



REVIEW ARTICLE

Medical management of opioid dependence in South Africa

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Medical practitioners in South Africa are increasingly confronted with requests to treat patients with opioid use disorders. Many do not possess the required knowledge and skills to deal with these patients effectively. This overview of the medical treatment of opioid dependence was compiled by an elected working group of doctors working in the field

of substance dependence. Recommendations are based on current best practice derived from scientific evidence and consensus of the working group, but should never replace individual clinical judgement.

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Extent of the problem

Heroin is the main illicit opioid of abuse, with an increasing trend in South Africa. Between 11% and 23% of all patients who presented for substance rehabilitation in the second half of 2006 stated that heroin was their primary or secondary drug of choice.¹

The use of heroin in combination with other drugs has also become popular. It includes 'nyaope' and 'pinch' (mixture of cheap heroin and cannabis) and 'sugars' (mixture of low-quality heroin and cocaine, mixed with cannabis). Heroin is mostly smoked in South Africa; the incidence of intravenous use varies geographically and is as high as 42% in Gauteng.¹ Owing to the purity of available heroin in many parts of South Africa, smoking and sniffing it can give a 'high' that is equal to that of injection use.

Between 5% and 8% of treatment seekers in addiction treatment facilities have problems with over-the-counter or prescription medication abuse as their primary or secondary drug of choice; these medications include codeine- and dextropropoxyphene-containing analgesics and cough mixtures. This makes up a significant group of opioid abusers with concerning morbidity, in part because of the toxicity of other ingredients, including paracetamol.¹

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What is opioid dependence?

Opioid dependence is a chronic relapsing disease that develops from repeated self-administration of opioids, including heroin, over-the-counter and prescription opioids. Genetic and environmental factors contribute to the development of this disease.² Repeated exposure to opioids can cause enduring structural and functional brain changes that are associated with distinctive behavioural patterns including compulsive substance seeking and repeated use despite horrendous consequences.

'Opioid' refers to all substances, natural and synthetic (such as pethidine) that act on the mu-opioid receptors in the brain. 'Opiate' refers to derivatives of opium (such as morphine, heroin or codeine). Routine drug screens test positive only for opiates and special testing is required for synthetic opioids.

Opioid dependence is associated with substantial morbidity and mortality. Heroin dependence has an annual mortality rate of about 1 - 2% and frequently requires long-term treatment. It is, however, encouraging that the proportion of clients who sustain abstinence increases with time, and the addicted proportion declines. In a British cohort of 86 heroin addicts followed up for 33 years after first contact, 42% were abstinent from all opioids and had been for at least 10 years; 22% had died, mostly with substance-related causes of death; 10% were on methadone; and 8% could not be located.³

Abuse v. dependence

Opioid abuse and dependence require different interventions.

Abuse implies that someone persistently or sporadically uses substances in a manner that causes negative consequences. The *Diagnostic and Statistical Manual of Mental Disorders, 4th revision (DSM-IV)*, defines it as a maladaptive pattern of substance use that leads to impairment or distress manifesting by any of the following: failing to fulfil important obligations at work, school or home; using substances in a manner that is physically hazardous; or having legal, social or interpersonal problems due to or exacerbated by the substance.



Dependence draws on the physical and psycho-behavioural aspects of addiction and is used by the *International Statistical Classification of Diseases and Related Health Problems*, 10th edition (ICD-10) and DSM-IV classification systems. Three symptom/sign domains are recognised:

- *Physical adaptation* of the body to the substance (tolerance; withdrawal)
- *Loss of control* over taking the substance (strong desire or sense of compulsion to take the drug; difficulties in controlling substance-taking behaviour; desire or unsuccessful efforts to cut down or control use), and
- *Salience* (great deal of time spent obtaining, using the drug or recovering from its effects; progressive neglect of alternative pleasures, interests, or important activities; continued use despite clear evidence of its harm).

Abuse is generally managed by using a psycho-educational approach, e.g. brief interventions,⁴ or motivational interviewing.⁵ This article deals with the medical management of opioid dependence.

Medical model for the treatment of opioid dependence

The aim of treatment for opioid dependence is total abstinence from all opioids. In clinical practice, the short-term success rate for total abstinence is low, even following inpatient treatment. In a 3-month follow-up of 242 opioid-dependent patients in residential treatment in the National Treatment Outcome Research Study, 34% of the patients relapsed to heroin use within 3 days and 60% after 90 days.⁶

Total abstinence does, however, remain an achievable goal for some patients. In 149 patients, following a 6-week residential programme followed by aftercare, a total abstinent rate of 23% after 2 - 3 years was found. Abstinence was significantly associated with programme completion and aftercare attendance.⁷ Over time, however, most users eventually achieve remission.⁸ Trends in treating opioid dependence have moved from only focusing on total opioid abstinence towards including strategies aimed at harm reduction (keeping patients alive until they eventually go into remission) and abstinence from illicit opioids. This may involve the use of long-term oral substitute opioids until the addict is ready to change behaviour and maintain sobriety. The two opioids used for this substitution therapy are methadone and buprenorphine.

