DRUGS OF DEPENDENCE WITHDRAWAL
Supporting information

This guideline has been prepared with reference to the following:

University College London Hospitals NHSFT. Managing opioid withdrawal for inpatients with substance dependency. 2022

BAP updated guidelines: evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP. 2012

https://www.bap.org.uk/pdfs/BAP_Guidelines-Addiction.pdf

Opiate withdrawal

On what evidence is the Short Opiate Withdrawal Scale based?
The scoring system is an adaptation of the Short Opiate Withdrawal Scale (SOWS) which was itself developed (Gossop, 1990) from the longer, 32-item Opiate Withdrawal Scale (OWS) (Bradley, 1987). The original checklist demonstrated criterion validity in that the scores were high during withdrawal and returned to normal in the weeks following cessation of opiate use. Discriminative validity was shown in that differentiation was possible between addicts in the withdrawal and post-withdrawal phases. Agreement was also seen with the recorded observations of nursing staff (Bradley, 1987). The abbreviated scale removed redundant items having a low loading score and/or overlapping with other items with a higher score (Gossop, 1990).
Blinded, pooled data from two trials assessing the efficacy of lofexidine hydrochloride in reducing withdrawal symptoms in patients undergoing opioid detoxification were used to evaluate the quantitative psychometric properties and score interpretation of the SOWS-Gossop (Vernon, 2016). The findings of this study indicate that the SOWS-Gossop included concepts that are relevant to patients' experiences with opioid withdrawal and has excellent psychometric properties. The authors concluded that the SOWS-Gossop is an appropriate, precise, and sensitive measure to evaluate the symptoms of acute opioid withdrawal in research or clinical settings.

Bradley BP, Gossop M, Phillips GT, et al. The development of an Opiate Withdrawal Scale (OWS). Br J Addict 1987;82:1139-42

Gossop M. The development of a Short Opiate Withdrawal Scale (SOWS). Addict Behav 1990;15:487-90

Vernon MK, Reinders S, Mannix S et al. Psychometric evaluation of the 10-item Short Opiate Withdrawal Scale-Gossop (SOWS-Gossop) in patients undergoing opioid detoxification. Addict Behav. 2016;60:109-16

Evidence Level: III

The following drugs are appropriate for symptomatic use: promethazine (anti-emetic/sedative), propranolol (for somatic anxiety), loperamide (for diarrhoea), hyoscine butylbromide (for stomach cramps)?
No controlled trials have been identified on the use of promethazine in drug withdrawal. This agent has been used for many years for its sedative and antiemetic properties (Erwin, 1957). A randomised, controlled trial in 30 patients recovering from surgery and receiving patient-controlled analgesia (Silverman, 1992) found that the group receiving promethazine along with morphine (n=15) experienced significantly less nausea and vomiting than did controls (Median and mean (+/- SD) symptom-therapy scores of 0 and 0.9 +/- 1.5 vs 2 and 2.4 +/- 1.7).
Only 1 controlled trial of propranolol in drug withdrawal was identified. A double-blind, placebo-controlled trial in 108 cocaine dependent subjects (Kampman, 2001) found that the propranolol group (n=52) had less severe withdrawal symptoms than did controls (n=56). The authors did, however, warn that these results would need to be replicated in a larger trial. Other randomised studies in alcohol withdrawal patients (Worner, 1994; Bailly, 1992) have found propranolol equal to diazepam in reducing symptoms of anxiety.
No controlled trials of loperamide in drug withdrawal were identified. Loperamide has been shown to be a safe and effective treatment for acute diarrhoea (Ericsson, 1990). A multicentre, double-blind study in 213 patients, comparing loperamide, diphenoxylate, clioquinol plus phanquone, and placebo

(Amery, 1975) found that loperamide had a more rapid onset of action than the other treatments, with a complete absence of non-gastrointestinal side effects.
No controlled trials of hyoscine butylbromide in drug withdrawal were identified. In gastrointestinal muscle spasm, Martindale (Sweetman, 2002) suggests 10-20mg orally, 3-4 times a day as an alternative to im or IV administration, despite also stating that the drug is poorly absorbed from the gastrointestinal tract.

