Pain in Hospitalized HIV-Positive Patients: Clinical and Therapeutical Issues

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Pain is frequently reported by patients infected with Acquired Immunodeficiency Virus (HIV), and its causes and specific treatment should be appropriately investigated. We evaluated 197 hospitalized HIV-positive patients with serial interviews and analysis of prescriptions and clinical evolution charts. The main characteristics of pain reported by these patients were: high intensity (60.7%), high frequency (72.0%) and well-known causes (88.8%). Fifty-two per cent of the patients reported persistent or frequent pain during the two weeks before hospital admission. Parameters such as gender, educational level and Karnofsky Index showed no direct relation to the presence or absence of pain. The most commonly affected sites were the head (28.0%) and the abdomen (26.2%). The frequency of indications of pain in the clinical evolution charts (46.2%) was considerably lower than the frequency of complaints reported by patients during the interviews (76.3%). Pain was undertreated in 83.2% of patients, both due to poor efficacy of the prescribed medications and to the excessive and inefficient use of standing order (“if necessary”) regimens. We observed that pain was better managed during the hospitalization period, although this cannot be explained by improvement of the analgesic treatment; it might be due to successful treatment of the underlying disease. We concluded that pain reported by hospitalized HIV-positive patients is often underestimated and inadequately treated by assisting doctors, in spite of its severity and frequency.

Key Words: Pain, HIV, AIDS, analgesic treatment, undertreatment, pain management index.
Materials and Methods

The trial was prospectively conducted at the Emílio Ribas Infectious Diseases Institute (IIER), São Paulo, Brazil, a public state referral center for the treatment of HIV-positive patients. The inclusion criteria were:

- Patients with confirmed diagnosis of HIV infection (ELISA and Western-blot), regardless of their immune status;
- Adults older than 18 years of age
- Admission to one of the seven hospital ward units within 90 consecutive days (March to May 1999).

The exclusion criteria were:

- Direct admission to the Intensive Care Unit;
- Premature discharge or death (within the first 48 hs after admission);
- Patient refusal to cooperate or in case of incapacity to understand the trial instructions.

Phase I – Initial Visit

Based on a daily inspection of the admission records in the Emergency Room (source of all hospital admissions), patients included in the study were submitted to a single bedside visit within 24-48 hours after admission. The following question was initially asked:

“have you felt any pain over the last two weeks?”

Based on the answer to this question, patients were assigned to one of the following groups:

Group 1 – patients reporting any pain;
Group 2 – patients reporting no pain;

Social, epidemiological and medical complementary information was collected from patient’ records and a form was completed for each case, with the identification data including name, hospital number, gender, education level, as well as specific information about the disease.

Phase II- First Interview

Only patients from Group 1 were included in this phase of the study (patients reporting any pain), with the aim of characterizing pain frequency, location, duration, intensity, and initial treatment, patient’s opinion on the use of pain relievers and their efficacy in the management of pain, and patients’ awareness of the cause of pain. A modified questionnaire based on the Wisconsin Brief Pain Questionnaire [4] (Table 1) was designed, using the Wong Baker pain rating scale [5,6] as a measure of pain (Figure 1). The interviews were preceded by an explanation of the questionnaire, certifying that each patient had thoroughly understood the procedure.

In Phase II, information from medical records, particularly related to the analgesic treatment (prescribed drugs, regimen, and medication actually administered) was once again collected, as well as the etiological diagnosis considered to be the cause of pain (routinely indicated by the medical team responsible for each patient).

Patient’s awareness of the etiology of pain was considered appropriate if it matched the medical diagnosis registered in charts. Pain was considered to be related to HIV/AIDS infection if it was a direct consequence of HIV, or if it occurred as result of tumors and opportunistic infections, their complications or therapies.