The medical management of opioid dependence can thus be conceptualised as involving two potential options:

- Achieving total abstinence rapidly using standard rapid detoxification procedures (withdrawal over 7 - 21 days), followed by relapse prevention strategies.
- Transferring the addict from abused opioids onto an individualised dose of substitution opioid (thus markedly reducing or preventing illicit drug use, allowing patients

to stabilise their lifestyle), and slowly detoxifying them when they are ready. This shift towards harm reduction is not widely accepted in South Africa as there is limited infrastructure and no legislation to accommodate opioid substitution therapy. It is important that South Africa develops the capacity to provide substitution prescription in a safe and controlled manner.

Rapid detoxification from all opioids and relapse prevention

Assisting opioid-dependent individuals to achieve the goal of abstinence from all opioids rapidly involves:

- Identification and motivation
- Detoxification
- Management of co-morbid medical and mental health problems
- Relapse prevention.

Identification and motivation

The problems of opioid-dependent individuals evoke shame, denial and defensiveness in the addict, and negative responses in health care workers. Social workers, educators, workers in the legal and judicial system, health care workers, and other persons involved with these individuals should be educated to recognise opioid use disorders early. Health care workers need to learn skills in dealing with resistance and motivating opioid abusers to engage in treatment services (e.g. brief interventions,⁴ motivational interviewing⁵) and should be familiar with treatment resources in their area.

Article 21/22 of the Prevention and Treatment of Substance Dependency Act (1992) and the draft copies of the revised version of this Bill, provide for the compulsory treatment ('committal') of clients who refuse treatment for substance dependence and who cause harm to themselves or their families.

Management of co-morbid medical and mental health problems

Heroin dependence is associated with a high incidence of co-morbid medical and mental health complications, which require separate identification and treatment. Fatal overdose is tragic and heroin is the drug most implicated in fatal accidental poisonings in addicts. Medical complications may arise from non-sterile injecting practices or needle sharing, and include skin or systemic infections, HIV or hepatitis B or C transmission, and complications because of adulterants, which may include talcum pneumonitis and renal complications. Common psychiatric problems include depression, protracted anhedonia (even with long-term abstinence) and personality disorders. Psychosis is rare but may arise from poly-substance abuse.



Detoxification

Detoxification, the first step of treatment, allows the addict to engage in the most important step of treatment, namely relapse prevention. It involves a graded and controlled reduction in tolerance to opioids, minimising unpleasant withdrawal symptoms. Two medication groups are used, often in conjunction: opioid substitution and symptomatic medication.

Substitution detoxification involves the use of either a full or partial opioid agonist, which is prescribed at an individualised dose that alleviates withdrawal symptoms without causing intoxication. It is then gradually reduced, usually over a period of 1 - 3 weeks, allowing the level of tolerance to normalise in a manner that is tolerable for the addict. It is important to ensure that patients are in withdrawal (objective rating scales may be useful, e.g. Clinical Opioid Withdrawal Scale (COWS)) before administering substitution opioids in order to prevent accidental overdose (full agonists) or precipitate withdrawal (partial agonists).

Symptomatic medications alleviate some of the withdrawal symptoms and are used for mild withdrawal or to reduce the requirement for substitution opioids.

Substitution detoxification options available in South Africa:

- *Full agonist:* Methadone⁹ (only available as Physeptone syrup (2 mg/5 ml) in South Africa; opioid detoxification is an off-label use); other – including codeine, morphine-SR, and the atypical opioid, tramadol (none of these medications are registered for detoxification, nor are they widely researched or accepted as medication of choice for detoxification).
- *Partial agonist:* Buprenorphine.¹⁰

Non-substitution detoxification

- *Alpha-2-agonist*, e.g. clonidine.¹¹
- *Symptomatic medications*, including antidiarrhoea drugs, anti-emetics (nausea and vomiting), hyoscine butylbromide (abdominal cramps), non-steroidal anti-inflammatory drugs (muscle aches), paracetamol (headaches), antacid (indigestion), sedative-hypnotics or hydroxyzine (insomnia) or benzodiazepines (cramps, irritability, dysphoria, anxiety). (Use benzodiazepines with *great care* because of the risk of overdose with opioids and partial opioid agonists and the risk of co-morbid abuse and dependence.) Non-medications like hot/cold packs, relaxation, baths, massages, rubbing ointments, music, acupuncture, aromatherapy, etc. may also be used.

Outpatient detoxification should be considered only in selected cases where it is considered safe to do so (risk of overdose and death). An infrastructure for daily supervised consumption of substitution opioids, regular follow-up and monitoring via random drug testing is required. Methadone should be used with great caution in outpatients, because of the risk of accidental overdoses; buprenorphine may be a safer option.

Inpatient detoxification is safer, especially with high levels of opioid tolerance, poly-drug use, other co-morbidities and in pregnancy. (Long-term supervised care is important during pregnancy and substitute prescribing may be appropriate.) Patients should be educated that their level of tolerance is reduced during detoxification. The dose of illicit opioid that was used prior to detoxification may subsequently cause overdose.

