ADDICTIVE DISORDERS & THEIR TREATMENT

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A Guide for Clinicians on ''Take Home'' Naloxone Prescribing

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Abstract

Overdosing is the most common cause of death among heroin addicts and it has been found that most such overdoses are witnessed by other drug users. Hence, it is only logical to argue that if naloxone (a full opioid antagonist and an effective antidote in reversing the effects of heroin overdose) could be administered immediately in such cases of opiate overdose (by anyone witnessing the overdose), lives could be saved. However, its distribution (''take home'' strategy) to heroin addicts or even their carers, as a public health/harm reduction strategy, in an attempt to reduce heroin overdose-related mortality, is a rather new approach. In this paper, we discuss the rationale and evidence base for prescribing take home naloxone and provide some practical guidance to clinicians who wish to prescribe it to their patients. This brief account is primarily intended to raise awareness among clinicians and other key stakeholders of the issues related to take home naloxone prescribing.

Key Words: heroin addiction, heroin overdose, harm reduction, take home supply, naloxone

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Naloxone is a full opioid antagonist and is an effective antidote in reversing the effects of heroin overdose—a standard and well-established treatment procedure in emergency medicine settings. However, its distribution (''take home'' strategy) to heroin addicts or even their carers, in an attempt to reduce heroin overdose-related mortality, is a rather new approach. Despite its critics, it is gathering momentum as a public health and harm reduction intervention in the United States, Europe, Australia, and now the United Kingdom.

In this paper, we aim to discuss 2 aspects of prescribing take home naloxone: its rationale and evidence base and some practical guidance to clinicians who wish to prescribe it to their patients. This brief account is primarily intended to raise awareness among clinicians and other key stakeholders of the issues relating to take home naloxone prescribing. For an in-depth account of the latest research in this field, see references.

RATIONALE FOR USE

Research worldwide indicates that between 40% and 70% of injecting drug users have overdosed at least once in their drug using careers[1–3] and that overdose is the most common cause of death in heroin addicts, most importantly, a preventable cause. Most of the heroin overdoses occur with other people present, and studies suggest that the people most likely to be present as witnesses are other drug users.[4,5] Administration of naloxone, because of its immediate antagonistic effects, can reverse opiate-induced respiratory depression and can prevent death. Hence there is a case for educating and distributing naloxone to drug users, in the hope that prompt provision of this antidote will save lives. Naloxone is a safe drug, which can be easily administered and is the most specific and crucial intervention that can reduce heroin overdose mortality.

KEY CLINICAL ISSUES RELATING TO HEROIN OVERDOSE

These are summarized below:

- Most common following a period of abstinence—that is, soon after release from prison or in the immediate post-detoxification period.

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- Nearly always occurs after intravenous (IV) heroin use.
- Respiratory depression resulting in cardiac arrest is the usual cause of death.
- Most heroin overdoses occur in the presence of others—usually other heroin users.
- Prompt resuscitation interventions can prevent fatal outcome in many cases.

PHARMACOLOGY OF NALOXONE

Naloxone is a μ-opioid receptor antagonist. It is a substituted oxymorphone that is derived from thebaine. Naloxone is ineffective orally and is to be administered parenterally (IV, intramuscular, or subcutaneous). Naloxone has an excellent safety profile and is virtually devoid of any side effect. In the absence of opiates, it has no pharmacologic action (hence no potential for abuse) and doses of up to 90 mg are well tolerated. Please see Box 1 for some of its key properties.

Chemical structure of naloxone (C_{19} H_{21} NO_4) (Fig. 1).

