The prevalence of pain in multiple sclerosis

A multicenter cross-sectional study

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Abstract—In a multicenter cross-sectional study, the authors assessed pain in patients with multiple sclerosis (MS) using a symptom-oriented approach. Out of 2,077 questionnaires, we used 1,672 for data analysis. Pain and frequencies included trigeminal neuralgia 2%, Lhermitte's sign 9%, dysesthetic pain 18.1%, back pain 16.4%, and painful tonic spasms 11%. Comparison between different groups showed significant differences for age, Expanded Disability Status Scale, disease duration, and disease course, but not for sex. This study underlines the relevance of pain in the clinical history of MS.

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Pain is estimated to occur in 29% to 86% of patients with multiple sclerosis (MS).[1-7] Studies usually classify pain symptoms following temporal criteria and not according to the World Health Organization (WHO) pain treatment guidelines.[8] WHO classifies pain using a symptom/sign-related approach rather than a disease-oriented approach, dividing pain syndromes into neuropathic pain, caused by injury anywhere in the nervous system; somatic pain, due to an inappropriate physiologic response when nociceptors are activated; and psychogenic pain. Moreover, it is difficult to assess the risk of developing pain during the course of the disease, making prospective studies unrealistic. On the other hand, evaluating pain through a retrospective study requires that subjects recall a subjective symptom and assign it an accurate classification.

In a multicenter cross-sectional study, we assessed pain in patients with MS using a structured questionnaire following the WHO guidelines for the classification of pain.

Materials and methods. We collected data from 26 MS centers (PaIMS group; see the Appendix) using a face-to-face structured questionnaire compiled by a neurologist. All consecutive patients with a definite diagnosis of MS (Poser criteria)[9] over a period of 2 months were interviewed. The only exclusion criterion was a relapse in the last month before the beginning of the study.

The questionnaire included demographic data, year of symptom onset and diagnosis, Expanded Disability Status Scale (EDSS), clinical course, disease modifying treatment, pain therapy, presence of neuropathic pain (trigeminal neuralgia, Lhermitte's sign, dysesthetic pain), somatic pain (back pain and painful tonic spasms), or visceral pain.[8] Headache, acute pain due to optic neuritis, and somatic pain other than back pain (tendonitis, capsulitis) were not considered.

We considered only symptoms present at the time of the interview. All data were registered in an SPSS database. Questionnaires with missing data were not included in the analysis. If a center incorrectly completed more than 30% of questionnaires or did not adhere to the recruitment criteria, all questionnaires for that center were excluded from the final analysis.

Statistical analysis. t-Test and χ^2 were performed to evaluate group differences. Variables included in the analysis were age, sex, disease duration (in years from the time of diagnosis), EDSS, and clinical course. A difference at $p < 0.05$ was considered significant.

Results. Out of 2,077 questionnaires collected, 405 were excluded from analysis due to incomplete data. Distribution of sex, age, and clinical characteristics (EDSS, disease course and duration) in excluded and included questionnaires was identical. Out of 1,672 subjects interviewed, 1,152 were female (69%) and 520 male (31%), mean age was 40 years (median 40; range 14 to 75), mean disease duration 10.5 years (median 8; range 0 to 47). A total of 1,234 (74%) subjects had a relapsing remitting disease course (RR), 343 (20.5%) were secondary progressive (SP), and 95 subjects (5.5%) were primary progressive (PP). Mean EDSS score was 2.9 (median 2.5; range 0 to 7). Types of pain and frequencies, considered on the total population, included trigeminal neuralgia 2%, Lhermitte's sign 9%, dysesthetic pain 18.1%, back pain 16.4%, visceral pain 2.9%, and painful tonic spasms 11%. A total of 550 subjects reported one painful symptom and 167 more than

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Table 1 *Clinical data and statistical correlations between different pain figures*

Clinical data	Male, %	Female, %	Mean age, y	Mean EDSS	Mean Dis Dur, y	RR, %	SP, %	PP, %
Pain, %								
Yes 42.9 (n = 717)	29.0	71.0	41.7*	3.5*	14.4*	64.7*	27.3*	7.9*
No 57.1 (n = 955)	32.5	67.5	37.6	2.5	9.2	80.2	15.4	4.4
Back pain, %								
Yes 16.4 (n = 275)	27.1	72.9	42.9*	3.5*	11.7*	62.2*	30.0*	7.9
No 83.6 (n = 1397)	31.9	68.1	38.7	2.8	9.9	76.2	18.6	5.2
Dysesthetic pain, %								
Yes 18.1 (n = 303)	28.4	71.6	43.6*	3.8*	11.9*	59.6*	30.1*	10.3*
No 81.9 (n = 1369)	31.7	68.3	38.5	2.7	9.8	76.9	18.4	4.7
Painful tonic spasms, %								
Yes 11.0 (n = 184)	24.1	75.9	44.2*	4.5*	13.5*	44*	44*	12*
No 89.0 (n = 1488)	32.0	68.0	39.0	2.8	10.0	76.7	18.0	5.3
Trigeminal neuralgia, %								
Yes 2.2 (n = 36)	19.2*	80.8*	48.5*	4.4*	15.3*	43.2†	37.8†	18.9†
No 97.8 (n = 1636)	31.4	68.6	39.3	2.9	10.2	74.1	20.3	5.6
Visceral pain, %								
Yes 2.9 (n = 48)	2.9†	97.1†	40.6	2.7	10.7	78.3	19.6	2.2
No 97.1 (n = 1624)	32.3	67.7	39.5	3.0	10.3	73.2	20.9	6.0
Lhermitte, %								
Yes 9.1 (n = 152)	36.0	64.0	39.2	3.1	10.2	74.8	18.4	6.8
No 90.9 (n = 1520)	30.7	69.3	39.4	2.9	10.2	73.7	20.7	5.6

EDSS = Expanded Disability Status Score; Dis Dur = disease duration; RR = relapsing remitting; SP = secondary progressive; PP = primary progressive; Yes = positive questionnaire; No = negative questionnaire.

