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Pain Treatment and Antiretroviral Medication Adherence Among Vulnerable HIV-Positive Patients

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Abstract

Pain represents a significant source of morbidity, function loss, and decreased quality of life among people living with HIV. The present study examined the associations among pain, pain treatment, and ARV adherence among indigent, HIV-positive substance abusers. Participants were recruited via targeted sampling strategies, and completed a one-time computer-assisted personal interview. ANOVA and chi-square tests were used to analyze differences in demographics, health and psychological status, health behaviors, by pain and pain treatment status; a multivariate logistic regression model was constructed to examine the contribution of pain/treatment status to recent ARV adherence. Results indicated that those with untreated pain had lower odds of achieving gold-standard 95% ARV adherence as compared to the pain-free and treated pain groups; higher substance dependence symptoms were also associated with significantly lower odds of 95% ARV adherence. Findings suggest that pain management is critical to the health of people living with HIV, specifically those with high levels of co-morbid health and psychological problems. The prevalence of untreated pain was elevated among this group, and contributed to reduced ARV adherence. Providers of clinical care to disadvantaged HIV-positive patients should emphasize routine assessment and appropriate treatment of pain in order to provide comprehensive HIV care.

Introduction

Pain is common among people living with HIV, with prevalence estimates indicating that some 40–80% of ambulatory HIV-positive patients endorse recent, clinically significant pain. The etiology of pain among HIV-positive individuals is varied, and includes infection-related inflammatory responses, secondary complications of progressive HIV disease, as well as adverse effects of treatment with antiretroviral (ARV) medications. Sensory neuropathy, for example, has been estimated to affect 40–60% of treated HIV-positive individuals, and often results in moderate to severe pain. Regardless of etiology, the experience of pain represents a significant source of morbidity, function loss, and decreased quality of life among individuals living with HIV, and has been associated with elevated levels of psychological distress, including depression, anxiety, and panic disorder, as well as greater HIV-related illness burden. Despite these indicators, recent literature suggests that pain is often under-recognized and under-treated in clinical care for HIV-positive individuals. Many HIV-positive individuals suffer from co-morbid mood disorders and/or substance abuse problems, and pain management among these patients can present special challenges. In particular, the risk for medication misuse may be heightened, and patients may require close monitoring; likewise, the under-treatment of pain may lead to aberrant drug-seeking behaviors. Despite these challenges, balanced and appropriate pain management among vulnerable HIV patients is critical to both individual and public health. A small but emerging body of literature suggests that pain experience among HIV-positive patients is associated with poor ARV adherence and reduced attendance at HIV-related care visits, both of which are key behavioral components of disease management to achieve viral suppression and prevent onward transmission. Although a handful of other studies has shown no link between pain and ARV treatment adherence, the dearth of research on this topic precludes consensus.

The purpose of this report is to examine the role that pain and its corresponding treatment may play in vulnerable patients’ behavioral repertoires for HIV disease management.
We recently documented substantial levels of ARV non-adherence, as well as the illicit diversion (selling and trading) of ARVs, among indigent substance abusing HIV-positive patients in South Florida. Prior research has not adequately examined the potential contribution of pain to these types of health risk behaviors, and to our knowledge, existing studies have been limited in investigating the influence of pain treatment as a potentially important moderator of these relationships. This article explores the associations of pain, pain treatment, ARV adherence, and diversion among a large, diverse sample of socioeconomically disadvantaged HIV-positive patients with high levels of co-morbid physical and psychological problems.

Methods

Study participants

Data were drawn from a large epidemiologic study designed to examine the patterns and predictors of ARV diversion among drug-involved people living with HIV in South Florida. Due to the focus on ARV diversion, we recruited a highly vulnerable sample of indigent HIV-positive substance users likely to have exposure to ARV street markets. Study eligibility criteria were: age 18 or older; cocaine or heroin use 12 or more times in the prior 3 months; documented HIV+ status; and current ARV prescription. In addition, diverters endorsed at least one occasion of ARV diversion in the prior 3 months.

Study recruitment

The study utilized targeted sampling techniques to guide recruitment. Study investigators identified specific geographic areas for recruitment based on publically available HIV prevalence and poverty-level indicator data. Initial recruitment efforts targeted the communities to the north of downtown Miami that are intersected by the highest rates of HIV prevalence and poverty-level indicator data. Initial recruitment efforts were expanded based on information from community key informants in the target areas (including treatment professionals, community outreach workers, HIV service providers, and street-level drug users). Professional field staff used direct outreach to distribute study information cards and flyers in a variety of street venues and community-based HIV service organizations within the identified target areas.

