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Self-Efficacy and Depression as Mediators of the Relationship between Pain and Antiretroviral Adherence

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Abstract

The goals of this study were to examine the association between pain and antiretroviral adherence, and to estimate the mediating effect of adherence self-efficacy and depression symptom severity. Surveys using audio computer-assisted self-interview were conducted among 70 HIV-infected current and former drug users enrolled in a methadone program. We assessed antiretroviral adherence and adherence self-efficacy using questions from the Adult Clinical Trials Group survey. We considered participants adherent if they reported taking at least 95% of prescribed antiretrovirals over the past seven days. We assessed depression symptom severity using the depression subscale of the Brief Symptom Inventory. Participants reported pain of any duration in response to a question from the Brief Pain Inventory. Participants reporting pain were 87% less likely to be classified as adherent compared to those without pain [OR_{unadj} = 0.13 (95%CI 0.03–0.52)]. When we examined adherence self-efficacy as a mediator of the relationship between pain and adherence, criteria for partial mediation were met. Adjusting for self-efficacy, the beta coefficient for pain decreased by 23% but the independent relationship between pain and antiretroviral adherence was maintained. Mediation criteria were not met when we examined the mediating effect of depression symptom severity on the relationship between pain and adherence. Adjusting for depression symptom severity, the beta coefficient for pain decreased by 9% and the relationship between pain and antiretroviral adherence remained significant. Our results indicate that neither adherence self-efficacy nor depression symptom severity fully mediated the relationship between pain and adherence. HIV providers should recognize the potential impact of pain on antiretroviral adherence among current and former drug users.

Keywords

pain; HIV; antiretroviral adherence; depression; self-efficacy

Introduction

Among patients with AIDS, those who report current or former injection drug use experience more physical pain than those with other HIV risk behaviors (Vogl et al., 1999). Physical pain has also been associated with two important predictors of antiretroviral adherence: depression and self-efficacy (Kalichman et al., 2005; Reynolds et al., 2004; Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000; Gifford et al., 2000; Murphy, Greenwell, & Hoffman, 2002; Molassiotis et al., 2002; Halkitis, Kutnick, & Slater, 2005). Despite these

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associations, neither the impact of physical pain on antiretroviral adherence, nor the roles of adherence self-efficacy or depression in mediating this relationship, have been examined.

Adherence self-efficacy is a set of cognitive beliefs regarding one's capabilities to take antiretroviral medications as prescribed. Self-efficacy in general is shaped by information from four sources: past accomplishments, perceptions of others' accomplishments, feedback regarding one's ability to perform the desired behavior, and one's physiological state (Bandura, 1977). Since pain is a reflection of one's physiological state, we examined adherence self-efficacy as a potential mediator of the association between pain and adherence. We hypothesized that pain is negatively associated with adherence self-efficacy. This hypothesis is supported by prevailing pain theories, which assert that the cognitive experience of pain can be examined by measuring self-efficacy (Jensen, Turner, & Romano, 1991; Fernandez & Turk, 1989).

Depressive symptoms are prevalent among those with HIV (Remien et al., 2006). Among those with pain, depression treatment may be less successful without concurrent pain treatment (Bair et al., 2004). How the complex relationships between depression and pain affect antiretroviral adherence is unknown. To address this question, we constructed a second mediation model to test the hypothesis that depression symptom severity mediates the association between pain and antiretroviral adherence.

Identifying modifiable correlates of adherence is necessary to inform the development of tailored interventions aimed at improving long-term antiretroviral adherence. Previous studies have found that pain is associated with both self-efficacy and depression, however associations between pain and antiretroviral adherence in HIV-infected drug users are unknown, and the potential mediating roles of self-efficacy and depression have not been examined. Our objective was to test two independent mediation models: the extent to which self-efficacy (model 1) and depression (model 2) mediate the relationship between pain and antiretroviral adherence.

Methods

Study population and setting

We recruited participants by screening patients in methadone clinic waiting rooms and posting flyers in common spaces. Patients were eligible if they were receiving methadone for opioid dependence, HIV-infected, and prescribed antiretroviral therapy. Surveys were administered in private offices at participants' clinics using audio computer assisted self-interview (ACASI) technology.

Adherence

The main outcome was self-reported antiretroviral adherence, which we assessed using questions from the AIDS Clinical Trials Group (ACTG) questionnaire (Chesney et al., 2000) and operationalized as [(number of pills taken)/(number of pills prescribed)]×100 during the prior seven days. We used a seven-day recall period to ensure inclusion of weekend days (Simoni et al., 2006). For each participant, we calculated an overall adherence rate by averaging individual rates for each medication. Participants were considered adherent if they took ≥95% of their medications (Paterson et al., 2000).