*$p < 0.001$; †$p < 0.05$.

one. A total of 1,175 (70%) subjects were in therapy with a disease modifying treatment for MS and 157 (9.4%) were currently taking pain medication.

Questionnaires were divided into pain (717, 42.9%) and no pain (955, 57.1%). In comparison with the no-pain group, patients in the pain group were significantly older (mean age 41.7 years vs 37.6), had a higher EDSS score (mean EDSS 3.5 vs 2.5), and a longer disease duration (mean duration 14.4 years vs 9.2 years). Moreover, the pain group included a significantly higher proportion of subjects with SP and PP disease than the no-pain group, while there was no significant difference in sex (table 1).

The statistical analysis showed a significant difference for trigeminal neuralgia between the two groups on all variables. When dysesthetic pain, back pain, and painful tonic spasms was considered, we observed between the two groups a significant difference for age, EDSS, disease duration, and disease course but not for sex. In contrast, when visceral pain was considered, statistical analysis showed a significant difference between the two groups for sex but not for age, EDSS, disease duration, and disease course (see table 1).

In order to confirm the hypothesis that pain is correlated with clinical characteristics including disease duration and severity, we conducted a second phase of the study using the same questionnaire, on consecutively seen MS patients with an EDSS of greater than 5. When we compared these results with those obtained in subjects from the first sample with an EDSS of greater than 5 (355 out of 1,672), clinical characteristics were identical (table 2).

Discussion. Management of pain in patients with MS is a challenge in clinical practice. In this study we have evaluated the prevalence of pain in patients with MS following a symptom-oriented approach rather than a temporal one. The importance of this type of classification is related to the different medical approaches for treating neuropathic or somatic pain due to different underlying pathophysiologic mechanisms. Previous studies have used relatively small samples conducted in single centers and have used either chart review or postal questionnaires to establish pain frequency. In one study pain was classified according to a temporal course of the symptom, i.e., acute and chronic.[2] This method grouped chronic pain, dysesthetic pain, and back pain into the same category, although these types of pain are different, regarding both pathogenesis and treatment approach. Pain was classified as somatic and neurogenic only in one study; however, the study population was small (85 subjects) and severely disabled (83% with EDSS > 6).[4] The correlation between pain frequency and clinical characteristics

Table 2 *Clinical characteristics of first and second studied group with EDSS >5*

	First group, n = 355		Second group, n = 220	
Characteristics	Yes, 70.1% (n = 249)	No, 29.9% (n = 106)	Yes, 72.7% (n = 160)	No, 27.3% (n = 60)
Male, %	29.7	32.2	31.8	37.8
Female, %	70.3	67.8	68.2	62.2
Mean age, y	50.3	49.7	48.6	48.7
Mean EDSS	6.5	5.8	6.4	5.6
Mean Dis Dur, y	17.6	16.2	16.9	15.3
RR, %	10.9	13.2	16.2	15.4
SP, %	69.2	67.1	65.3	69.5
PP, %	19.9	19.7	18.5	15.1

EDSS = Expanded Disability Status Score; Dis Dur = disease duration; RR = relapsing remitting; SP = secondary progressive; PP = primary progressive; Yes = positive questionnaire; No = negative questionnaire.

varies in different reports. Some studies report a correlation between pain and sex[2] while others have found no correlation on these same variables.[1] Some studies correlate pain with disease severity[1] or not,[5] while age has also been correlated with pain[2] but then contradicted in a subsequent study.[5] The current study has shown a correlation between pain and age, EDSS, disease duration, disease course, but not sex. Moreover, this correlation was present for both typical neurogenic pain, such as dysesthetic pain and trigeminal neuralgia, and for typical somatic pain, including back pain and painful tonic spasms. It is possible that the correlation with disease severity could be due, in dysesthetic pain and painful tonic spasms, to spinal involvement and, in back pain, to abnormal posture and gait impairment.

A recent report on the prevalence of pain in a population-based study[7] found no association between disease duration and pain. The study reported a high prevalence of back pain (40.7%), although not higher than in the control group, but three times higher than in our sample. In this study disease course and disability information was unavailable.

The accuracy and reliability of the data collection is demonstrated by the fact that clinical characteristics and pain prevalence in the second-phase group were identical to patients with EDSS of greater than 5 in the original sample studied.

Regarding the correlation between pain frequency and medication use, 22% of subjects with pain were currently taking pain medication. This discrepancy confirms a previous study in which we found, in an epidemiologic survey, that the use of symptomatic medications was significantly lower than symptom frequency.[10]

Appendix

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