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Review

Association of opioid agonist therapy with the initiation of antiretroviral therapy - a systematic review

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ABSTRACT

Objectives: People who inject drugs are at high risk of HIV infection but often face barriers in accessing medical care including access to antiretroviral therapy (ART). Evidence is available about the effectiveness of opioid agonist therapy on drug dependency and risk behaviors. However, it remains scattered regarding access to ART among HIV-positive people who inject drugs. We conducted a systematic review to examine the association of opioid agonist therapy with ART initiation among HIV-positive people who inject drugs.

Methods: We searched the literature for evidence from seven databases. We conducted a narrative synthesis and meta-analysis to examine the association of opioid agonist therapy with ART initiation.

Results: Five out of 2,901 identified studies met the inclusion criteria. Three out of five studies reported that, HIV-positive people receiving opioid agonist therapy initiated ART more than those not receiving opioid agonist therapy. In meta-analysis, opioid agonist therapy was associated with ART initiation among HIV positive people who inject drugs (pooled odds ratio: 1.68; 95% confidence interval: 1.03–2.73).

Conclusions: Opioid agonist therapy is positively associated with ART initiation among HIV-positive people who inject drugs. It is important to scale up opioid agonist therapy among people who inject drugs to improve their ART initiation.

1. Introduction

People who inject drugs are at high risk of contracting human immunodeficiency virus (HIV) infection, owing to their high-risk injecting,[1] and sexual behaviors.[2] About 1.7 out of 12.2 million people who injected drugs were infected with HIV in 2013.[3] This population is recognized as a point source of HIV infection for the general populations, both in concentrated and generalized epidemics. They may engage in high-risk sexual behaviors with their injecting or non-injecting drug use partners. Unrestricted access of HIV care by people who inject drugs is necessary to control the HIV epidemic.

Many people who inject drugs do not have access to antiretroviral therapy (ART) despite their need. ART improves morbidity and mortality[4,5] and prolongs lives of HIV-positive individuals. ART may also decrease the transmission of HIV infection.[6–8] Only four out of 100 HIV-positive people who inject drugs receive ART in 47 countries where reports of ART use were available among people who inject drugs.[9] People who inject drugs face various barriers to access ART and other health care services. People who use drugs do not often trust the health care system and expect that they will be treated punitively.[10] They sometimes perceive discrimination and fear of negative reactions from health workers.[11] In addition, people who use drugs may be denied treatment due to co-morbidity of medical conditions[12,13] and medical practitioners' fear of inadequate compliance to treatment, once initiated.[12,14]

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Treatment of opioid dependence may improve access to ART among people who inject drugs.[15,16] Medications for opioid dependence can either be agonists such as methadone or partial agonists such as buprenorphine or antagonists such as naloxone.[17] However, provision of opioid agonist therapy to people who inject drugs is still low. For instance, less than 2% of people who inject drugs are provided with opioid agonist therapy in each of the following five countries: China, Malaysia, Russia, Ukraine and Vietnam. Almost half of all HIV-positive people who inject drugs live in these five countries.[18] In an opioid agonist therapy program, people who inject drugs receive medications to treat opioid dependence.[19]

Opioid agonist therapy programs may be linked to medical services. This allows provision of medical care at the harm reduction sites[20,21] Additionally, people who inject drugs may be referred to nearby medical clinics or specialized care facilities when in need.[22] Such medical care may include primary medical care, ART, and hepatitis treatment services. In addition, opioid agonist therapy improves physical and social functioning of clients.[23,24] These provisions are more likely to help people who inject drugs achieve physical and social stabilization and overcome barriers of access to ART. Although such evidence is available, no systematic review has been conducted to examine the association of opioid agonist therapy with ART initiation among HIV-positive people who inject drugs. Therefore, we conducted this systematic review to examine the association of opioid agonist therapy with ART initiation among HIV-positive people who inject drugs. The results of this review will assist policy makers in making decisions about the problem of low ART coverage among people who inject drugs.