Study procedures

Potential participants were given information about the project, and were asked to participate in telephone screening for eligibility. Those meeting eligibility requirements were scheduled for an appointment at the field site, where they were re-screened by a research staff member. After eligibility was confirmed on-site, informed consent procedures were completed. 503 individuals were ultimately enrolled into the study; by design, we included approximately equal numbers diverting their ARV(s) (n = 251) and not (n = 252). Participants completed a single, standardized interviewer-administered questionnaire, which took approximately 1 h. Participants were paid a $30 stipend for their time and travel costs to complete the interview. Research staff completed the requirements for National Institutes of Health (NIH) web-based certification for protection of human subjects, and study protocols were subject to regular review by the University Institutional Review Board. A Certificate of Confidentiality from the National Institutes of Health was obtained and a copy was offered to participants.

Data collection and measures

Trained, bilingual research staff conducted computer-assisted personal interviews (CAPI) in either English or Spanish, according to the participant’s language preference. The Global Appraisal of Individual Needs (GAIN, v. 5.4) was the primary data collection instrument. The GAIN captures information on demographics, physical and mental health status, including DSM-IVR depression and anxiety measures, substance use and DSM-IVR dependence, and sexual risk behaviors, and has established reliabilities. Standardized instruments also assessed HIV diagnosis/treatment history, ARV adherence, and a newly developed instrument assessed ARV diversion.

Demographic information gathered on study participants included age, race/ethnicity, gender, and years since initial HIV diagnosis. As an indicator of economic need, we assessed food and housing insecurity with a single item adapted from a validated life stress scale. “In the 3 months prior to interview, did you go without food, housing, or other necessities because you did not have the money?”

Health status was measured by five items. HIV-related health status was assessed by self-report of: (1) most recent CD4 count, and (2) most recent viral load. For the present analysis, viral load was dichotomized into undetectable versus not. Pain was assessed using a single item adapted from the Health Distress Scale of the GAIN instrument. Participants were asked, “During the past 90 days, have you had a lot of physical pain or discomfort?” A separate item queried related treatment: “Are you currently prescribed any pain medication?” If appropriate, participants were permitted to endorse multiple medications. Finally, we assessed other medical diagnoses among the target sample, excluding HIV. This included a range of chronic and acute health conditions; participants were instructed to endorse all current medical diagnoses.

Mental health subscales in the GAIN are based on DSM-IVR criteria: nine items assess depression symptoms, and twelve items assess anxiety symptoms over a 12-month period. In all cases, higher scores indicate greater problem severity. Alpha reliability coefficients for the depression and anxiety scales were 0.87 and 0.88, respectively. A separate item queried recency of depression and anxiety symptoms: “When was the last time, if ever, you had any of those significant nerve, mental or psychological problems that we just talked about?” To obtain a measure of current psychological distress, we dichotomized this variable into “within the past month” or “not within the past month.”

Substance dependence in the past month was assessed using DSM-IVR criteria, which consists of seven items measuring drug problem severity (e.g., using more or longer than intended, withdrawal problems). The present analysis examined past month dependence symptom count as a
Data analysis

Data from the interview questionnaires were analyzed using SPSS for Windows, Version 21. The primary independent variable of interest was recent pain and its associated pharmacological treatment. We constructed three analytic groups from the data: (1) pain-free: those individuals reporting no pain in the past 90 days; (2) pain/untreated: individuals reporting pain in the past 90 days and denying a current pain medication prescription; and (3) individuals endorsing both 90-day pain and a current prescription for pain medication. Descriptive statistics were calculated to describe the sample in terms of pain and treatment status. ANOVA and Chi-square tests were utilized to examine differences in socio-demographics (age, gender, race, food/housing insecurity, years HIV diagnosed); health status (CD4, viral load, other medical conditions); psychological status (depression, anxiety, current psychological problems, substance dependence), and health behavior domains (ARV adherence, ARV diversion) by pain and pain treatment status. Post-hoc Bonferroni tests were computed to identify specific group differences for significant ANOVA main effects.

