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Original Research Article

The occurrence and characteristics of pain in HIV-1 positive persons – A challenge in the aging population

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ABSTRACT

Aim: To investigate epidemiology and characteristics of chronic pain in HIV-1 positive persons.
Background: Chronic pain is vital but still understudied problem in HIV clinical practice; therefore we have designed a study to analyse the prevalence and attributes of pain symptoms in the group of HIV-positive patients in the Out-Patient HIV Clinic in Warsaw.
Materials and methods: During their routine visit patients were asked to fill in a general information form and the Alcohol Use Disorders Identification Test Consumption (AUDIT-C) form. All patients reporting any pain were additionally asked to fill in the Brief Pain Inventory (BPI) form and were subject to a brief examination performed by a physician who afterwards completed a DN4 (Douleur Neuropathique en 4 Questions) form. Logistic regression models were used to identify factors associated with chronic pain occurrence.
Results: Forty nine patients completed the questionnaires. Nineteen patients (37.2%) reported chronic pain, occurring once daily in 39.4%, and in 42.9% lasting several hours. In univariate logistic regression analyses factors increasing the odds of chronic pain were age at the time of evaluation (OR = 1.07; 95% CI 1.02–1.08, $p = 0.01$), starting antiretroviral treatment with didanosine, zalcitabine and stavudine (OR = 6.75; 1.18–38.4, $p = 0.03$) and last CD4+ lymphocyte count (OR = 0.99; 0.99–1.00, $p = 0.07$). After adjusting for the three above only age at the evaluation time remained significant factor increasing the odds of experiencing chronic pain (OR = 1.07 [1.01–1.13]; $p = 0.03$).
Conclusion: Almost 40% of respondents reported chronic pain. We have found a strong correlation between age and chronic pain in the HIV infected population with the 7% increase in the odds of experiencing pain with each year of age.

1. Background

Only in the United States over 100 million people suffer from chronic pain, which contributes to 20% of outpatient visits [1]. The prevalence of average chronic pain in European Union is reported as 27% of general adult population [2]. In HIV infected population pain is even more predominant. The recent study by Miaskowski et al. showed that over 90% of patients reported any kind of pain and/or the use of pain medication in the recent week [3].

Through the spread of effective and accessible antiretroviral treatment HIV persons survival is now comparable to their age and gender matched population controls [4,5]. In result up to 50% of existing HIV cohorts population consists of persons over 50 years of age. With this change we observe significant alterations in the causality of both morbidity and mortality [6–9]. Thus HIV clinicians are facing many new challenges such as age-related co-morbid diseases management, aging of body organs essential for HIV treatment metabolism and polypharmacy [10–13].

The management of chronic pain can be especially difficult in HIV-infected patients, taking into account the multifactorial origin of its nature and frequent history of drug abuse [14–18]. For example the use of nucleos(t)ide reverse transcriptase inhibitors is the most common reason for peripheral neuropathy, whereas factors such as alcohol and psychoactive substances abuse can also lead to such condition [17].

At the same time chronic pain is an important factor affecting daily activity, causing sleep disorders and decreasing the quality of life achieved by antiretroviral treatment [19]. It can significantly affect adherence to antiretroviral therapy, which is especially important in older HIV infected persons, increasing the risk of treatment failure or discontinuation [20,21].

Chronic pain is vital but still understudied problem in HIV clinical practice; in particular there is a lack of studies in patients

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on antiretroviral treatment [22–24]. Therefore we have designed a study to investigate the prevalence and character of pain symptoms in the group of HIV-positive patients in the Out-Patient HIV Clinic in Warsaw.

2. Methods

All patients of 18 years of age or older were considered eligible for the study. Patients with the diagnosis of ongoing psychiatric disorder or actively using illicit drugs intravenously were excluded from the study.

Patients were enrolled consecutively from the 1st of January 2014 and preliminary analyses were planned at the time when approximately fifty questionnaires being completed.

During their routine visit in the HIV clinic, after signing the informed consent, patients were asked to fill in a general information form and the Alcohol Use Disorders Identification Test Consumption (AUDIT-C) form. All patients reporting any pain were additionally asked to fill in the Brief Pain Inventory (BPI) form and were subject to a brief examination performed by a physician who afterwards completed a DN4 (Douleur Neuropathique en 4 Questions) form.

In the general information form patients were asked whether they suffered from any pain, about the frequency of its occurrence, duration, use of any psychoactive substances, other than illicit infectious drugs, and patterns of adherence to antiretroviral therapy.

Chronic pain was defined as lasting 6 months or longer according to duration reported by study participants.

The AUDIT-C form is a three-item alcohol screening questionnaire which allows to identify persons as hazardous drinkers. A maximum of 12 points is possible to obtain. A score of 4 in men and 3 in women is considered as "positive" indicating hazardous drinking or active alcohol abuse [25,26].

