Assessing the efficacy of antidepressant treatment in opioid-dependent patients undergoing methadone maintenance treatment: A literature review

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ABSTRACT

Introduction. Opioid dependence and co-occurring depressive disorders represent a significant clinical challenge within the field of psychiatry, necessitating effective interventions to improve patient outcomes. Antidepressant treatment has emerged as a potential therapeutic approach, yet its efficacy in the context of Methadone Maintenance Treatment (MMT) remains inconclusive.

Methods. To address this critical knowledge gap, a comprehensive literature review was conducted. Databases including PubMed, the National Institutes of Health (NIH), Google Scholar, and Cochrane Drugs and Alcohol Reviews were meticulously searched for relevant publications from January 2010 to June 2022, using targeted keywords (“antidepressants,” “opioid addiction,” “methadone”).

Results. The review uncovered a complex landscape of studies, highlighting the challenges in evaluating the efficacy of antidepressant treatment in opioid-dependent individuals receiving MMT. While some investigations have reported modest benefits in alleviating depressive symptoms, others remain inconclusive or contradictory. Desvenlafaxine, a dual-action antidepressant, demonstrated some effectiveness in this population, suggesting a potential treatment option. However, these findings necessitate further exploration through large-scale, complex studies with a focus on diverse patient populations.

Discussion. The multifaceted nature of opioid dependence, comorbid depressive disorders, and the complexities of MMT underscore the challenges in ascertaining treatment outcomes definitively. Additionally, the potential for adverse effects and drug interactions, particularly in cases of relapse, complicates the therapeutic landscape. Patients often resort to self-medicating depressive symptoms with other substances, further clouding the interpretation of treatment results.

Conclusion. The literature review reveals the need for continued research to elucidate the role of antidepressant treatment in opioid-dependent patients undergoing MMT. As patients’ needs vary widely, a comprehensive approach to managing affective symptoms should encompass not only pharmacotherapy but also various psychotherapeutic and social interventions. By addressing these complexities, future research may pave the way for more tailored and effective treatment strategies, ultimately enhancing the well-being of individuals grappling with the dual burdens of opioid dependence and depressive disorders within the MMT context.

Keywords: opioids, addiction, methadone, antidepressants

INTRODUCTION

Addictive behavior poses a substantial challenge within the realm of psychiatry, warranting meticulous attention and comprehensive strategies for intervention. The imperative of fostering a secure therapeutic environment and formulating a pharmacological framework to mitigate and manage associated risks effectively has garnered heightened interest and scrutiny among dedicated healthcare practitioners.

Methadone maintenance treatment (MMT) is a medication-supported strategy that utilizes Metha-
done to assist people dealing with opioid use disorder in abstaining from or reducing their use of illegal opioids (e.g., intravenous heroin) or the unauthorized misuse of prescription opioid medications. Typically, methadone doses are provided daily at the methadone treatment center to minimize the risk of diversion. Nevertheless, individuals may qualify for take-home doses based on their consistent attendance at the clinic, absence of behavioral issues, recent clean drug history, absence of criminal activity, and a stable home environment with secure methadone storage capabilities. It is important to note that individuals in MMT remain dependent on Methadone, and MMT is not regarded as an abstinence-based approach. The duration of methadone treatment is open-ended, with the primary goals being the reduction or elimination of illicit opioid use and the subsequent reduction of associated negative consequences [1].

MMT for opioid dependence offers multiple benefits, both in the short and long term. Depression is one of the most important diagnoses in psychiatry, which is also evident in this population group. It represents one of the most critical risk factors in morbidity and mortality for those undergoing MMT, negatively influencing their course and prognosis. Depression associated with opioid dependence can exist as an independent psychiatric comorbidity or can result from the psychosocial stress associated with substance use and the effects of substance use or withdrawal. Although the prevalence of depression in this population group is significantly higher than in the general population (approximately 50% compared to 16%), studies focusing on antidepressant treatment remain incompletely explored [2].

Among individuals dependent on opiates, having a high level of depression is linked to several negative consequences. For instance, those with opiate-use disorders and coexisting mood disorders are more likely to have a history of suicide attempts, experience severe depression, report a lower quality of life, achieve poorer treatment outcomes, continue using other substances despite treatment, and face higher relapse rates after treatment compared to those without these comorbidities [3].

OBJECTIVES AND METHODOLOGY

This literature review aims to evaluate the effectiveness and impact of antidepressant treatment within the specific cohort of opioid-dependent individuals engaged in MMT. A methodical search was conducted, utilizing academic databases such as PubMed, the National Institutes of Health (NIH), Google Scholar, and the Cochrane Drugs and Alcohol Reviews, selecting publications from January 2010 to June 2022, using a set of keywords which included the terms “antidepressants,” “opioid addiction”, “methadone”.