Subsequently, a multivariate logistic regression model was constructed to examine the potential contribution of pain/treatment status to past week ARV treatment adherence, while controlling for all variables displaying significant associations in the initial bivariate analyses. To reduce the potential for multi-collinearity among our independent variables in the regression analysis, we included only the recency of achieving 95% medication adherence as the outcome of interest and was treated as a dichotomous variable. Variables were entered simultaneously into the logistic regression model.

Results

The median age of the sample was 46 years; 59.4% were male. More than three-quarters (81.4%) of study participants had monthly incomes below $1000, and 39.2% reported homelessness in the prior 3 months. Self-reported ARV adherence in the past week was 95% or better among 54.1% of participants (data not shown).

The prevalence of recent pain among this sample of indigent HIV-positive substance users was 51.3%. Of those endorsing pain, 41.5% indicated no current prescription for pharmacotherapy. Among those who reported medication treatment, 48.3% were prescribed an opioid, 39.1% a non-steroidal anti-inflammatory drug (NSAID), and 21.9% indicated another type of prescribed pain medication (data not shown). Participants could endorse multiple prescription types.

As shown in Table 1, pain experience and treatment status were associated with a number of health and psychosocial problems in this vulnerable sample. In terms of demographics, food/housing insecurity was more prevalent among both pain groups (treated and untreated) compared to the pain-free ($\chi^2 = 9.48; p = 0.009$). No significant differences in HIV-related health status were observed between the groups.

Nearly three-quarters of the sample (74.6%) indicated diagnosis with at least one other medical condition (excluding HIV), and the mean number of health diagnoses in the sample was 2.2 (data not shown). The highest prevalence diagnoses included high blood pressure (31.2%), neuropathy (24.9%), high cholesterol (22.5%), sleep disorders (21.3%), and arthritis (20.3%). The presence of pain and its corresponding treatment status were associated with other diagnosed health problems endorsed by the sample. Higher illness burden was associated with pain experience ($F = 61.0; p = 0.000$), as both pain groups had significantly higher numbers of medical diagnoses than the pain-free group. Patients receiving pain treatment also reported significantly more medical diagnoses than their nontreated counterparts ($p = 0.000$).

Analyses revealed disparities in mental health functioning associated with pain and treatment status. In this regard, both pain groups (treated and untreated) displayed significantly higher levels of psychological distress when compared with their pain-free counterparts, including past year symptoms of depression ($F = 34.3; p = 0.000$) and anxiety ($F = 33.7; p = 0.000$). Past month psychological symptoms were also more prevalent among those with pain ($\chi^2 = 35.1; p = 0.000$), regardless of treatment status. Substance dependence symptoms in the prior month were elevated among those with untreated pain compared to both the pain-free and treated pain groups ($F = 14.1; p = 0.000$).

Pain was also associated with poorer disease management, as indicated by ARV diversion and adherence. Nearly 40% of those with untreated pain endorsed diversion of their ARV medications in the past month, which was a significantly higher proportion than either the pain-free or treated pain groups ($\chi^2 = 6.62; p = 0.04$). Past week ARV treatment adherence levels were also reduced among HIV+ individuals with pain. The pain-free group displayed a higher likelihood of achieving 95% medication adherence than either pain group, regardless of treatment status ($\chi^2 = 11.81; p = 0.003$).

Table 2 presents the results of the multivariate logistic regression model examining the impact of food and housing insecurity, pain and treatment status, other medical diagnoses, past month psychological problems, past month substance dependence symptoms, and past month ARV diversion on recent ARV adherence.

In the multivariate model, pain/treatment status, substance dependence symptoms, and ARV diversion demonstrated significant associations with ARV adherence. Those with untreated pain had 42% lower odds of achieving 95% medication adherence in the past week compared with the pain-free ($p = 0.043$). Substance dependence symptoms adversely affected ARV adherence as well, with 11% lower odds of...
95% adherence per symptom endorsed \( (p=0.007) \). ARV diversion displayed a strong association with adherence; endorsement of past month HIV medication diversion resulted in 74% lower odds of achieving 95% adherence \( (p=0.000) \).

