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Original Article

Self-reported sleep disturbances in HIV-infected people: a meta-analysis of prevalence and moderators

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ABSTRACT

Objective: Our goal was to estimate the pooled prevalence of self-reported sleep disturbances in HIV-infected people through meta-analysis, taking into account variations in geographic region, gender, age group, CD4 counts, and instrument used to measure sleep disturbances.
Methods: The authors conducted systematic searches of PubMed and PsycINFO to include studies that met our criteria. A random effect meta-analysis model was used to estimate the pooled prevalence of self-reported sleep disturbances in HIV-infected people. The potential moderators of self-reported sleep disturbances were explored with meta-regression analysis.
Results: Twenty-seven articles comprising a total of 9246 HIV-positive participants were finally included in our analysis. The overall prevalence of self-reported sleep disturbances in HIV-infected people was 58.0% (95% CI = 49.6–66.1). Meta-regression analysis indicates that geographic region, gender, and instrument significantly explain part of the heterogeneity of the prevalence estimates between the included studies.
Conclusion: The findings suggest that HIV-infected people suffer from a heavy burden of sleep disturbances. It is therefore recommended that sleep quality should be routinely assessed in HIV-infected people in order to identify the medical treatment needs and the potential impact of sleep problems on antiretroviral therapy outcomes in this population.

1. Introduction

Sleep disturbances among human immunodeficiency virus (HIV)-infected people have been recognized as serious issues ever since the early stage of the HIV epidemic [1]. They have been reported at all stages of HIV infection from the beginning of the infection to its progression to AIDS [2]. Sleep disturbances have also been identified as common and debilitating illnesses for people living with HIV/AIDS both in the pre-combined antiretroviral therapy (cART) and post-cART era with a reported prevalence ranging from 30% to 100% [3–6], as compared to 10–35% [7–9] in the general population.

The pathophysiology of sleep disturbances among HIV-infected patients is still largely unknown, but previous studies have suggested possible clues, including the ability of HIV to affect the central nervous system (CNS), CNS opportunistic infections, pharmacological impact of antiretroviral medications (eg, efavirenz (EFV)), mental health issues, and substance abuse in HIV-infected populations [10,11]. Despite the uncertainty of their etiology, sleep disturbances have clinically important consequences on this population. For example, sleep disturbances are associated with daytime sleepiness, fatigue, depression, cognitive impairment, neurobehavioral dysfunctions, and reduced quality of life in HIV-infected people [5,12–15]. Furthermore, HIV-infected patients complaining of sleep disturbances are more likely to show poor adherence to recommended cART [10,16], which may further cause loss of virologic control, development of drug-resistant strains of HIV, and treatment failure in this population [17,18].

Recent studies have suggested that sleep may play an important role in the immune system. There is increasing evidence supporting an association between sleep and immune function as well as inflammatory response. For example, sleep deprivation decreased NK cell, T cell, and monocyte function [19], and increased the secretion of cytokines, such as interleukin (IL)-6, tumor necrosis factor (TNF)-α, IL-1, and IL-2 [20,21]. It is generally known that HIV infection is characterized by destruction of the immune system and disruption of inflammatory response. HIV-associated immune deficiency results from a decline in the number of CD4 T lymphocytes, defective immunological function of both T cells and macrophages, as well as dysregulation of cytokine production. The close relationship between sleep, immune system, and HIV infection may further underline the importance of examining the sleep disturbances in HIV-infected individuals.

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Although a large body of studies has documented the sleep disturbance burden in HIV-infected people, few of them have explored which covariate may moderate the sleep disturbances in HIV-infected persons. Our meta-analysis aims to use the UCSF symptom management conceptual model (University of California, San Francisco School of Nursing, 1994) to explore the potential moderators of sleep disturbances in HIV-infected individuals. The UCSF symptom management conceptual model consists of three interacting dimensions: symptom experience, symptom management strategies, and outcomes. Our study only adopted the symptom experience dimension of the conceptual model. There are three elements within the symptom experience dimension: perception, evaluation, and response to the symptom. The symptom experience dimension classifies variables that are related to symptom perception into three categories: person, health/illness, and environment, which can guide the identification of the potential moderators to be examined in our study and had been applied in the previous sleep disturbance study [22]. In the person category, we assessed whether patients' gender and age moderate the prevalence of sleep disturbances in HIV-infected persons. Patients' immune status was used in the health/illness category. Since we cannot obtain the detailed environmental variables in each study setting, we used geographic region as a proxy for the environment. In addition, we included instrument assessing sleep disturbances in our meta-analysis because prior studies indicated instrument has a great moderate effect on the prevalence of diseases. Understanding the moderates of sleep disturbance prevalence is clinically important because these moderates may help health professionals to identify high-risk groups that should especially be screened and treated.

