LETTER TO THE EDITOR

Is It Time to Consider Other Treatment Options for Opioid Use Disorder in Saudi Arabia?

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Over the last 20 years, the steady increase in the prevalence of substance use disorder had been accompanied by changes in the overall patterns of substance use in Saudi Arabia[1]. Here, opioid use disorder (OUD) deserves special attention. Although the rates of heroin misuse continue to decrease in Saudi Arabia[1], OUD encompasses a range of substances other than just heroin. In North America, the misuse of prescription opioids has reached epidemic proportions[2].

A recent study by Al Maharbi *et al.*[3], involving patients with chronic pain, who were treated in a tertiary care hospital in Riyadh, had raised concerns regarding OUD. They reported that 12.8% of the 219 patients studied had engaged in the misuse of prescribed opioids and were at consequential risk of OUD[3]. Roughly 10% of these patients already had OUD[3]. While a significant proportion of patients with chronic pain do not require maintenance treatment with prescription opioids for their pain relief, the only current option for OUD in Saudi Arabia is the abstinence-based treatment, which may not be feasible for these patients. Furthermore, another recent retrospective study involving patients with heroin use disorder admitted to a Riyadh hospital reported that over half of the study population, *i.e.*, 56.6%, had blood-borne infections, such as HIV, hepatitis B, or hepatitis C[4]. This study highlights the need for an opioid agonist treatment in Saudi Arabia[4].

The stigma of using opioid agonist therapies as a treatment, which is like "treating opioids with opioids," might be the main barrier to abstinence-based treatment as the only treatment option. The potential physical dependence from opioid agonist therapies might be the biggest fear for prescribers. Although this dependence is a major concern, harm-reduction must be necessary to save lives and improve the quality of life of those suffering with the disorder. The diagnosis of opioid use disorder, just like in the diagnoses of other substance use disorders, requires at least two out of the 11 DSM-5 criteria[5]. These criteria consist of the symptoms that affect the individual's functioning, such as craving, spending a lot of time to get opioids, and giving up important social, occupational, or recreational

activities. When opioid agonist therapy is introduced to an individual with OUD, these OUD criteria become immaterial, and therefore, the therapy is considered as a treatment for OUD.

Unsurprisingly, many patients become dependent on opioids after their initial exposure. Among the four opioid receptors, the most well-known are the mu and the kappa receptors, which are responsible in triggering the reward and anti-anxiety effects[6]. Individuals with undiagnosed/untreated psychiatric disorders may use opioids to self-medicate for psychiatric symptoms, as well as for pain relief[7]. It is also not surprising that an abstinence-based treatment does not protect against contracting infectious diseases. Opioid use disorder is a highly relapsing, chronic disease that is associated with high rates of morbidity and mortality, especially following a relapse[8]. Similar to other substance use disorders, OUD requires a long-term treatment, which consists of pharmacotherapy and psychotherapy[8]. Therefore, abstinence-based treatment may not be effective for all patients. The treatment with opioid agonists may be more suitable for patients, who take prescription opioids and those who are at high risk, such as those individuals, who use injectable drugs.

In addition to psychotherapy, there are several pharmacological strategies that can be employed for the treatment of OUD. A general summary and worldwide recommendations for OUD treatment are presented in Table 1.

Multiple treatment options for OUD exist worldwide, allowing clinicians to customize their treatments, based on their patient's needs. However, the abstinence-based treatment, *i.e.,* the management of withdrawal symptoms only, is currently the only available option for patients with OUD in Saudi Arabia. This option is not recommended by the leading experts worldwide[8] due its strong association with the risk of relapse, which, in turn, increases the risk of overdose and needle-sharing. These latter factors may explain the high rates of blood-borne infections, observed in a previous study[4]. Opioid withdrawal is associated with symptoms, such as diarrhea, vomiting, piloerection, mydriasis, and severe pain. These symptoms can be traumatic for some individuals and may force them to continue using opioids despite the desire to stop, *i.e.*, promoting negative reinforcement. Even if the physical withdrawal period has passed, the psychological craving for opioids continues long after the cessation of the opioid use, thereby increasing the risk of relapse. Alternatively, monthly treatment with an opioid antagonist, such as injectable naltrexone, can be initiated following the opioid cessation in order to ensure adherence[6]. A previous study reported that this option is equally effective, when compared with the opioid agonist therapies[6]. Although this option may provide a sense of security for patients, who fear opioid relapse[6], it may not be feasible for patients with chronic pain, who require ongoing treatment with painkillers.