**Discussion**

Pain is estimated to affect some 30% of adults in the US, making it one of the most frequently occurring health disorders in the nation.²⁶,²⁷ Among indigent, HIV-positive substance abusers in South Florida, the present study documented recent pain prevalence of 51.3%. Although elevated with respect to the general population, this finding is in line with prior research on HIV-positive patients, which has gauged pain prevalence to be between 40% and 80%.¹⁻⁴ Our data confirm that pain is an exceedingly common co-morbid health condition among HIV-positive individuals, including the non-elderly and those treated in an era of ARVs with lower side effect profiles.

Although this study did not gather information on pain intensity or duration, prescribed pharmacotherapy to treat pain was modest, with 41.5% of those endorsing pain being untreated. Pharmacotherapy for pain was more likely for those with more diagnosed medical conditions; nevertheless, those with untreated pain reported 2.4 medical diagnoses on average, not including HIV infection. These data would appear to indicate substantial levels of physical health co-morbidities among this vulnerable sample. Opioid therapy was most common among those prescribed pharmacotherapy at 48%, followed closely by NSAIDs at 39%. The relatively common selection of non-opioid medications may reflect

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**Table 1. Sample Characteristics by Past 90-Day Pain and Treatment Status Among Indigent HIV+ Patients in South Florida \( (N=503) \)**

<table>
<thead>
<tr>
<th></th>
<th>Pain (treated) ( N=151 )</th>
<th>Pain (untreated) ( N=107 )</th>
<th>No pain ( N=245 )</th>
<th>F- or chi-square</th>
<th>Sign. level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>46.9 (7.4)</td>
<td>46.8 (8.0)</td>
<td>45.3 (7.9)</td>
<td>2.50</td>
<td>0.08</td>
</tr>
<tr>
<td>Male gender, ( n )</td>
<td>79 (52.3)</td>
<td>64 (59.8)</td>
<td>156 (63.7)</td>
<td>5.01</td>
<td>0.08</td>
</tr>
<tr>
<td>African American, ( n )</td>
<td>101 (66.9)</td>
<td>71 (66.4)</td>
<td>169 (69.0)</td>
<td>0.32</td>
<td>0.85</td>
</tr>
<tr>
<td>Food/housing insecurity, ( n )</td>
<td>71 (47.0)</td>
<td>57 (53.3)</td>
<td>90 (36.7)</td>
<td>9.48</td>
<td>0.00</td>
</tr>
<tr>
<td>**Years HIV diagnosis, mean (SD)( a )</td>
<td>13.5 (7.3)</td>
<td>13.7 (7.4)</td>
<td>12.9 (7.2)</td>
<td>0.56</td>
<td>0.57</td>
</tr>
<tr>
<td><strong>Health status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current CD4, mean (SD)( a )</td>
<td>480.3 (293.9)</td>
<td>449.5 (264.0)</td>
<td>480.1 (285.3)</td>
<td>0.46</td>
<td>0.63</td>
</tr>
<tr>
<td>Undetectable viral load, ( n )( % )( a )</td>
<td>65 (49.2)</td>
<td>48 (49.0)</td>
<td>103 (46.2)</td>
<td>0.39</td>
<td>0.82</td>
</tr>
<tr>
<td>Other medical conditions, mean (SD)</td>
<td>3.4 (2.4)</td>
<td>2.4 (2.2)</td>
<td>1.2 (1.4)</td>
<td>61.05</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Psychological status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression symptoms past yr., mean (SD)</td>
<td>6.3 (2.6)</td>
<td>6.4 (2.7)</td>
<td>4.3 (3.0)</td>
<td>34.34</td>
<td>0.00</td>
</tr>
<tr>
<td>Anxiety symptoms past yr., mean (SD)</td>
<td>5.8 (3.5)</td>
<td>5.9 (3.6)</td>
<td>3.3 (3.3)</td>
<td>33.70</td>
<td>0.00</td>
</tr>
<tr>
<td>Psychological symptoms past mo., ( n )( % )( a )</td>
<td>122 (80.8)</td>
<td>87 (81.3)</td>
<td>138 (56.6)</td>
<td>35.13</td>
<td>0.00</td>
</tr>
<tr>
<td>Dependence symptoms past mo., mean (SD)</td>
<td>3.4 (2.5)</td>
<td>4.5 (2.5)</td>
<td>3.0 (2.4)</td>
<td>14.14</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Health behaviors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% ARV adherence past week, ( n )( % )</td>
<td>77 (51.0)</td>
<td>45 (42.1)</td>
<td>150 (61.2)</td>
<td>11.84</td>
<td>0.00</td>
</tr>
<tr>
<td>ARV diversion past month, ( n )( % )</td>
<td>38 (25.2)</td>
<td>42 (39.3)</td>
<td>68 (27.8)</td>
<td>6.62</td>
<td>0.04</td>
</tr>
</tbody>
</table>
| \( a \)\( N=502; N=464, N=453, N=502 \)