NALOXONE SUMMARY

• Onset of effects	2 to 4 minutes (depending on route of administration)
• Duration of action	Up to 45 minutes
• Metabolism	Hepatic
• Half-life	60 to 90 minutes
• Excretion	Urine and bile
• Dose	0.4 to 2 mg repeated if necessary, every 2 to 3 minutes
• Maximum dose	10 mg (recommended in the United Kingdom)
• Preparations available	0.4 mg per 1 mL ampoules or minijets (in the United Kingdom) 0.4 mg/1 mL and 1 mg/mL strengths (in the United States)
• Side effects	None
• Contraindications	Hypersensitivity
• Abuse potential	Nil

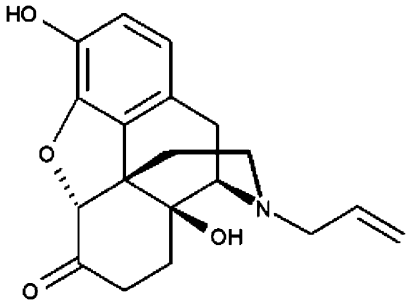

FIGURE 1. Chemical structure of naloxone (C_{19} H_{21} NO_4).

EVIDENCE BASE FOR NALOXONE DISTRIBUTION PROGRAMS

It has to be borne in mind that naloxone is to be prescribed only as part of an overall overdose management training program, which should include resuscitation training and cardiopulmonary resuscitation (CPR). This point cannot be overemphasized as adequate resuscitation training is a strong determinant of successful outcomes (lives saved) in heroin overdoses. Our experience of prescribing naloxone to patients and carers suggests that at a clinical level, this can easily be incorporated into a one-to-one or group training session on overdose management, including resuscitation and CPR training.

Note that the supply of naloxone to take home, as a specific harm reduction strategy is very recent and the evidence available to date is limited. However, emerging trends are very positive and encouraging. From our experience, we would like to highlight to practicing clinicians that such naloxone distribution programs and related training programs can easily be delivered outside research settings—that is within clinic settings. Although its use is limited in the United Kingdom, there is sufficient evidence from the United States, Australia, and Europe to support its use in reducing heroin overdose mortality. The Chicago Recovery Alliance (2004) in an evaluation of their naloxone distribution program concluded that over 200 lives were saved by use of naloxone.[6] Dettmer et al[7] found that 90% of the usages of naloxone by 22 people were

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appropriate. A national, multicenter trial of the possible impact and acceptability of take home naloxone is underway at the National Addiction Centre, London. Although it is only logical to assume so, the public health benefits and cost effectiveness of naloxone distribution have not yet been systematically evaluated.

USEFUL SOURCES OF INFORMATION ON NALOXONE TRAINING, OVERDOSE MANAGEMENT, AND BASIC LIFE SUPPORT

- www.bhf.org.uk (British Heart Foundation)
- www.exchangesupplies.org
- www.anypositivechange.org

ARGUMENTS FOR AND AGAINST NALOXONE PRESCRIBING

Akin to some other drug-related harm reduction measures such as needle exchange, prescribing heroin and safer injecting rooms, supply of naloxone to take home too deeply polarizes opinion among clinicians, researchers, policy makers, and general public. Here is a brief summary of some of the issues raised by its proponents and protagonists:

For

- Effective in reducing heroin overdose mortality.
- A very safe medication with no significant risks.
- Could potentially save lives at relatively little cost.
- Fairly simple training program and prescribing procedure.
- Has important public health (harm reduction) benefits.
- Empowers drug users and their carers.
- Most overdoses are witnessed and hence bystander intervention is crucial and life saving.
- Prompt provision of naloxone can save lives.

Against

- Could be interpreted as professionals condoning injecting behavior.
- Not effective in nonopiate overdoses.
- Not useful in drug users who inject alone.
- Naloxone alone is not sufficient in all cases to resuscitate victims: rescue breathing and CPR are important.
- Administration of naloxone may put people off from calling for an ambulance.
- Possession of naloxone may encourage heavy drug use.
- No robust evidence base to support the assertion that take home naloxone decreases overdose mortality.