In order to examine the effectiveness of treatment, the pain management index – PMI [7] was used to compare the potency of prescribed analgesics with the severity of pain reported by each patient. Patients reporting pain intensity grade 4-5 (Figure 1) were considered “patients with severe pain” and coded as “3”. Patients reporting pain intensity grade 2-3 were considered “patients with moderate pain” and coded as “2”. Patients reporting pain intensity grade 1 were considered “patients with mild pain” and were coded as “1”. Patients without pain were coded as “0” (zero). Similarly, the potency of the analgesic received by each patient was classified according to the WHO analgesic scale [8], i.e., patients receiving strong opioids were classified as
“3”, those receiving mild opioids were classified as “2” and patients receiving nonopioid analgesics were classified as “1”. Patients were classified as “0” if no analgesic medication was prescribed. The PMI was calculated by subtracting the score of pain intensity from the score of prescribed analgesics. The PMI index varied from -3 to +3. Analgesic therapy was considered appropriate if the patient had a score ≥ 0.

Any adjuvant medication prescribed for purposes other than pain management (eg. antipyretics, antidepressants, and anticonvulsants) was not considered as an analgesic drug.

**Phase III- Serial Interviews**

In this phase, a next interview (within a period not greater than seven days) was excluded for any patient who was discharged, died prematurely, became mentally confused or refused to participate. All remaining patients were assessed weekly, using the same questionnaire used in phase II at each visit. Data on the evolution of symptoms and specific treatment over the entire period of hospitalization were prospectively collected.

Statistical analysis of qualitative variables was performed using the chi-squared test for 2 x 2 tables and the Kolmogorov-Smirnov test for larger tables. For quantitative variables, the Kolmogorov-Smirnov test was used when the distribution was normal; otherwise, the Mann Whitney test was used. The difference was considered statistically significant whenever p<0.05.

This project was approved by the Ethics Committee and the Institutional Review Board of IIER.
Table 2. Comparison between Group 1 (patients with any pain) and Group 2 (patients with no pain)

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>107</td>
<td>90</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>74</td>
<td>69.2%</td>
</tr>
<tr>
<td>Female</td>
<td>33</td>
<td>30.8%</td>
</tr>
<tr>
<td>Age*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>34.0 years</td>
<td>34.9 years</td>
</tr>
<tr>
<td>18-40</td>
<td>92</td>
<td>86.0%</td>
</tr>
<tr>
<td>&gt;41</td>
<td>15</td>
<td>14.0%</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td>0.9%</td>
</tr>
<tr>
<td>Incomplete elementary education</td>
<td>56</td>
<td>52.3%</td>
</tr>
<tr>
<td>Full elementary education</td>
<td>50</td>
<td>46.8%</td>
</tr>
<tr>
<td>Karnofsky Index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>69.8 points</td>
<td>68.6 points</td>
</tr>
<tr>
<td>70-100</td>
<td>75</td>
<td>70.1%</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>32</td>
<td>29.9%</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

*p<0.05.

Table 3. Characteristics of pain, prescribed medications and Pain Management Index (PMI) in Phase II and III interviews

<table>
<thead>
<tr>
<th></th>
<th>Phase II 107 interviews</th>
<th>Phase III 134 interviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent pain*</td>
<td>60 56.0</td>
<td>26 19.4</td>
</tr>
<tr>
<td>Severe pain*</td>
<td>65 60.7</td>
<td>15 11.2</td>
</tr>
<tr>
<td>Only “if necessary” medication prescribed</td>
<td>52 48.7</td>
<td>67 50.0</td>
</tr>
<tr>
<td>Non-administered standing order medication</td>
<td>39 75.5</td>
<td>55 82.1</td>
</tr>
<tr>
<td>PMI&lt;0*</td>
<td>89 83.2</td>
<td>41 30.6</td>
</tr>
</tbody>
</table>

*p<0.05.

Results

Four patients were discharged and readmitted during the trial. These were considered “new cases”, regardless of each patient’s complaint or the reason for admission. Eighty-six (30.4%) out of 283 patients initially included in this study were discontinued. Therefore, the total population consisted of 197 patients.

Phase I – Initial Visit

A hundred seven patients were assigned to Group 1 (with pain) and 90 patients were assigned to Group
2 (no pain). The comparative data between Groups 1 and 2 are presented in Table 2 (distribution by gender, age, educational level, and Karnofsky Index).