RESULTS

A study published after the mid-2010s highlights the difficulties and challenges this issue has faced, citing the literature up to that point, concluding that there is no certainty regarding the use of antidepressants in patients undergoing MMT [2]. A meta-analysis of antidepressant treatment for depressive disorder and dysthymia in patients with opioid dependence undergoing MMT observed a slight difference between antidepressant treatment and placebo (42.1% vs. 33.3%) [4]. Among concurrent psychotropic treatment options, antidepressant medication is the most commonly encountered in patients undergoing MMT for opioid dependence (approximately 35% of them receive antidepressants). However, recent studies underline contradictory results regarding its effectiveness [5].

Desvenlafaxine is a dual-action antidepressant inhibiting serotonin and norepinephrine reuptake (SNRI). Unlike tricyclic antidepressants, it has a superior tolerance profile in terms of cardiotoxicity, with minimal effect on the QT interval. Unlike other more frequently prescribed SNRIs (Duloxetine, Venlafaxine), Desvenlafaxine has a different metabolic profile that bypasses hepatic metabolism, reducing potential drug interactions. An 8-week study conducted on 18 participants, of which 14 completed all stages of the study, yielded favorable results regarding the administration of Desvenlafaxine to patients undergoing MMT with concurrent depressive disorder. The administered doses were 50 mg/day for the first two weeks and 100 mg/day for the following six weeks. The results were favorable regarding depressive and anxious symptomatology (highlighted by a significant improvement in Montgomery-Asberg and Hamilton test scores). Additionally, plasma levels of Methadone remained stable, and the QT interval did not undergo substantial changes. Therefore, Desvenlafaxine not only can be considered a therapeutic option for alleviating depressive symptoms in patients undergoing MMT, but its favorable profile of adverse reactions and drug interactions makes it a clear choice for individuals with hepatic or cardiac pathologies [6].

The use of tricyclic antidepressants has also yielded ambiguous results. While treatment with Doxepin at doses of 25-100 mg/day had favorable results regarding both depressive and anxious symptomatology, Imipramine showed a significant reduction in depressive symptoms in one study, and Desipramine did not provide additional benefits for affective symptoms when combined with MMT. Other tricyclic antidepressants have not been studied [7].
Selective serotonin reuptake inhibitors (SSRIs) can increase the bioavailability of Methadone. Clinical evidence shows that adding Fluvoxamine to Methadone can improve its response rate. Those who benefit particularly from this property of Fluvoxamine, which increases plasma methadone concentration (even up to 200%), are individuals who develop withdrawal symptoms before each daily administration, probably due to rapid metabolism. Furthermore, those who obtain unsatisfactory responses to methadone treatment at 100-150 mg/day may benefit from adding Fluvoxamine to their treatment regimen [7].

The use of monoamine oxidase inhibitors has been found to be dangerous for this population group due to the risk of developing maladaptive consumption patterns and poorer dietary control [7].

CONCLUSIONS AND DISCUSSIONS

In conclusion, the landscape of clinical research examining the effectiveness of antidepressant treatment in individuals undergoing MMT for opioid dependence presents a complex and multifaceted picture. While some recent studies have pointed to the potential efficacy of Desvenlafaxine in ameliorating depressive symptoms in MMT patients, it is imperative to acknowledge the lack of unanimity and the need for more robust investigations. The existing body of evidence, while promising, is still insufficient to draw definitive conclusions regarding the utility of antidepressants in this specific population. Therefore, a critical imperative emerges: the necessity for comprehensive studies characterized by larger sample sizes. Such research endeavors should strive to provide a more nuanced and precise scientific outcome, thus contributing significantly to the existing knowledge base.

Furthermore, the therapeutic landscape in the context of MMT remains marked by its inherent complexity. Patients grappling with opioid dependence often face many challenges, including adverse effects, potential drug interactions, and the ever-present specter of relapse. In this context, it becomes evident that a one-size-fits-all approach is unlikely to yield optimal results. It is crucial to recognize that individuals undergoing MMT frequently resort to self-medication with other substances, such as the misuse of benzodiazepines to address insomnia. Consequently, it becomes increasingly arduous to ascertain the true impact of antidepressant treatment alone.

Therefore, it is imperative to broaden the scope of our therapeutic strategies. Beyond pharmacotherapy, the comprehensive management of affective symptoms in MMT patients necessitates exploring and integrating diverse therapeutic modalities. These may encompass various forms of psychotherapy, ranging from cognitive-behavioral interventions to psychosocial support, as well as social interventions designed to address the broader spectrum of needs within this unique patient population. In this multifaceted approach lies the potential to enhance the overall well-being and treatment outcomes of individuals undergoing MMT while grappling with comorbid depressive symptoms.

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REFERENCES


