

Drug treatment for opioid dependence

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SYNOPSIS

The number of Australians dependent on heroin is increasing. This is resulting in more deaths and disease. Treatment of heroin dependency usually begins with detoxification, followed by maintenance treatment. Some patients become abstinent. While non-drug therapy has a role there is more evidence to support the use of pharmacotherapy for drug dependence. Methadone is a cost-effective maintenance treatment. Other options include buprenorphine and naltrexone, but further evaluation of these treatments is needed in Australian practice.

Index words: buprenorphine, heroin, methadone, naltrexone.

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Introduction

Heroin is the most commonly injected illicit drug in Australia. Heroin injecting began in Australia in the late 1960s. Using several different methods, it was estimated that there were about 70 000 heroin-dependent persons in Australia in 1997.¹ In the last few years, the number of heroin injectors in Australia has increased more rapidly than in the previous quarter century.

Reported deaths from heroin overdose have increased in Australia fifty-five fold from six in 1964 (1.3/million people aged 15-44 years) to 600 in 1997 (71.5/million).² In 1998, there were 737 such deaths. HIV remains under good control among injecting drug users in Australia, but an estimated 11000 hepatitis C infections in 1997 were attributed to the sharing of injection equipment.³

Heroin dependency is a poorly understood, chronic, relapsing, remitting condition. Mortality, estimated to be 1-2% per annum, is about 15 times that expected in a population of similar age and sex who do not inject drugs.

Heroin-dependent persons benefit from treatment.⁴ Evidence for the persistence of benefit after treatment is less impressive. Pharmacological treatments attract and retain many more drug users than non-pharmacological interventions and are also far better supported by evidence of benefit. Psychosocial interventions play an important role in pharmacological treatments, but the optimal nature and extent of these psychosocial components remains controversial. Some heroin-dependent persons are not suitable for pharmacological treatments or are unwilling to consider them. We therefore need a diverse range of treatment options, including non-pharmacological interventions.

Benefits of treatment

Treatment can improve social and economic outcomes as well as the patient's health (see box). As a generalisation, heroin use falls dramatically. The longer patients stay in treatment, the lower it falls. Reducing the use of heroin will result in decreased deaths, fewer infections and less crime. Although not all patients will completely stop using drugs, the reduction in deaths from overdose makes treatment worthwhile.

Detoxification

The aim of detoxification is to provide a safe and comfortable withdrawal from mood-altering substances. Detoxification should not be regarded as the sole treatment, but it is often a useful prelude to other forms of treatment. Furthermore, some patients undergoing detoxification manage to achieve enduring abstinence without proceeding through subsequent formal treatment. In Australia, most detoxification provided to heroin-dependent persons is still provided in residential care. Outpatient detoxification is increasing, although not all patients are suitable for or will accept this approach.

Benefits of treatment

Health

- Reduction in deaths (all-cause mortality but especially drug overdose)
- Reduction in morbidity (mainly infections – HIV, hepatitis B, hepatitis C, also bacterial infections both proximal, e.g. abscesses around injection sites, and distal, e.g. sub-acute bacterial endocarditis – but also reduction in non-fatal overdoses)
- Improvement in mental health

Social

- Improved relationships and parenting
- Reduction in crime
- Increased employment
- Improved residential status (i.e. less homelessness)
- Increased education and training
- Reduction in drug use (all sorts)
- Reduced heroin use (including abstinence)

Economic

- Earning income legally, or social security
- Less debt
- Benefits outweigh costs to individuals and society

Clonidine, an α_2 -adrenergic agonist, helps to ameliorate some of the more distressing symptoms of heroin withdrawal. It is usually used in combination with several other oral drugs to provide symptomatic relief. These drugs include paracetamol for bone pain, diphenoxylate or loperamide for control of diarrhoea and hyoscine to control abdominal cramps. Benzodiazepines such as nitrazepam can be used for the short-term treatment of insomnia. A small proportion of patients prescribed clonidine may develop hypotension. Some patients who cease clonidine abruptly develop rebound hypertension. Lofexidine, which has many of the useful features of clonidine but possibly fewer adverse cardiovascular effects, may become available in Australia.

Relapse following detoxification is very common. Doctors, their patients and the patients' families should be prepared for the possibility of relapse and not despair if this occurs. Relapse should either prompt a repeat attempt at detoxification, or alternatively, a review of all available options.

Methadone maintenance

Methadone, an opioid agonist which is well-absorbed orally, was introduced for the treatment of heroin dependence in 1964. The rationale involves replacing an illegal, short-acting, expensive drug injected intravenously with an oral drug which is legal, inexpensive and has a longer half-life (requiring only once-daily administration). Patients attend a clinic or pharmacy every day (or several days a week) to be dispensed methadone under supervision. Detoxification is not required for patients starting methadone. Psychosocial interventions are an important part of treatment.

Methadone maintenance is one of the most thoroughly investigated interventions in medicine. A vast scientific literature provides compelling evidence that methadone maintenance reduces heroin consumption, death from drug overdose, HIV infection and criminal activity.⁴ Methadone maintenance is generally very safe, but injudicious use can prove fatal. Methadone also appears to be cost-effective³ and in most countries, demand for treatment exceeds the availability of methadone programs.