Phase II – First Interview

Only the 107 patients with pain (Group 1) were included in this phase.

The mean pain intensity, based on the visual scale presented in Figure 1, was 3.6. Thirteen patients (12.2%) reported mild pain, 29 (27.1%) moderate pain and 65 (60.7%) patients reported severe pain; 77 patients (72.0%) reported persistent pain or several episodes during the day.

Among these 107 patients, 29 (27.1%) reported headache, 28 (26.2%) abdominal pain, 13 (12.1%) pain in the lower limbs and 12 (11.2%) chest pain. The syndromic diagnosis was visceral pain in 44 (41.1%) patients, headache in 29 (27.1%), somatic pain in 13 cases (12.1%), and other types of pain classified as neuropathic in 9 (8.4%) patients.

Pain was related to HIV infection, its complications or therapy in 44 patients (41.1%). In 23 cases (21.5%) it was not possible to establish this relationship.

The accurate etiology of pain was determined in 95 cases (88.8%). Sixty-nine patients (64.5%) had pain due to infection, 9 patients (8.4%) experienced neoplastic pain, and, in 7 cases (6.5%), the pain was of inflammatory origin. Neurocryptococcosis was the most prevalent infection causing pain (11.2% of the total of pain episodes), followed by all forms of tuberculosis (7.5%), neurotoxoplasmosis (5.6%) and candidiasis (5.6%). The reasons for feeling pain were well explained by 64 (59.8%) patients.

Seventy-five patients (60.0%) believed they were receiving specific medication for the treatment of pain, and among these 57 (88.0%) considered the analgesic treatment effective. However, the analysis of prescription charts showed otherwise; in 54 (50.5%) out of 107 cases only regular analgesics were prescribed for the treatment of pain (in spite of usually severe and frequent symptoms), whereas 16 (15.0%) patients were treated only with antiinflammatory drugs. Only 8 (7.4%) patients received strong or mild opioids.

In 52 (48.7%) charts, the analgesics were prescribed without fixed intervals, i.e., a standing order of: to be administered “if necessary”; in 39 (75.5%) of these patients, the drugs were not actually administered. The pain management index (PMI < 0) was the criterion used to identify undertreatment, and thus 89 (83.2%) patients were undertreated.

Phase III - Serial Interviews

Sixty-two patients were followed-up during hospitalization, accounting for 134 new weekly interviews (mean of 2.16 visits per patient – minimum = 2, maximum = 7). Pain was still present in 47.0% of the new interviews.

During the course of hospitalization, pain became progressively less persistent and less intense (Table 3), indicating a better PMI. However, a continuous review of prescription charts showed that in 65 (48.5%) cases only regular analgesics were prescribed, 18 patients (13.4%) received non-hormonal antiinflammatory drugs, 5 (3.7%) mild opioids and in only 4 (3.0%) cases strong opioids were prescribed. In 67 prescription charts (corresponding to half of the 134 serial interviews of Phase III) analgesics were still been prescribed as standing orders on an “if necessary” recommendation and in 55 (82.1%) these were never actually administered. Therefore the improvement of symptoms described in Table 3 was not a result of better analgesic treatment.

Among 173 medical records, complaints of pain were registered in only 80 (46.2%) clinical evolution charts, whereas patients reported pain in 132 (76.3%) interviews. This difference was statistically significant.

Forty-eight patients (45.2%) still had pain at the last interview before discharge or death. In spite of the high percentage of medications prescribed as standing orders that were never actually administered, in 153 (63.5%) of 241 interviews (sum of Phases II and III), patients blindly believed they had received pain medication and, among these, 68 (87.2%) believed that it helped to relieve pain.
Discussion

The demographic data of this study is consistent with the general overview of AIDS in Brazil in the end of the nineties [9], i.e., the prevalence of AIDS was higher among young male adults (between 18 and 40 years of age) with a low degree of education (incomplete elementary education).

Phase I showed the symptom “pain” in about 55% of HIV patients. However, this study included only hospitalized patients whose communication level could be assured. Other studies on pain in AIDS patients indicate an outpatient prevalence of approximately 60-88% [10-13].