GUIDANCE NOTES FOR THE CLINICIAN WISHING TO PRESCRIBE TAKE HOME NALOXONE

Naloxone Prescribing

Naloxone is a prescription only drug in most countries and can only be prescribed by a doctor. Analogous to the injection of epinephrine by anyone witnessing a patient with severe anaphylactic reaction, naloxone can also be administered by any member of the public, in case of a witnessed opioid overdose. A naloxone prescription should only be issued within the context of injection training and a comprehensive training in overdose management. The prescription must specify the dose, formulation, quantity supplied, and the route of administration. Naloxone is available in the United Kingdom in 0.4 mg/1 mL ampoules and in minijets or prefilled syringes (0.4 mg/1 mL). A needle should also be supplied with a prescription of naloxone.

Advice to Patients on Administration of Naloxone

Naloxone is not intended for self-administration but for use by any bystander who witnesses an overdose, who may be another drug user, carer, or a member of the public. As establishing IV access in overdose victims can be difficult, patients are advised

to administer naloxone intramuscular—it is easier, is as effective as IV and has a longer duration of action than IV administration.[8] There is less agreement on the exact dose of naloxone to be administered. But recommendations drawn from clinical experience would dictate that after an initial dose of 0.4 mg, further doses could be repeated at 2 to 5 minutes intervals if necessary. It is important to administer the correct dose of naloxone as too high a dose can result in intense and distressing withdrawal symptoms, whereas too low a dose is likely to be ineffective. Patients have to be advised to call for an ambulance as soon as they have administered naloxone in all cases. This is because even in patients who may seem to recover immediately, there is always the possibility of a delayed occurrence of respiratory depression. Patients and carers are also advised to initiate CPR techniques while waiting for expert help to arrive. Clinicians need to remember that some drug users, for fear of arrest and prosecution, do not wait till paramedics and/or police arrive.

Other Factors to Consider in the Use of Naloxone

- One or more doses of naloxone (one standard dose is usually 0.4 mg/1 mL) may be supplied at a time.
- Users are advised to call an ambulance soon after administering naloxone.
- Patients or carers are instructed to give additional doses if required.
- As naloxone precipitates an acute and severe opiate withdrawal, the victim might be agitated or angry on resuscitation.
- Naloxone is safe to administer in mixed overdoses (heroin with other central nervous system depressants such as alcohol and benzodiazepines).
- Naloxone is ineffective in reversing respiratory depression owing to nonopioids.
- Equivalence—1 mg of naloxone will antagonize approximately 25 mg of IV heroin.
- Only prescribe naloxone as part of a more comprehensive overdose management-training program including CPR.
- As the risk of opioid overdose increases with reduction in tolerance (eg, on discharge after detoxification or release from prison), it is useful to give a supply of naloxone on discharge/release.
- Take home naloxone prescribing is only useful in witnessed overdose.
- Even if the patient responds to the first dose of naloxone, observe for delayed recurrence of respiratory depression.

Naloxone prescribing flowchart (Table 1).

Monitoring

Prescribing naloxone to take home is not to be seen as a one-off event but rather as a process that requires regular monitoring. Key issues to consider at reviews (at least 3 monthly) are:

- Use of supplied naloxone.
- If used, assess appropriateness, impact, and experiences.
- Reassess knowledge and understanding.
- Assess need for refresher training.
- Check if the naloxone ampoule/minijet is within its expiry date.

CONCLUSIONS

Overdosing is the most common cause of death in heroin addicts and studies indicate that most such overdoses occur in the presence of other heroin users. Hence, it is only logical to argue that if naloxone (an immediate acting opiate antagonist) could be administered immediately in cases of opiate overdose, lives could be saved. However, for a range of social and political reasons, naloxone distribution programs, as a harm reduction and public health strategy, has not gained much popularity. Preliminary evidence from such program across the world points to encouraging trends. This paper will hopefully increase the awareness of this intervention among professionals and also provide practical guidance for clinicians on how to prescribe take home naloxone.