The Brief Pain Inventory (BPI) short form is an instrument assessing pain interference with function and pain severity [27]. The severity of pain was classified according to Numeric Rating Scales (NRS) as mild (1–4 points), moderate (5–6 points) and severe (7–10 points).

The DN4 form is a questionnaire to identify neuropathic characteristics of pain. The questions on the form relate to pain quality and to associated paresthesia and/or dysesthesia. A score of 3 or more is indicating a neuropathic characteristics of pain [28].

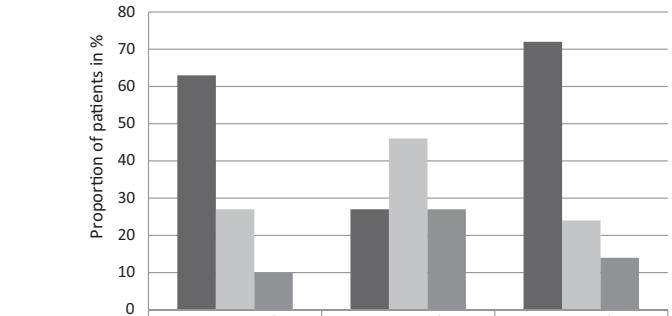
All questionnaires used in the study were translated into Polish and all necessary approvals and copyrights obtained.

In statistical analyses Chi-square and Kruskal–Wallis tests were used as appropriate for group comparisons. Univariable logistic regression models were used to identify factors associated with chronic pain occurrence. A multivariable model was developed including all variables with $p < 0.1$ in univariable models. The potential predictors tested in univariate models were: age at the time of evaluation, age at the registration in HIV clinic, gender, mode of HIV transmission, antiretroviral regimen, time from starting antiretroviral treatment, most recent CD4+ lymphocyte cell count and HIV RNA. Confidence interval (CI) of 95% was accepted. All analyses were performer with SAS version 9.3 (SAS Institute, Cary, NC).

The study was approved by the Bioethical Committee of the Medical University of Warsaw.

3. Results

Fifty one patients fulfilled inclusion criteria and completed the questionnaires, clinical data were available for 49 patients and the median follow-up time was 6.14 (1.13–11.32) years.



	Average pain	Worst pain	Least pain
Mild intensity	63	27	72
Moderate intensity	27	46	24
Severe intensity	10	27	14

Fig. 1. The proportion of patients with mild, moderate and severe intensity in the Numeric Rating Scales (NRS) reported for the pain at its average, worst and least in the last 24 h (according to Brief Pain Inventory form).

In general 81.6% of patients were male. In terms of mode of HIV transmission 20.4% were infected through heterosexual intercourse and 42.8% were man having sex with man (MSM), 16.3% were infected through injecting illicit substances (IDU), 6.1% reported other and 14.3% unknown mode of infection.

The vast majority of patients (91.8%) were on antiretroviral treatment, 17% were ever on antiretroviral therapy containing ddI, ddC or d4T. Over one third (36.7%) of patients admitted to forget to take their antiretroviral treatment with 52.6% of the patients reporting to forget more than one dose per month. However the majority (91.1%) of patients were on fully suppressive treatment, with HIV RNA below 50 copies/ml, according to the most recent viral load measurement.

Almost two thirds (57.1%) of patients presented late into care, with the CD4+ lymphocyte count below 350 cells/μl.

In total 34 (66.7%) patients reported to have any pain in the last week, 26 (51%) reported using any pain relief treatment and 31.6% received professional help in relation to pain symptoms. The pain intensity scaling is presented in Fig. 1. In nineteen patients (37.2%) the pain was classified as neuropathic (12 defined as chronic pain) according to DN4 form and the characteristics are presented in Fig. 2.

Twelve and a half percent of the patients reported to be using psychoactive substances and 16.3% were indicated by AUDIT-C form as having hazardous drinking pattern or active alcohol abuse.

Nineteen patients (37.2%) reported chronic pain, occurring once daily in 39.4%, and in 42.9% lasting several hours. Patients experiencing chronic pain were more likely to be older, with lower most recent CD4+ lymphocyte count, the latter two being of borderline significance. The comparative characteristics are presented in Table 1.

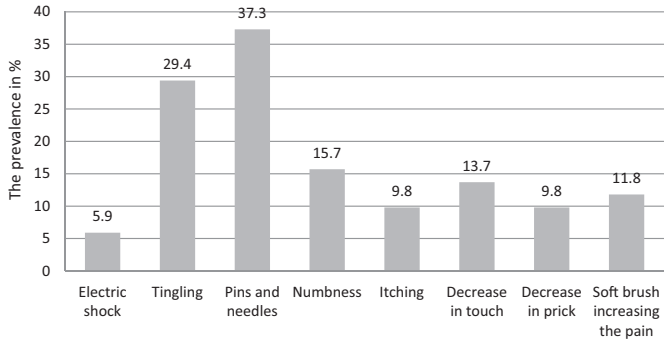


Fig. 2. Neuropathic characteristics of pain in HIV-infected patients according to DN4 questionnaire evaluation.