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**Table 2. Multivariate Logistic Regression Model Predicting 95% ARV Adherence Among HIV+ Substance Abusers in South Florida \( (N=502) \)**

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>Sign. level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food/housing insecurity( a )</td>
<td>-0.066</td>
<td>0.936</td>
<td>(0.628, 1.40)</td>
<td>0.744</td>
</tr>
<tr>
<td><strong>Health status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain( a )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated</td>
<td>-0.538</td>
<td>0.584</td>
<td>(0.346, 0.984)</td>
<td>0.043</td>
</tr>
<tr>
<td>Treated</td>
<td>-0.492</td>
<td>0.611</td>
<td>(0.372, 1.01)</td>
<td>0.052</td>
</tr>
<tr>
<td>No. of other medical conditions</td>
<td>0.037</td>
<td>1.037</td>
<td>(0.939, 1.15)</td>
<td>0.469</td>
</tr>
<tr>
<td><strong>Psychological status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological symptoms past mo.( a )</td>
<td>-0.199</td>
<td>0.820</td>
<td>(0.526, 1.28)</td>
<td>0.380</td>
</tr>
<tr>
<td>No. of dependence symptoms past mo.</td>
<td>-0.113</td>
<td>0.893</td>
<td>(0.822, 0.970)</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>Health behaviors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARV diversion past month( a )</td>
<td>-1.322</td>
<td>0.266</td>
<td>(0.172, 0.413)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

\( a \)Reference category is ‘no’.
caution among health care providers and prescribers treating a population with known substance abuse issues. Among our vulnerable sample of socioeconomically disadvantaged HIV-positive substance users, pain likely arose from multiple sources, including aging, long-standing participation in street lifestyles that entail drug use and exposure to violence, the presence of multiple chronic health conditions, as well as poverty-driven limitations on health care access and basic subsistence needs. Our bivariate analyses demonstrated that food and housing insecurity were significantly associated with pain endorsement. This finding is consistent with the notion that environmental living conditions, in this case inadequate access to food and safe housing, engender circumstances that may cause, exacerbate, or perpetuate pain. In this regard, prior research has linked housing instability to both high pain prevalence and multiple barriers to care. An additional limitation is the cross-sectional nature of the interview data that were gathered; the lack of temporal data limits our ability to demonstrate causal relationships among the key variables. Finally, our measures of pain were limited, and no information was collected on pain intensity, duration, or etiology, so it is not definitive that medication therapy would have been indicated; similarly, it is unknown if patients were receiving alternative therapies for pain. We believe that this study provides compelling evidence that pain assessment and management warrant more attention among health care providers who serve disadvantaged HIV-positive patients. Given the competing needs of these vulnerable patients and limited access to both routine and specialized medical care, the assessment and treatment of pain may fall to HIV care providers, particularly in locations where the phenomenon of interest was occurring. This limits generalizability of the findings to other HIV-positive patient populations. A second limitation involves reliance on self-report data. It is possible that recall problems and social desirability biases influenced participant responses to the interview items; nevertheless, the high levels of substance use, ARV diversion, and low ARV adherence reported suggest that participants did not substantially under-report these behaviors. Measures of CD4 and viral load were also obtained from participant self-report; recall problems may have impacted the reliability of these measures and limited our ability to detect relationships in the data. An additional limitation is the cross-sectional nature of the interview data that were gathered; the lack of temporal data limits our ability to demonstrate causal relationships among the key variables. Finally, our measures of pain were limited, and no information was collected on pain intensity, duration, or etiology, so it is not definitive that medication therapy would have been indicated; similarly, it is unknown if patients were receiving alternative therapies for pain. This research is supported by PHS Grant Number R01DA023157 from the National Institute on Drug Abuse. NIDA had no further role in study design; in the collection, analysis and interpretation of data; in the writing of this report; or in the decision to submit the article for publication.
**Author Disclosure Statement**

There are no financial conflicts of interest to report.

**References**