Experts recommend that OUD should be treated using opioid agonists. First-line options include medicating with buprenorphine and methadone, although the former is preferred due to its superior safety profile[8]. Buprenorphine is a partial agonist of the mu opioid receptor and exhibits a ceiling effect on opioid toxicity[6]. To address this issue, patients can be treated with a combination of buprenorphine and naloxone (Suboxone). Naloxone is a short-acting opioid antagonist that is added to prevent diversion, in case buprenorphine has been injected. Naloxone has a

Table 1. Brief description of the treatment options for opioid use disorder that are available worldwide

Treatment Option	Description	Recommendation
Abstinence-based treatment, *i.e.*, the management of withdrawal symptoms only	Treatment consists of supportive management, detoxification, and medication of withdrawal symptoms, *e.g.*, with clonidine, diazepam, naproxen. No long-term agonist, *e.g.*, buprenorphine, or antagonist, *e.g.*, naltrexone, treatment is provided.	Not recommended
Abstinence-based treatment, *i.e.*, withdrawal management, followed by long-term opioid antagonist treatment	In patients who are actively using opioids, detoxification is followed by an antagonist treatment, which typically involves long-term/monthly injections of naltrexone.	Recommended in some individuals
Opioid agonist therapies, *i.e.*, maintenance therapies	Individuals with OUD, who are either abstinent or actively using drugs, are treated with buprenorphine (sublingual or injection), methadone, or slow-release morphine in some cases.	Highly recommended
Opioid agonist therapy, *i.e.*, slow taper therapy	After receiving the above treatment, patients are slowly tapered off from the opioid agonist therapy over weeks, months, or years.	Recommended

limited bioavailability and does not interfere with oral/sublingual ingestion. The manufacturer has recently developed a monthly injection that can be delivered in specialized clinics/hospitals. Methadone is a full mu opioid receptor agonist that can be useful, when buprenorphine treatment is ineffective[8]. In some cases, such as when the treatment with buprenorphine or methadone is contraindicated, slow-release morphine presents an alternative treatment option.

Pharmacists and other health care professionals need additional training in treating and monitoring patients with the disorder, who are receiving opioid agonists. There is also a need to coordinate with the prescribing physicians in order to ensure the safety of everyone involved. If opioid agonist therapies were to be approved for the treatment of OUD in Saudi Arabia, the author recommends initiating the therapy with buprenorphine injection, which was recently developed, until the full training protocol has been completed for sublingual films and methadone. This extended-release monthly injection of buprenorphine has been observed to be well tolerated and showed superior results to those of the placebo[9]. Maintenance therapy may include long-term treatment with opioid agonists in some patients, although, sometimes, it may be useful to specify an approximate window, *e.g.,* weeks to years, within which the treatment should be tapered off. The author recommends this option for the initial treatment. In addition, physicians should continually monitor the patient's progress and adjust their advice and treatment accordingly. This should minimize the risks of relapse and deterioration.

In summary, the rate of blood-borne infection is high among users of injectable opioids in Saudi Arabia, and a small but alarming number of patients are known to abuse prescription opioids, *i.e.,* patients with chronic pain, who are taking painkillers. The abstinence-based treatment is not recommended by experts due its high risk of relapse, which increases the rates of death and infection. Therefore, the need in devising other treatment options for OUD in Saudi Arabia is urgent. Multiple OUD treatment options can reduce the fear of withdrawal symptoms, enhance help-seeking, and promote patient autonomy. Initially, treatment with opioid agonists is recommended, although clinical and epidemiological trials, investigating the feasibility of these treatment options in Saudi Arabia, are warranted. Physicians, pharmacists, nurses, and other health care providers should receive appropriate training to ensure the success of this program.

Conflict of Interest

The author declare that there is no conflict of interest that is related to this study and this article.

Disclosure

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Ethical Approval

The study was approved by the Ethics Committee of the KAUH in Jeddah, Kingdom of Saudi Arabia, also known as the Institutional Review Board of Hospitals.

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