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PAIN IN PARKINSON'S DISEASE

Analysis of 50 cases in a clinic of movement disorders

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Abstract – **Introduction:** Pain is a common symptom in Parkinson's disease (PD), and is often related to the illness itself. **Objective:** To prospectively establish the ocurrence of pain in PD patients. **Method:** This study was conducted within a population composed of 50 patients with PD to evaluate the presence of pain. **Results:** Twenty-eight patients reported pain; comparing the group with pain and the group without pain, there were no differences related to the beginning of the illness and the motor symptoms of PD. However, many patients related an improvement of pain when antiparkinsonian therapy was initiated or adjusted. **Conclusion:** The use of techniques for analgesia and the adjustment of PD medication contribute to improve the manifestations of pain and the life quality of patients with PD.

KEY WORDS: Parkinson's disease, pain, pathophysiology, treatment.

Dor na doença de Parkinson: análise de 50 casos em uma clínica de transtornos do movimento

Resumo – **Introdução:** Dor é um sintoma comum na doença de Parkinson (DP) e, às vezes, está relacionada à própria patologia de base. **Objetivos:** Estabelecer prospectivamente a ocorrência de dor em pacientes com DP. **Método:** Foram avaliados consecutivamente 50 pacientes com DP, para comparação entre os que referiam e os que negavam quadro álgico. **Resultados:** Entre os entrevistados, 28 referiam episódios dolorosos, não havendo diferenças quanto ao início da doença e os sintomas motores da DP, na comparação entre os dois grupos. Porém, muitos pacientes referiam melhora da dor com a introdução ou ajuste da terapia antiparkinsoniana. **Conclusão:** O uso de analgesia e ajuste da terapia para a DP ajudam na melhora do quadro álgico e na qualidade de vida dos pacientes.

PALAVRAS-CHAVE: doença de Parkinson, dor, fisiopatologia, tratamento.

In century XIX, Charcot had already discovered a relation between Parkinson idiopathic disease (PD) and pain. This was related to parkinsonian symptoms or due to rheumatologic modifications resulting from a more advanced age, demonstrating that the effects of this disease are not limited to cognitive and motor aspects[1-4].

Pain as a primary symptom is usually located on the side of the body that is most compromised by the disease, suggesting a relation to modifications of the cerebral neurotransmission, mainly on the basal ganglia. In addition, pain usually appears prematurely in patients, and can appear before the occurrence of motor symptoms, and is therefore not recognized as a symptom of PD until further symptoms appear. Pain disappears when the disease is finally diagnosed and treated[4-6]. The main motor symptom related to pain is rigidity, which occurs frequently on the "off" episodes, i.e. during the period in which the antiparkinsonian medication loses its effect until the next administration of the doses. In more advanced stages of the disease, an instability of the therapeutic effect occurs, occasioning a loss of the effect of the medication during the "on" period, which is entitled "wearing-off" effect, and during this period the symptoms of pain can be emphatic[2,3,5,7]. The treatment always demands a great adjustment of dopamine agonist, local injections of steroids, massages, physiotherapy and analgesic therapy, which improve the life quality of patients[8-10].

The objective of this prospective study was to estab-

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lish the frequency of pain among these patients, in addition to seeking clinical characteristics and pharmacological therapy that could be related to pain manifestations.

METHOD

During the period July 2004 to March 2005, 50 patients with PD diagnosis were interviewed, consecutively followed up at the Movement Disorders Outpatient Unit of the Department of Neurology, State University of Campinas Teaching Hospital (HC/UNICAMP). The PD diagnoses were based on the criteria of London Brain Bank[11].

The patients were submitted to a questionnaire, comprising their epidemiologic data and motor symptoms. The clinical analysis was conducted using the UPDRS (Unified Parkinson's Disease Rating Scale)[12] for the subscales I (mental state, behavior and humor), II (daily routine activities), III (motor examination), IV (therapy complications), Hoehn and Yahr's staging; and the Schwab and England's scale (classifying the patient's dependence on a caretaker for daily routine activities, being defined in dependence percent).