Relapse prevention

A programme, including psychosocial rehabilitation and pharmacological interventions, to prevent relapse back to opioids must be in place prior to embarking on detoxification. Psychosocial interventions provide individuals in recovery with the skills to maintain sobriety and include cognitive behavioural therapy, motivational enhancement therapy, spiritual 12-step programmes and addressing social needs, such as homelessness, unemployment and family reintegration.

Limited pharmacological interventions are available. Naltrexone is an opioid antagonist blocking opioid receptors without producing an effect, making it difficult to get high. It has been used orally, as a depot monthly injection or as a longer-term implant formulation. Naltrexone is unfortunately no longer registered in South Africa, but can be prescribed with Medicines Control Council (MCC) approval per patient and then ordered from overseas, e.g. using an online pharmacy. Only doctors experienced in treating opioid disorders should prescribe naltrexone.

Opioid dependence is a chronic disorder and relapse is common. Relapse could be viewed as a learning and growth opportunity. Many clients find that engaging in an aftercare programme, for example a self-help support group like Narcotics Anonymous, provide them with a useful support structure and may reduce relapse.

Substitute opioid prescribing

Some addicts are unable to give up their opioids, and interventions to reduce harm may be considered until they are able to achieve total abstinence.

Given the chronic relapsing nature of opioid dependence and frequent poor results of rapid detoxification and relapse prevention, treatment to reduce drug-related harm has become an important intervention in many countries. Substitution prescription of opioids, though not widely used in South Africa, is well established internationally and is supported by a large body of research literature and clinical practice.¹² Cochrane reviews confirm that maintenance treatment with methadone¹³ and buprenorphine¹⁴ has proven effectiveness, provided that adequate dosages are prescribed and appropriate supervision is given.

Substitution is suitable for addicts who want to stop illicit opioid use, but are unable to achieve abstinence from all opioids at that time. They receive a prescribed individualised dose of methadone or buprenorphine at suitable doses



to suppress withdrawal and craving, and in the case of buprenorphine, to block the 'high' if illicit opioids are used on top. This provides the opportunity to stabilise their lifestyle, develop insight and reduce harm from illicit drug use.

Methadone maintenance treatment has been shown to reduce morbidity,¹⁵ including HIV risk,¹⁶ incarceration,¹⁷ other substance use¹⁸ and mortality¹⁹ associated with heroin dependence, and improves treatment retention. Compared with detoxification and psychosocial interventions, methadone maintenance treatment has a better outcome²⁰ and the same is true for buprenorphine.²¹

The only formulation of methadone available in South Africa is Physeptone syrup, at a concentration of 2 mg/5 ml. This alcohol-containing cough syrup has a high sugar content and high viscosity, making accurate dispensing difficult. Users have to consume large volumes of the diluted formulation syrup (v. the 5 mg/5 ml formulation available abroad). Methadone is not currently registered for the management of opioid dependence in South Africa (off-label use). Methadone has good oral bioavailability and its long half-life allows for daily oral dosing. Because of its full agonist action, methadone substitution could be associated with a risk of accidental overdose. Ideally, the sugar-free 5 mg/5 ml elixir (not currently available in South Africa) rather than the cough syrup should be used for substitution prescribing.

Buprenorphine is available as a sublingual 2 mg or 8 mg tablet and its long half-life allows for once-daily or alternate-day supervised consumption. Because it is a partial agonist, with increasing dose the active effects plateau, making it safer and less likely to result in accidental overdose than full agonists. Individuals also report a 'clearer head' with buprenorphine, in contrast to the 'mental clouding' sometimes experienced with methadone. The choice of substitution drug rests with the prescribing physician. A higher level of tolerance, patient preference and contraindications to use buprenorphine may be indications for choosing methadone.

Patients should be carefully selected for substitution treatment. They must have a diagnosis of opioid dependence with evidence of physical dependence (tolerance, withdrawal). Ideally they should have had at least one failed attempt at standard detoxification and rehabilitation, be well motivated and give informed consent.

Concomitant medical or psychiatric problems increase the complexity of management and may increase the risk of overdose and death. Other precautions include high-risk poly-drug use, especially drugs that cause sedation such as alcohol or benzodiazepines, and individuals who are at risk of self-harm.

Substitution prescription poses risks if unregulated, including the potential for unsafe or unethical practices by medical professionals, black-market diversion and 'doctor hopping'. It is therefore important that accreditation, guidelines and proper legislation be put into place to ensure that doctors

who do substitution prescribing are properly trained and regulated to ensure patient safety. Only medical practitioners who have received training or have experience in substitution prescribing should provide this treatment. Important elements include regular monitoring of patients, random drug screening to pick up relapse to illicit opioids or other addictive substances, and ongoing psychosocial interventions.

Diversion of medication to the black market remains a valid concern, and adequate supervision of patients with regard to opioid dispensing and consumption is essential. A patient register would help to prevent 'doctor-hopping'.

The ultimate aim of opioid substitution treatment is eventual dose reduction and abstinence when the individual is ready, and treatment goals should be reviewed every 3 - 6 months. Some argue that a small number of addicts require lifelong substitution therapy owing to a relative endogenous opioid deficiency. Better results are obtained when opioid substitution is continued for at least 1 year before attempts are made to reduce the dose.

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