Physical Pain

To capture a variety of pain syndromes, we used the following question from the Brief Pain Inventory: “how long have you had pain of any type?” This question has been used to characterize pain in drug users (Rosenblum et al., 2003). We classified participants as not

having pain if they endorsed the response option "I have no pain," and as having pain if they endorsed any other response option indicating that they were currently experiencing pain ranging in duration from "less than one month" to "more than five years."

Adherence self-efficacy

Self-efficacy for taking antiretroviral medications as prescribed was assessed using the following question from the ACTG questionnaire: "How sure are you that you will be able to take all or most of your medication as directed?" (Chesney et al., 2000; Reynolds et al., 2004). Reponses on a 4-point Likert scale ranged from zero (not at all sure) to three (extremely sure). We treated adherence self-efficacy continuously because beta coefficients increased linearly when dummy variables for the 4-point scale were entered into a logistic model with adherence as the outcome.

Depression symptom severity

Depression symptom severity was assessed using the six-item depression subscale of the Brief Symptom Inventory (BSI). Respondents were asked to rate their level of discomfort from the following six symptoms over the past week: "feeling lonely", "feeling blue", "feeling no interest in things", "thoughts of ending your life", "feeling hopeless about the future", and "feelings of worthlessness." Responses on a 5-point Likert scale ranged from 1 (not at all) to 5 (extremely). Scores on these six items were averaged to obtain a continuous score ranging from one to five (Derogatis LR, 1993). In our sample, the depression subscale of the BSI had a Chronbach's alpha of 0.87.

Statistical analysis

We followed standard procedures to test for mediation (Baron & Kenny, 1986). Necessary criteria for mediation are met when the predictor is significantly associated with both the outcome and the proposed mediator; and the proposed mediator is significantly associated with the outcome. In the first step of model building, we examined the predictor (pain) alone. In step two, we added the proposed mediator (adherence self-efficacy or depression symptom severity) to the model. Comparing the results of these models allows determination of whether mediation is supported. The size of the reduction in the beta coefficient of the predictor variable after adding the mediator reflects the potency of the mediator. Partial mediation occurs if the direct effect is reduced but still present and full mediation occurs if the direct effect is eliminated.

Results

Participant characteristics

The sample of 70 participants was 54% female, 50% Hispanic, 43% Black, and the mean age was 46. The median methadone dose was 120mg (interquartile range (IQR) 90-170mg), and the median duration of methadone treatment was nine years (IQR 5-15 years).

Forty participants (57%) reported pain. Nineteen (27%) participants were classified as non-adherent, indicating that they missed at least 5% of their antiretroviral medications over the prior seven days. Participants reporting pain were 87% less likely to be classified as adherent compared to those without pain [OR_{unadj} = 0.13 (95%CI 0.03–0.52)].

Overall, mean (sd) adherence self-efficacy was moderate: 1.81 (0.86) on a scale of zero to three. Participants with greater adherence self-efficacy were less likely to report pain than patients with lower adherence self-efficacy; the odds of reporting pain were decreased by 58% for each unit increase in adherence self-efficacy (on a four point scale) [OR_{unadj} = 0.42 (95% CI 0.22 – 0.81)]. Further, participants with greater adherence self-efficacy were more

likely to be adherent. Each unit increase in adherence self-efficacy was associated with a greater than 5-fold increased odds of being classified as adherent [OR_{unadj}=5.50 (95%CI; 2.12–14.25)].

In the entire sample, depression symptom severity was low [median 1.5 (IQR) 1.0-2.0]. Participants with worse depression symptoms were more likely to report pain. For each unit increase in depression symptom severity (on a 5 point scale) the odds of reporting pain were increased by a factor of two [OR_{unadj}=2.17 (95%CI;1.01–4.69)]. Lastly, worse depression was associated with non-adherence; for each unit increase in depression symptom severity, the odds of being classified as adherent were decreased by 50% [OR_{unadj}=0.50 (95%CI; 0.25–0.98)].

Analysis of mediators of the relationship between physical pain and antiretroviral adherence

Results supported adherence self-efficacy as a partial mediator of the relationship between pain and antiretroviral adherence (Table; Model 1). When adherence self-efficacy was added to the model, the beta coefficient of pain decreased from −2.03 to −1.56 (23%), but the independent relationship between pain and adherence was maintained. This suggests that those with pain were less likely to adhere to antiretroviral medications, despite adjustment for differences in adherence self-efficacy. The Sobel test indicated that self-efficacy's role as a mediator of the association between pain and adherence was significant (z=-2.17; p=0.03).