Patients with painful symptoms were submitted to a questionnaire in which pain was evaluated, as well as the numerical graduation of pain (a scale of 1–10, in which 1 represented the less possible pain, and 10 represented the maximum possible pain) before and after the administration of medication.

This study was approved by the Research Ethics Committee of the Medical Science School of the UNICAMP, and the patients were informed as to the objectives of the evaluation, and signed a consent term.

The percentage and average calculations as well as the chi-square test were used for the statistics when indicated.

RESULTS

Among the 50-interviewed patients, 34 (68%) were men and 16 (32%) women, presenting the initial clinical manifestations of PD with an average age of 53.2±10.3 years, ranging from 31 to 74 years old. The time elapsed from the origin of the symptoms and the interview was 8.7±5.2 years (ranged from 1 to 22 years).

Resting tremor was observed in 42 patients (84%), rigidity in 41 (82%), bradykinesia in 44 (88%), and modification of postural reflexes in seven patients (14%).

The medication used by these patients in monotherapy or in association to improve the parkinsonian symptoms were levodopa and dopamine agonist.

Twenty-eight (56%) patients – 12 women and 16 men – reported the presence of pain; Table 1 show the relation between the patients with and without pain in the gender, age, time of PD history, main symptoms of disease (tremor, rigidity and bradykinesia) and use of main medication to PD. There was not statistically significant difference between these patients.

The manifestation of pain in 28 patients ranged from one to 30 years (average of 8.3±6.7 years); however, some patients (12) manifested pain before manifestating PD symptoms.

Table 2 show the type of pain among the patients, and unspecified pain was a gastrointestinal pain in burning and was not related the parkinsonian symptoms. Dystonia was a pain with primary origin, related with rigidity or bradykinesia.

Pain episodes occurred daily in 16 (57.1%) patients, two patients (7.1%) presented more than one episode a month, and nine patients (32.1%) presented pain sporadically; one patient presented pain only during the "off" periods.

Among the 28 patients with pain, 78.6% used mainly nonhormonal and anti-inflammatory analgesics. One patient used amitriptyline and 14.3% of the patients with pain

Table 1. Relation in patients with or without pain.

Pain	Presence	Absence
Male	16	18
Female	12	4
Age	53.6±10.9	52.6±9.8
Time of PD symptoms	8.8±5.8	8.5±4.4
Resting tremor	24	18
Rigidity	21	20
Bradykinesia	25	19
Use of levodopa	21	18
Use of dopamine agonist	6	8

p>0.05 compared among patients with or without pain.

Table 2. Frequency of patients in every type of pain.

Pain	Total (%)
Muscle-skeletal	14 (50.0)
Dystonia	6 (21.4)
Radicular	3 (10.7)
Articular	2 (7.1)
Headache	2 (7.1)
Unspecified	1 (2.6)

Table 3. Frequency of patients in every classification of Hoenh and Yahr's stage, according to presence or absence of pain.

Hoehn and Yahr / Pain	Presence	Absence	Total
1.0	2	0	2
1.5	5	1	6
2.0	5	5	10
2.5	6	7	13
3.0	4	8	12
4.0	6	1	7

p>0.05 compared among patients with or without pain.

underwent other analgesic methods (gabapentin, carbamazepine, opioids, acupuncture, and physiotherapy). Only one patient used no analgesic at all during periods of pain.

There was a significant improvement of pain during the effect of the antiparkinsonian medication in eight patients (28.6%), i.e. during the "on" period, and pain increased during the "off" period. Seven patients used levodopa and three used dopamine agonist.

The degree of pain, considering a numerical scale of 0–10 (being 10 for the maximum possible pain), was of 6.1±1.8 points before the use of medication and, of 3.3±2.3 after medication therapy. There was a significant difference in the improvement of pain with the administration of medication ($p<0.05$), however a comparison of self-given scores among the patients using medication and those not using was not possible as only one patient claimed no to make use of any analgesic treatment.