Methadone treatment is often subjected to relentless ill-informed criticism in the lay press despite strong scientific support. This criticism undermines community support and makes authorities ambivalent towards funding programs. Local opposition to programs is also not uncommon. Much of the opposition to methadone arises from the fact that it involves giving a patient with drug dependence another drug of dependence. This concern does not arise with nicotine replacement therapy for cigarette smokers even though 20% of patients experience great difficulty stopping nicotine chewing gum.

As many as 85% of patients will stay on methadone for 12 months. Patients retained in treatment on a larger dose and for a longer duration generally achieve better results. For most patients, optimal results are achieved with a dose of 60–100 mg per day. Many patients require treatment for at

least two years. Some heroin-dependent persons will not consider methadone maintenance treatment, while others who agreed to enrol achieve unsatisfactory outcomes. Better results are often achieved in older patients. Not uncommonly, patients who have had poor results from earlier episodes of treatment achieve better results from a subsequent treatment episode. There is good evidence to suggest that as much as 80% of the variance in treatment outcome results from treatment rather than pre- or post-treatment factors.⁵ Important treatment factors include the dose of methadone and the morale of the clinic staff.

Methadone maintenance therapy is provided in a diverse range of programs. New patients or those with more difficult medical or psychosocial problems are often better managed in large public or private clinics. Patients who have achieved some stability are often better managed in general practice with methadone dispensed from a community pharmacy. (Methadone programs are not available in the Northern Territory.)

Naltrexone

Naltrexone is a long-acting opioid antagonist which is well-absorbed orally. A severe withdrawal reaction may be precipitated if the patient has recently taken heroin or another opioid. The manufacturer recommends that naltrexone is not commenced until seven to 10 days after the last use of heroin. If heroin or another opioid is taken by a patient who has already been taking naltrexone, all opioid effects are blocked. The results of naltrexone maintenance treatments are consistently modest for street drug using populations.⁶ Better results may possibly be achieved if naltrexone administration is supervised as part of a comprehensive treatment program, or if more 'motivated' patients are selected (white-collar professionals, persons on parole, probation or in jail).

Some concern has recently been raised about the possibility of an increased risk of death from overdose during naltrexone maintenance. The proposed explanation is that opioid tolerance declines during naltrexone administration. If naltrexone is taken intermittently and then heroin consumed in intervening periods, the risk of death from overdose may be increased.

Accelerated detoxification with general anaesthesia or heavy sedation has been added recently to naltrexone maintenance. This is sometimes referred to as Ultra Rapid Opiate Detoxification (UROD) or Rapid Opiate Detoxification (ROD). Published evaluations have substantial methodological shortcomings and accelerated detoxification can only be considered to be experimental.⁷ Nevertheless, astonishing success is often claimed for this intervention in the lay press.

Buprenorphine

This partial agonist is taken sublingually as it has a high first-pass metabolism when taken orally. It has been used extensively in France and evaluated in a number of countries. Results overall are generally comparable with methadone maintenance, but each drug has particular advantages

(and some special disadvantages). Buprenorphine can be taken on alternate days.

The risk of overdose is minimal but people on large doses of heroin may experience some withdrawal symptoms. Although buprenorphine is more expensive than methadone it may become the treatment of choice for detoxification.

Leva-alpha-acetylmethadol (LAAM)

LAAM (also known as levomethadyl acetate) is a methadone derivative. It has a longer half-life than methadone, but has similar effects. Administration on alternate days reduces the cost of providing the drug and also reduces the burden on patients who are doing well. The metabolites are active and other drugs can interfere with the production of the metabolites. LAAM may be available in Australia within the next few years.

Sustained release oral morphine (SROM)

Few studies have been conducted. A trial has commenced in Australia.

Prescription heroin

Heroin prescription has been available for the management of heroin dependence in the UK since 1926. It has never been studied or utilised commonly in that country. A handful of papers of variable quality suggest that results might be comparable to methadone. A heroin trial conducted in Switzerland in the 1990s obtained some impressive results but lacked a control group. Nevertheless, results were sufficiently impressive to stimulate research in other European countries. The major argument in favour of heroin prescription is for the management of heroin injectors refractory to other treatments.

Intravenous methadone

Intravenous methadone has been prescribed in the UK for decades although evaluation studies are scant.

Non-pharmacological treatments

These include drug-free outpatient counselling, residential rehabilitation (therapeutic communities) and self-help groups (Narcotics Anonymous). Retention is often poor and good

evidence of benefit is difficult to find. Residential rehabilitation is more expensive than outpatient pharmacological treatment and is difficult to combine with continued employment.

Summary

Pharmacotherapeutic treatments attract and retain large numbers of heroin-dependent patients. Evaluation studies show that agonist treatments are safe, effective and cost-effective. The range of pharmacotherapeutic options for management of heroin dependency in Australia is now being expanded. Demand for all forms of treatment (especially pharmacological treatments) for heroin dependence far outstrips supply.

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Self-test questions

The following statements are either true or false (answers on page 23)

- Buprenorphine is taken sublingually because of its low oral bioavailability.
- The long half-life of methadone allows it to be given once a day.

Thyroxine interacts with celery seed tablets?

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Introduction

Interactions between so-called 'natural therapies' and clinical medicines are an unquantified problem in the Australian community, due to a lack of awareness and reporting from consumers and health professionals alike.

The Queensland Medication Helpline is a direct link to consumers and their medication concerns. Over the past five years we have reported, to the Adverse Drug Reactions Advisory Committee, a variety of suspected adverse effects and interactions between clinical and herbal/nutritional