Results did not support depression symptom severity as a mediator of the relationship between pain and adherence. When depression symptom severity was added to the model, the independent relationship between pain and adherence remained highly significant (Table; Model 2). This model suggests that differences in depression severity did not explain why individuals with pain were less likely to adhere to antiretroviral medications.

Discussion

In this sample of methadone maintained HIV-infected drug users, we found a strong association between pain and antiretroviral non-adherence. The initial bivariate model, which included only pain, correctly classified 72% of participants as adherent or non-adherent. Because this association was only partially mediated by adherence self-efficacy, and not mediated by depressive symptoms, clinicians who care for HIV-infected drug users should assess and treat pain.

There are several possible explanations for the observed association between pain and adherence self-efficacy. Pain is strongly associated with psychological distress (Breitbart et al., 1997), which is a known determinant of low self-efficacy (Reynolds et al., 2004; Maly, Costigan, & Olney, 2006; Dohnke, Knauper, & Muller-Fahrnow, 2005). Pain may also decrease one's sense of mastery or self-esteem, both of which may weaken self-efficacy beliefs (Lacroix, Clarke, Bock, & Doxey, 1986; Manning & Wright, 1983). Alternately, pain may influence self-efficacy through its effect on social relationships; both pain and poor self-efficacy are associated with negative provider interactions (Johnson et al., 2006; Feuchtl et al., 2004; Kenny & Faunce, 2004) and lack of social support (Simoni, Frick, Lockhart, & Liebovitz, 2002; Reynolds et al., 2004; Foster, Marshall, Myers, Dunkley, & Griffiths, 2003). Because measuring presence or absence of pain precludes identifying precisely what aspect of pain is associated with self-efficacy, this analysis should be considered exploratory rather than conclusive. To facilitate tailoring of adherence interventions for HIV-infected drug users with pain, future research should focus on understanding mechanisms through which pain influences adherence self-efficacy.

Though depressive symptom severity was associated with non-adherence in bivariate analysis, this association did not persist in models adjusted for pain. Potential explanations for this unexpected result include our small sample size or poor validity of our depression measure. Though this measure has been used among drug users (Knowlton et al., 2006), we did not evaluate performance of the subscale in our sample. Empirical studies are needed to understand the relationship between pain, depression symptom severity, and antiretroviral adherence.

Our study is exploratory for several reasons. Because the prevalence of pain among methadone maintained drug users may be higher compared to other HIV-infected populations, these findings may not be widely generalizable. In addition, the proportion of participants who reported 95% or greater adherence was higher than expected and may be explained by the use of self-report to measure adherence. Further, though the single-item measure has been utilized by investigators in multicenter studies to assess adherence self-efficacy (Reynolds et al., 2004), more recent studies have demonstrated psychometric validity of multi-item adherence self-efficacy scales (Kalichman et al., 2005; Johnson et al., 2007). Lastly, the strong relationship between adherence self-efficacy and adherence may reflect overlap between the constructs being measured. However, to the best of our knowledge, the validity of adherence self-efficacy as a measure of antiretroviral adherence has not been formally evaluated.

Additional methodological issues may have influenced our results. Though the application of mediational analysis to cross-sectional data is not uncommon (Johnson et al., 2006; Sacco et al., 2005; Wolf et al., 2006), it precludes determination of causality and the true direction of hypothesized associations may be reversed. Future studies should examine these causal assumptions, as the relationship between pain and adherence self-efficacy may in fact be bi-directional.

Our results suggest that pain is negatively associated with antiretroviral adherence, and that this association is partially mediated by adherence self-efficacy but not by depressive symptom severity. Because the association between pain and adherence remained robust in both mediation models, HIV providers should identify and treat pain in HIV-infected drug users.

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Table

Analysis of adherence self-efficacy (Model 1) and depression (Model 2) as mediators of the relationship between pain and antiretroviral adherence

Independent variables in logistic regression models	**Beta coefficient**	**OR (95% CI)**	**Beta coefficient**	**OR (95% CI)**
Model 1	Step 1 AUROC[a]=0.72		Step 2 AUROC=0.84	
Pain	-2.03	0.13 (0.03-0.52)	-1.56	0.21 (0.05-0.92)
Adherence self-efficacy [b]	--	--	1.42	4.12 (1.61-10.50)
Model 2	Step 1 AUROC=0.72		Step 2 AUROC=0.78	
Pain	-2.03	0.13 (0.03-0.52)	-1.85	0.16 (0.04-0.63)
Depression symptom severity [c]	--	--	-0.49	0.61 (0.29-1.27)

[a] AUROC indicates Area Under the Receiver Operating Curve

[b] Defined continuously on a 4-point Likert scale question from the AIDS Clinical Trials Group questionnaire

[c] Defined continuously by the score on the six-item depression dimension of the Brief Symptom Inventory

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