually with MS patients and matched controls (1:2). Participants were assessed for mood disorders (depression, anxiety) and pain, using validated instruments. In addition, their use of alcohol, tobacco and illicit drugs was assessed.

Results: Thirty-three patients with MS and 66 controls were enrolled in the study. Ninety percent of the patients with MS reported having one or more types of chronic pain, and headache was the most frequent type. Among the controls, the prevalence of chronic pain was 10.6%. Anxiety, depression and the use of tobacco, illicit drugs, depression or anxiety were similar between the two groups.

Conclusion: Patients with MS frequently presented chronic pain, which may be an additional burden of this disease.

Keywords: Multiple sclerosis; Pain; Alcohol; Illicit drugs

Introduction

Multiple sclerosis (MS) is a chronic inflammatory and degenerative disease of the central nervous system. Accumulated neurological disability is the main concern of doctors and patients alike, and all MS treatments aim at reducing the relapse rate of demyelination as well as postponing the moment when disability will become established.

MS lasts for decades and several symptoms are associated with the neurological manifestations of MS over this time. Fatigue [1], cognitive impairment [2], pain [3,4] and depression [5] are a few of the conditions that frequently accompany MS. Although depression and fatigue can be diagnosed in patients in the early stages of MS, pain does not follow a similar pattern [6]. Pain can originate from a large variety of situations in MS and there is no simple way of assessing this [4]. While some patients may suffer from neuropathic pain due to specific lesions in the central nervous system [7], others may suffer from pain due to treatment injections [8]. As expected, patients with MS who suffer from pain have worse outcomes in quality of life assessments [9].

Some studies have addressed the matter of pain in patients with MS in relation to control subjects. However, their results have not been uniform. Svendsen et al. showed that patients with MS had no more pain than the general population, although the former might have greater intensity of pain than the latter [10]. In other studies, a comparison between the prevalence and types of pain in patients with MS was assessed in relation to other chronic diseases [11]. Other evaluations have concentrated on the importance of pain as a condition that is not taken into consideration by the universally used expanded disability scale score (EDSS) in MS [12].

The aim of the present study was to assess the prevalence and types of pain in patients with MS in relation to controls, in a direct and comprehensive manner. Additionally, their use of alcohol, tobacco and illicit drugs was observed to see whether these habits were more frequent in patients with MS presenting pain.

Methods

This study was approved by the Ethics Committee of Universidade Metropolitana de Santos, under the number CAAE 25172713.2.0000.5509, in July 2014. All participants were aware of the characteristics of the study and signed a written consent form for enrollment.

This was a cross sectional study, assessing patients with MS and healthy controls from the general population by means of interviews with specific questionnaires and scales. Two controls for each patient were included, matched for gender, age and socioeconomic level. No financial compensation was given for participation in the study. Only patients who had not experienced a clinical relapse over the previous three months were included, since relapses may be accompanied by pain without reflecting a chronic condition.

All patients and controls were individually interviewed in an appropriate environment and data were collected on the demographic and socioeconomic aspects of each participant. The control group was selected from the general population in the same area, with the aim of adequate matching for gender, age and socioeconomic level. Patients and controls were defined as having pain if they presented daily or nearly daily pain for at least three months.

The interview consisted of simple questions about demographics and the presence of chronic or recurrent pain and its characteristics (duration, intensity, recurrence, etc). Once it had been established

Table 1: Demographic data on patients with multiple sclerosis (MS) and healthy controls. Socioeconomic level was assessed using the IBGE scale (*Instituto Brasileiro de Geografia e Estatística*) which classifies the individual as belonging to classes A1 to E, in decreasing levels of wealth. EDSS = expanded disability scale score, which classifies the individual's neurological disability between zero (normal) and 10 (death due to MS).

	Gender	Average age \pm SD (range) in years	Average socioeconomic level	Average disease duration \pm SD (range) in years	Average EDSS \pm SD (range)
Patients (n=33)	Male= 12 (36.3%) Female = 21 (63.7%)	37.7 \pm 12.5 (18-59)	24.4 – class B2 (13-39) (classes A2 to C)	6.6 \pm 2.1 (1 to 16)	2.8 \pm 1.1 (zero to 6.0)
Controls (n=66)	Male= 24 (36.6%) Female = 42 (63.7%)	38.2 \pm 16.8 (18-61)	24.8 – class B2 (17-40) (classes A2 to C)		

that painful conditions lasting for at least three months (continuously or recurrently) were present, the visual analogue scale and face scale were administered to the participant in order to grade that particular pain. Characteristics of the painful condition were also assessed as an attempt to classify the type of headache and the presence of fibromyalgia, for example. In addition, depression and anxiety were assessed by means of the Hospital Anxiety and Depression scale (HAD) and the AUDIT scale (alcohol use disorder identification test). One question regarding use of tobacco and any illicit drug (past or present) was also included in the interview.

Sample size was calculate and established to be 10. Statistical analysis on the results was performed using the Student t-test, one-way ANOVA, Fisher exact and chi-square tests, taking the cutoff for significance to be 5% ($p \leq 0.05$).

Results

The group of patients consisted of 33 individuals regularly attending the outpatient service at the Department of Neurology, Universidade Metropolitana de Santos. Patients were randomly chosen for participation: typically the first three or four cases coming for consultation on every outpatient day for six consecutive weeks. In total, 33 patients and 66 controls participated in the study. The study was sensitive enough to detect large (effect size $d = 0.78$) mean differences between groups at standard alpha and power levels (0.05 and 0.95 respectively) using t-tests.

Demographic and clinical data are presented in Table 1. Briefly, the average age of both groups was circa 37 years, and the male-to-female ratio was 1:2.5. The groups were comparable with regard to age, gender and socioeconomic level (Student t-test).