There was a significant difference between age of patients when Groups 1 (patients with any pain) and 2 (patients without pain) were compared among; pain was most prevalent in younger individuals. This is a surprising finding not seen in other populations, possibly due to a methodological bias. Therefore, it was not possible (nor recommended) to reach a definite conclusion on this subject. A direct relationship between the frequency of pain and a worsened immune status was observed in another study [11].

Although not assessed in this study, it is well known that pain has a negative impact on daily life activities, mood and affective relationships of each patient [14]. Suicidal idealization is two-times higher in HIV-positive patients with pain than in such patients without pain (40% and 20%, respectively) [15]. Therefore, if any patient reports frequent and severe pain, it must be considered of significant importance and should not be regarded as irrelevant or minor.

The incidence of visceral pain was high (41.1%), when compared to somatic pain (12.1%), which is opposite to the tendency reported by Hewitt [10] (15 and 45%, respectively) in outpatients.

Neuropathic pain may have been underestimated (8.4% of the total number of pains), as only the main pain reported by each patients was considered as a “single” pain, overlooking chronic symptoms of lower intensity. Another difference observed in this study was the higher incidence of secondary headache (24.0% of the total number of all types of pain and 86.6% of headaches). In outpatient studies [16] primary headaches (migraine and tension headache) occur more frequently.

Pain was related to HIV infection in 45% of patients, similar to the results obtained by Hewitt [10]. This means that in a significant number of patients, pain is not related to the underlying disease, suggesting the need to evaluate other etiologies to explain the symptoms.

Concerning treatment, many studies have shown that up to 85% of patients with pain receive inappropriate analgesic therapy and less than 8% receive opioid medication to relieve episodes of severe pain in developed countries [17,18].

In our study, although 60% of patients had severe pain and 72% reported the occurrence of persistent symptoms or pain episodes several times a day, common analgesics (almost always dipyone) were the only medication prescribed in 50% of the cases, while mild and strong opioids were prescribed in only 6.1 and 3.1% of the cases, respectively.

The Pain Management Index (PMI) reinforces the impression of the high frequency of undertreatment (83.2% of patients). The main explanations for undertreatment are: failure to assess the reported pain, lack of physician knowledge on the use of drugs, administrative impediments to prescribe opioids, difficult access to pain specialized services, cultural barriers imposed by patients (unwillingness to report pain to avoid being perceived as “not a good patient”, fear of dependency, fear that pain could mean disease progression) [19]; about 70% of the patients thought that they had received analgesics and believed that these non-existing medications had helped to relieve pain.

Improvement in PMI was observed during hospitalization, as inadequately treated pain was detected in 83.2% of patients in Phase II versus 29.0% in Phase III. Considering that the rate of prescription mistakes had not improved (Table 3), we conclude that the symptoms were gradually relieved because the etiology of pain had been well understood, and therefore the underlying disease was appropriately...
treated. However, many days of hospitalization were needed in order to achieve these results, which is not consistent with one of the basic principles of pain treatment: to introduce analgesic medication at the beginning of treatment, even before the diagnosis is made [8].

Conclusions

Pain is a frequent symptom in hospitalized HIV-positive patients at our institution, and generally it is severe, persistent or presents several episodes a day. The causes of pain are usually known; in most cases they are of infectious origin and potentially treatable. However, pain treatment has not been clearly appropriate, either due to a lack of attention to patients’ complaints or to inadequate prescription of analgesics.

In this context, a multidisciplinary team for palliative care (established at IIER since 1998) indicates progress in clinical practice of pain management.

Discussions among physicians and nurses have been stimulated and updating seminars and exhibitions for professionals have been promoted. In addition, our palliative care team has been successful in extending technical and emotional support to the patient’s family and other caregivers [20]. Such pedagogic activities have been increasingly requested, focused mainly on quality of life and on integral assistance to the patient, considering not only the physical and organic aspects of the disease but also its psychological, social and spiritual implications.

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References