A previous systematic review of insomnia prevalence in patients with HIV infection was published almost 10 years ago [6]. In addition, to the best of our knowledge, meta-analytic research estimating the prevalence of self-reported sleep disturbances across different characteristics of HIV-infected subjects is still lacking. Therefore, we conducted an updated meta-analysis aiming to estimate the prevalence of self-reported sleep disturbances in HIV-infected persons, taking into account variations in geographic regions, genders, age groups, CD4 counts and instruments used to measure sleep disturbances.

2. Methods

The systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard [23]. Our study protocol was registered with the PROSPERO database of systematic reviews (http://www.crd.york.ac.uk/prospero). The registration number is CRD42014013834.

2.1. Search strategy

We searched PubMed and PsycINFO for articles published up to September 1, 2014. We searched in the title, abstract, or text fields with the keywords: *sleep disturbances*, *sleep disorders*, *insomnia*, *sleep difficulties*, *AIDS*, and *HIV*. Reference lists of articles identified through database searches were manually screened to locate additional relevant studies. All articles were downloaded, stored, and reviewed with EndNote (version X4).

2.2. Inclusion criteria

In order to be included in the current meta-analysis, a study had to meet the following criteria: (a) it was published in English and presented with original data (excludes reviews and commentaries); (b) participants had HIV infection (either tested or self-reported) and were aged over 18 years of age; (c) self-reported frequency data for sleep disturbances (of any type or diagnostic criteria) or specific sleep problems/symptoms/complaints were reported or could be calculated; and (d) sample size was greater than 10 (excludes very small samples and case studies). We excluded studies that specifically recruited participants who already had the presence of sleep disturbances. In addition, if several studies reported the prevalence with the same sample, one study that provided the most comprehensive covariate information of interest to our meta-analysis was selected. If multiple studies provided the same covariate information, we selected the latest published study to ensure only one sample contributed to our analysis.

2.3. Data extraction

Two independent investigators (JW and HW) conducted data extractions, with discrepancies resolved by consensus meeting. The following information was extracted from each included study: the first author of the paper; the year of publication; the country in which the study was conducted; study design; proportion of male participants; participants' age (mean or median); CD4 counts (mean or median); instrument used to determine sleep disturbances; number of HIV-positive participants and the self-reported frequency of sleep disturbances or the proportion.

2.4. Statistical analysis

In the first place, we calculated the prevalence of self-reported sleep disturbances and 95% confidence intervals (CIs) using Wilson's score method for each included study. This method for estimation of two-sided CIs of proportions (prevalence) prevents overshoot of zero or one, and it does not have a sample size requirement [24]. Secondly, a meta-analysis with a random effect model was performed to obtain an estimation of overall and covariates-stratified prevalence of self-reported sleep disturbances in the population with HIV infection. Those studies with missing covariates information, such as CD4 cell counts and age, were omitted in the stratified meta-analysis. The effect size used for meta-analysis was the proportion, but all analyses were performed by converting proportion $\left(p=\frac{n}{N}\right)$ to double arcsine transformation $\left(t=sin^{-1}\sqrt{\frac{n}{N+1}}+sin^{-1}\sqrt{\frac{n+1}{N+1}}\right)$. Previous simulation study indicated that double arcsine transformation is preferred over proportion and logit transformation to stabilize variance when the proportion becomes very small or big [25]. However, for ease of presentation, all final results were back-transformed to proportions using the method recommend by the paper. Sensitivity analysis was employed to explore the influence of one individual study on the overall estimate. Thirdly, since heterogeneity was expected, we used a random effect meta-regression model, in which several study characteristics were incorporated, including geographic area, gender (≥95% male, mixed sample, and female), age (≤40 and > 40), and instrument used to define sleep disturbances (standardized sleep scale and informal criteria), to explore the moderators of prevalence. The categorizations of gender and age were based on the availability of data. Furthermore, the categorizations warrant the distribution of studies is even across different categories to maximize statistical efficacy. All statistical analyses were conducted with the version 12.0 STATA software.

3. Results

A total of 2734 studies were initially retrieved; 27 studies [3–5,26–49] were finally selected for the meta-analysis (Fig. 1); 1102 records were removed because of duplicity. A total of 1425 papers clearly did not match our inclusion criteria after reviewing the title