All the patients presented the relapsing-remitting form of MS and were undergoing treatment: intramuscular (IM) interferon beta 1a (n=6), subcutaneous (SC) interferon beta 1a (n=5), SC interferon beta 1b (n=5), glatiramer acetate (n=11), natalizumab (n=3), and fingolimod (n=4). Headache was remarkably more frequent in patients undergoing treatment with interferon beta in comparison to other drugs, irrespectively of the IM or SC formulation ($p < 0.01$).

Among the group of 33 patients with MS, only three did not report having any pain on a regular basis. A summary of pain and its characteristics is presented in Table 2, along with the presence of anxiety and depression and the use of alcohol, tobacco or illicit drugs. Headache (48%), joint pain (21%) and backache (15%) were the most frequent complaints among the patients, and the intensity of pain was moderate or severe in 78.8% of all individuals with MS. When headache was investigated in more detail, migraine was the most frequent diagnosis (75% of all patients with MS who referred headache). From this group of patients with headache, only 18.7% of

patients referred previous similar pain, but always of lower intensity than that found after the diagnosis of MS.

Over 80% of the patients reported that these painful conditions had not been present before the diagnoses and treatment of MS. In comparison with the controls, pain was significantly more frequent and more intense in patients with MS ($p < 0.0001$ for both parameters, using one-way ANOVA). None of the patients with joint pain presented other immunological diseases that could suggest rheumatologic disease. Three patients scored values in HAD that were suggestive of moderate to severe anxiety disorder and one of them also scored values suggestive of severe depression. Similar findings were observed among the control subjects. Alcohol consumption was significantly more prevalent among the control subjects ($p = 0.01$, Fisher exact test, chi-square). The frequency of smoking was typically low among patients and controls, as was the use of illicit drugs. There were no significant differences in smoking and use of drugs between the two groups (Fisher exact test, chi-square).

Presence of pain was not related to the use of alcohol, tobacco or drugs among these patients, and no specific relationships were found between pain and disease duration, degree of disability, symptoms of depression or anxiety ($p > 0.05$ for all correlations, one-way ANOVA).

Discussion

The findings from the present study demonstrate the high prevalence of pain, particularly of moderate or severe intensity, in patients with MS. Headache was found in virtually half of patients with MS, more frequently related to the use of interferon beta. The same findings have been reported by other authors [13]. Patients with MS may present headache more often due to a chronic inflammatory condition and/or as an adverse event to disease modifying drugs [13].

Although studies on MS and pain are marked by heterogeneity of methods, the conclusion that patients with MS often suffer from chronic and recurrent pain seems to be widely accepted [14]. In a recent systematic review of over 7,000 patients with MS presenting pain, headache was the most frequent finding (43%), followed by neuropathic extremity pain (26%), back pain (20%), painful spasms (15%), Lhermitte sign (16%) and trigeminal neuralgia (3.8%) (Foley). In the present study, headache, back pain, fibromyalgia and joint pain were the most prevalent conditions, and no cases of painful spasm, Lhermitte or trigeminal neuralgia were identified. A limitation to the conclusions of the present study is the sample size, which is relatively small. Should the database be expanded, other (less frequent) types of pain would perhaps be registered. The authors are equally aware that the scales used for assessing the intensity of pain (visual analogic and faces) are simplistic, but they are useful for screening patients with different educational levels. Since the aim of the present paper was to evaluate the presence and general characteristics of pain, as well

Table 2: Number of patients with MS and controls in each of the above categories. Note that more than one type of pain was possible for the same individual. Pain was significantly more frequent in patients with MS than in controls (** p=0.0001), while the use of alcohol was significantly higher among controls (* p=0.01). Other parameters did not show statistical significance difference or correlation for either patients or controls.

Types of pain		Headache	Low back pain	Fibromyalgia	Joint pain	Both hands
		Patients **	16 (48.5%)	5 (15.2%)	3 (9.1%)	7 (21.2%)
	Controls	4 (6.1%)	1 (1.5%)	0	1 (1.5%)	1 (1.5%)
		Yes	No	Previous		
Smoking	Patients	6 (18.2%)	23 (69.7%)	4 (12.1%)		
	Controls	10 (15.2%)	51 (77.3%)	5 (7.5%)		
		Yes	No	Previous	Nearly daily drinking	
Drinking	Patients	13 (39.4%)	18 (54.5%)	2 (6.1%)	0	
	Controls*	42 (63.7%)	18 (27.3%)	4 (6%)	2 (3%)	
		Yes	No	Previous		
Use of drugs	Patients	2 (6.1%)	29 (87.8%)	2 (6.1%)		
	Controls	2 (3%)	64 (94%)	0		
		No	Mild	Moderate	Severe	
Symptoms of Depression	Patients	29 (87.9%)	2 (6.1%)	1 (3%)	1 (3%)	
	Controls	62 (97%)	1 (1.5%)	0	1 (1.5%)	
		No	Mild	Moderate	Severe	
Symptoms of Anxiety	Patients	31 (94%)	0	1 (3%)	1 (3%)	
	Controls	62 (94%)	1 (1.5%)	2 (3%)	1 (1.5%)	

as the presence of mood disorders and lifestyle noxious habits, the scales were chosen appropriately for this purpose. The results from the present study indicate that the most painful conditions among patients with MS were not of neuropathic or demyelinating origin and, therefore, they were similar to what is found in the general population, albeit with greater prevalence. In addition, patients with pain, longer disease duration or higher degrees of disability were not more likely to make use of alcohol, tobacco or illicit drugs.

Conclusion

Patients with MS are more prone to painful conditions that are not necessarily related to demyelination or neurological disabilities. Regular investigation of the presence and characteristics of pain in patients with MS could lead to better care for these patients.

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