Amery W, Duyck F, Polak J, et al. A multicentre double-blind study in acute diarrhoea comparing loperamide (R18553) with two common antidiarrhoeal agents and a placebo. Curr Ther Res 1975;17:263-70

Bailly D, Servant D, Blandin N, et al. Effects of beta-blocking drugs in alcohol withdrawal: a double-blind comparative study with propranolol and diazepam. Biomed Pharmacother 1992;46:419-24

Ericsson CD, Johnson PC. Safety and efficacy of loperamide. Am J Med 1990;38(6A):10S-14S

Erwin HJ. Clinical observations on the use of promethazine hydrochloride in psychiatric disorders. Am J Psychiatry 1957;113:783-7

Kampman KM, Volpicelli JR, Mulvaney F, et al. Effectiveness of propranolol for cocaine dependence treatment may depend on cocaine withdrawal symptom severity. Drug Alcohol Depend 2001;63:69-78

Silverman DG, Freilich J, Sevarino FB, et al. Influence of promethazine on symptom-therapy scores for nausea during patient-controlled analgesia with morphine. Anesth Analg 1992;74:735-8

Sweetman SC (ed). Martindale: the complete drug reference, 33rd ed. London, Pharmaceutical Press, 2002. p469

Worner TM. Propranolol versus diazepam in the management of the alcohol withdrawal syndrome: double-blind controlled trial. Am J Drug Alcohol Abuse 1994;20:115-24

Evidence Level: II

Methadone mixture is the preferred drug (and administration route) for use in opiate withdrawal?
The first clinical trial of oral methadone was conducted nearly 60 years ago (Dole, 1965). 22 patients previously dependent upon heroin were started on 10-20 mg of oral methadone, twice daily, rising over a 4-week period to a stabilisation dose of 50-150 mg per day. Patients were then discharged and maintained on a single daily dose. All patients were able to return to normal life.
A later trial established that the optimum dose was 40 –50 mg, once daily (Strain, 1999), although there is evidence that only doses as high as 120 mg completely block the effects of heroin as well as suppressing withdrawal symptoms (Donny, 2002).
Methadone is of equal potency to morphine if given as a subcutaneous injection but approximately half as potent if administered orally (Martin, 1973). Its slow onset of action blunts the euphoric effect, making it unattractive as a principal drug of abuse (Anon, 1998).
An updated Cochrane review of 23 RCTs in a total of 2,467 subjects (Amato,2013) concluded that compared to any other pharmacological treatment, tapered oral methadone showed no clinical difference, and was superior to placebo, in reducing symptoms of opiate withdrawal.

Amato L, Davoli M, Minozzi S et al. Methadone at tapered doses for the management of opioid withdrawal. Cochrane Database of Systematic Reviews 2013, Issue 2. Art. No.: CD003409
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003409.pub4/full

Anon. Effective medical treatment of opiate addiction. National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction. JAMA 1998;280:1936-43

Dole VP, Nyswander M. A medical treatment for diacetylmorphine (heroin) addiction: a clinical trial with methadone hydrochloride. JAMA 1965;193:646-50

Donny EC, Walsh SL, Bigelow GE, et al. High-dose methadone produces superior opioid blockade and comparable withdrawal suppression to lower doses in opioid-dependent humans. Psychopharmacology 2002;161:202-12

Martin WR, Jasinski DR, Haertzen CA, et al. Methadone: a reevaluation. Arch Gen Psychiatry 1973;28:286-95

Strain EC, Bigelow GE, Liebson IA, et al. Moderate-vs high-dose methadone in the treatment of opioid dependence: a randomized trial. JAMA 1999;281:1000-5

Evidence Level: I

Sedative withdrawal

Once symptoms are controlled, a long-acting benzodiazepine (chlordiazepoxide or diazepam) should be given in the doses indicated?

Long-acting benzodiazepines are used in sedative withdrawal, as short-acting benzodiazepines such as lorazepam do not allow for a smooth decline in blood and tissue concentrations of the drug (Kosten, 2003; Ashton, 2002). Diazepam has a half-life of up to 200 hours, which means that the blood level for each dose falls by only half in about 8.3 days, and chlordiazepoxide is similar, converting to a diazepam metabolite in the body (Ashton, 2002). The equivalent dosages in the table agree with Table 1 in the “Ashton Manual” (Ashton, 2002).

Ashton CH. Benzodiazepines: how they work and how to withdraw (aka The Ashton Manual). Revised August 2002.
http://www.benzo.org.uk/manual/bzcha01.htm

Kosten TR, O’Connor PG. Management of drug and alcohol withdrawal. N Engl J Med 2003;348:1786-95

Evidence Level: V

Last amended August 2023
Last reviewed January 2026