2. Methods

This systematic review aimed to answer the following population, intervention, comparator, and outcome (PICO) question: "What is the association of opioid agonist therapy with ART initiation among people who inject drugs who are on opioid agonist therapy compared to those who are not on such therapy?" In this review, we defined the population as people who use illicit drugs by means of injection and are living with HIV regardless of their age. The intervention was being on opioid agonist therapy. In such interventions, clients receive medications such as buprenorphine and methadone for treating opioid dependence.[19,25] The comparison group consisted of people who use illicit drugs by means of injection and are living with HIV but are not on opioid agonist therapy. The outcome of interest was ART initiation.

We excluded studies which included people who inject drugs enrolled in detoxification centers from our review. These centers are used to minimize withdrawal symptoms of addicted clients in a safe and effective manner. We excluded these studies because, detoxification processes in such centers may or may not involve the use of medications such as methadone and buprenorphine.[26]

We first developed a protocol and registered it at the PROSPERO database for systematic reviews (Supplementary file 1). The registration number of the protocol is CRD42014009118.[27] In this registered protocol, the primary outcome variables were access to general medical care and the initiation of treatment for HIV and hepatitis. However, in the current study, we have reviewed and reported the results on the outcome of the initiation of HIV treatment only.

2.1. Data sources for existing reviews

Two reviewers (LBM and BFS) independently searched for the presence of systematic reviews or protocols similar to the one used for this review. This search was conducted in the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, the Campbell Library of Systematic Reviews, and the National Institute for Health and Care Excellence. No similar review was found.

2.2. Evidence search strategy

We used sets of prepared Boolean phrases and search terms to retrieve evidence from various medical and academic databases. Similarly, the two reviewers (LBM and BFS) independently conducted a literature search in PubMed, the Education Resources Information Center, PsycINFO, the European Monitoring Centre for Drugs and Drug Addiction, the National Institute on Drug Abuse, the United Nations Office on Drugs and Crime, and World Health Organization databases. For the PubMed database, we used a Boolean combination search term (Supplementary file 2). We used similar text words to conduct searches in the other databases. We also conducted a hand search from references of journal articles that we retrieved. The last search for this review was conducted on 1st November 2014. The searches for various databases were conducted within three months. We limited our screening to studies which were reported in English language. No limit was set for the dates of publication of the articles. The two reviewers compared their results for each database, resolved minor differences and reached a final article inclusion list. We adopted the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (Supplementary file 3) and used the PRISMA flow diagram to retrieve and report the evidence (Figure 1).[28]

2.3. Inclusion and exclusion criteria

We included studies of prospective cohort design with control groups or those comparing an outcome before and after the intervention. We also included cross-sectional studies with control groups. We also searched for randomized controlled trials however none was found which addressed our PICO question. We excluded qualitative studies, reviews, case reports, or editorials.

2.4. Data extraction

The two researchers (LBM and BFS) independently extracted data. The differences were resolved by consensus. We conducted data extraction using an excel spreadsheet. It contained the following elements: study author, year of publication, country in which the study was conducted, study design, intervention characteristics including the medications used for opioid agonist/antagonist therapy and length of follow-up of the intervention, participants of the study, and results of the study.

2.5. Data synthesis and analysis

Five studies were included in this review.[29–33] A narrative synthesis was described for all five studies and a meta-analysis was conducted for four studies[29,30,32,33] for the outcome of ART initiation (Figure 1). A fifth study[31] was not included in the meta-analysis because it had no control group.

For meta-analysis, we calculated the odds ratio (OR) and 95% Confidence Interval (CI) using the Mantel-Haenszel analysis in a random-effect model. We assessed heterogeneity of studies using Chi-square (χ^2) and I^2 statistics. The I^2 statistic describes the percentage of variation in the observed estimates of effect from the included studies due to heterogeneity rather than chance. We used an alpha level of 0.05 for meta-analysis, except for testing heterogeneity, where we used $p < 0.10$. We used Review Manager 5.3[34] to conduct meta-analysis.