The total score in the UPDRS scale was of 52.0±24.0; therefore, there was no statistically significant difference among the patients with or without pain ($p=0.41$), as observed in Table 3.

Analyzing the UPDRS parameters separately, we observed a statistical significance regarding patients with pain, who complained of having a greater difficulty of getting and walking in relation to the patients without pain, $p=0.00430$ and $p=0.00435$, respectively.

According to the Schwab and England's scale, which classifies the patient's dependence on a caretaker for daily activities, there was no statistically significant difference between patients with or without pain, despite the degree of dependence.

DISCUSSION

The frequency of pain in patients with PD ranges from 30 to 70% according to the literature[2-4,13-15], and was also observed in this study, which revealed a 56% of patients with pain. There was no statistically significant difference related to gender.

The age of patients with pain did not differ from those without pain, in contrast to other studies[2,6], where patients presenting pain were younger, in age addition, there was no difference between the two groups of patients (with/without pain)at the moment when parkinsonian signs appeared. But these studies did not explicate the cause of this difference, so pain is more evident in patients with rigidity and/or akynesia and they are older.

There was no difference in the presence of clinical signs between the patients with or without pain; therefore there was no relation between motor and sensory symptoms, despite the fact that patients with pain claimed to have a greater difficulty to get dressed or walk, with a significant difference between the groups.

This difference was not made clear on the motor analysis by UPDRS, which was similar between the patients with and without pain, as observed in a recent study[16], contrary to two previous studies[17,18] that demonstrated motor fluctuations between the groups with and without complaints of pain.

Contrary to other studies[2,7,17], we found only one patient asserting that pain occurred only during the "off" period of medication, 28.5% of the patients with pain claimed to feel better when using the antiparkinsonian medication, similar to previous studies[6,12], suggesting that pain could be occurring due to the "wearing-off" effect, but the improve was relate to the correct use of medication.

The most frequent manifestation reported was muscle-skeletal pain, with a daily frequency, which could be improved or not with the use of medication; this manifestation was characterized having a rheumatologic origin as pain was not related to the period of effect of the antiparkinsonian medication.

Rare forms of pain, such as comprising oral or genital parts[19], were not observed in our study, and that was not used other medications, like subcutaneous apomorphine, that shown improve in a case report[20].

There was no difference among the self-given score for the Schwab and England's scale regarding daily-life activities between the patients with or without pain, although some reports demonstrated that patients with pain had more symptoms of depression[15,17], which could reduce the graduation in these patients. However, this study did not analyze the presence of depression; therefore, it was not possible to make a comparison with previous studies[5,6,9,10,13].

The patients classified in the Hoehn and Yahr's stage 1.0, 1.5, and 5.0 presented pain in 100, 90 and 85 per cent of cases, the stage 2.0, 2.5 and 3.0 presented pain in 50 per cent or less of cases; that shown the patients in the first years of disease had lower pain threshold than in the other patients, maybe because this patients did not used antiparkinsonian medication in the early phase of the disease, and in the later phase, the medication was less effective.

None of the patients mentioned aggravation of symptoms after using PD medication, however there has been one case cited in the literature[3].

The physiopathogenic mechanism resulting from this scenario is not yet clear like the relation between PD and olfactory dysfunction[21], however recent studies[16,22] points out that patients with PD have a lower pain threshold than healthy people, highlighting a relation between pain and PD. In addition to serotoninergic nociceptive pathways, other factors can be involved, such as depression – a common symptom in these patients[23].

In conclusion, the manifestation of pain occurs with a certain frequency in parkinsonian patients, and these manifestations present a significant improvement with the use of medication and analgesics used to decrease the symptoms of the disease, in addition to the therapeutic adjustment of levodopa. The knowledge of the primary and secondary causes of PD pain and of the correlation with the dose of levodopa allow therapeutic changes that could contribute to the improvement of the treatment of these patients. The treatment of chronic pain helps patients improve their performance of daily-life activities, as well as their life quality. The pain threshold is lower in the earlier and later phases of the disease, when the patients use little or have not good response to the use of levodopa, that is showing this medication is related in the pain way.

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