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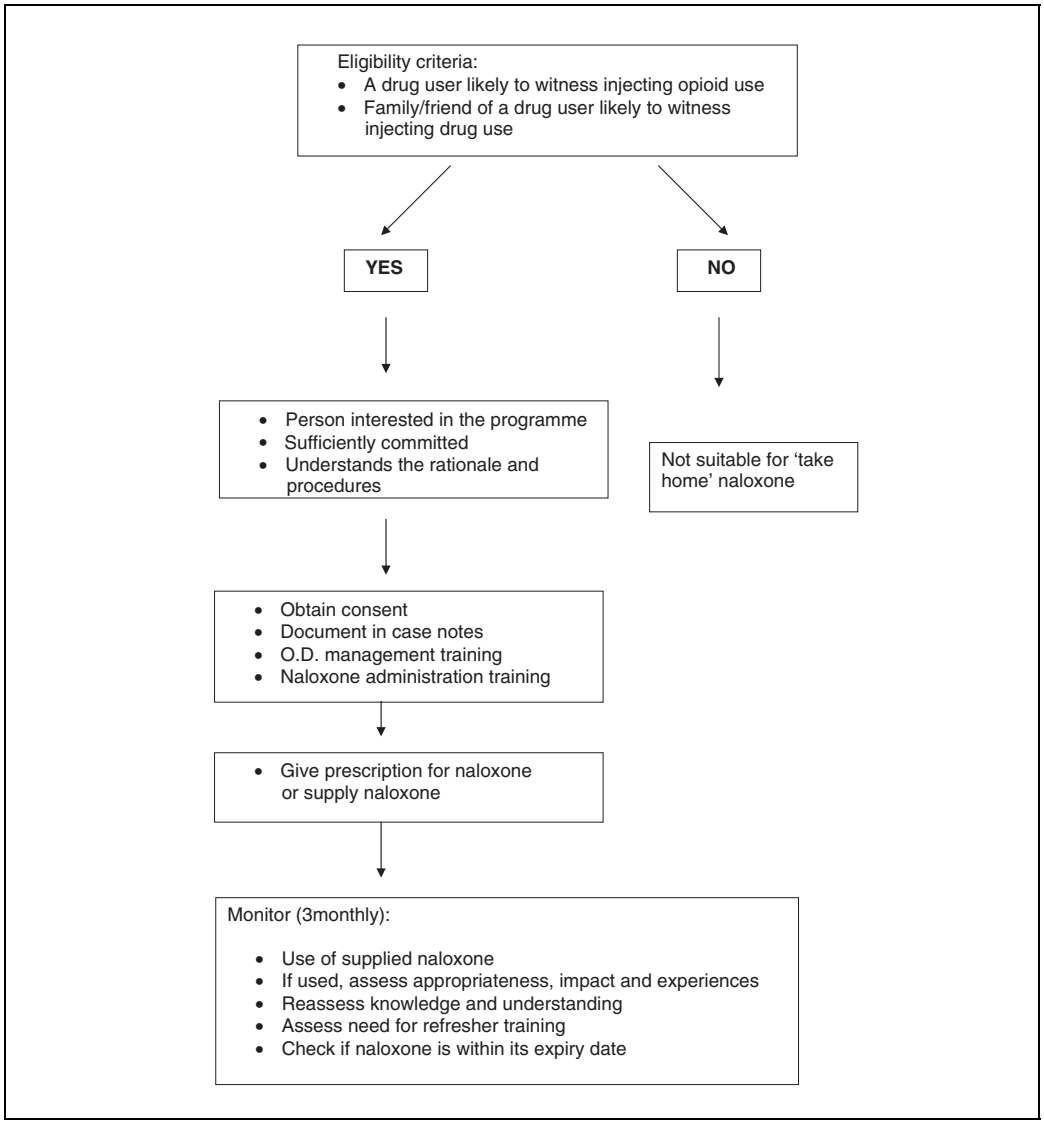
TABLE 1. Naloxone Prescribing Flowchart



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