ALCOHOL WITHDRAWAL
Supporting information

This guideline has been prepared with reference to the following:

NICE. Alcohol-use disorders: diagnosis and management of physical complications. 2017. London. NICE

http://www.nice.org.uk/guidance/cg100/

Stewart S, Swain S; NICE et al. Assessment and management of alcohol dependence and withdrawal in the acute hospital: concise guidance. Clin Med (Lond). 2012;12:266-71

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4953492/

Recognition and assessment

The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar) allows accurate grading of the patient into mild, moderate, or severe withdrawal states?
This scale was validated using subsets of the 137 patients involved in the creation of the original scale. The revised scale was found to have improved efficiency with no significant loss in accuracy (r=0.99) and inter-rater reliability was also found to be high (r>0.8) (Sullivan, 1989).

Sullivan JT, Sykora K, Schneiderman J, et al. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). Br J Addict 1989;84:1353-7

Evidence Level: IV

Immediate treatment

What is the evidence in support of pharmacological interventions?
A Cochrane Review of 114 studies in a total of 7333 participants (Amato, 2011) compared 5 pharmacological treatments with placebo and each other. Compared with placebo, benzodiazepines performed better for seizures (three studies, 324 participants, RR 0.16 (95% CI 0.04 to 0.69), moderate quality of evidence). Comparing each of the five treatments versus specific class of drugs, benzodiazepines performed better than antipsychotics for seizures (4 studies, 633 participants, RR 0.24 (95% CI 0.07 to 0.88) high quality of the evidence). Comparing different benzodiazepines and among themselves (28 comparisons), results never reached statistical significance but chlordiazepoxide performed better.

Amato L, Minozzi S, Davoli M. Efficacy and safety of pharmacological interventions for the treatment of the Alcohol Withdrawal Syndrome. Cochrane Database Syst Rev. 2011, 6. CD008537
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008537.pub2/full

Evidence Level: I

Symptom-triggered treatment using CIWA-Ar is appropriate?
Although fixed-dose schedules have the advantage of convenience and are widely used, individualised (symptom-triggered) dosing has been shown to result in shorter hospital stay, less total benzodiazepine use, and shorter periods of sedation in two randomised trials in 117 and 101 patients respectively (Daeppen, 2002; Saitz, 1994). The success of the symptom-triggered approach relies on a scoring system, the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale, and staff trained in its use.
A systematic review of RCTs (Six studies involving 664 patients) concluded that there was moderate strength evidence to suggest that symptom-triggered therapy improved duration of therapy and total benzodiazepine dose in specialized detoxification settings of low-risk patients but the applicability of this evidence in general hospital settings is low (Holleck, 2019). There was insufficient evidence for any conclusions about symptom-triggered therapy for the major outcomes of mortality, seizure, and delirium in any setting. Four studies reported delirium, which occurred in 4 out of 164 patients randomized to symptom-triggered therapy compared to 6 out of 164 randomized to fixed dose therapy (odds ratio, 0.64 [95% CI, 0.17 to 2.47]). Three studies reported duration of therapy, which was 60.4 h

less with symptom-triggered therapy (95% CI, 39.7-81.1 h; p < 0.001). Six studies reported total benzodiazepine dosage, which was 10.5 mg in lorazepam-equivalent dosing less with symptom-triggered therapy (95% CI, 7.1-13.9 mg; p = 0.011).

Daeppen JB, Gache P, Landry U, et al. Symptom-triggered vs fixed-schedule doses of benzodiazepine for alcohol withdrawal: a randomized treatment trial. Arch Intern Med 2002;1117-21
http://archinte.jamanetwork.com/article.aspx?articleid=211434

Holleck JL, Merchant N, Gunderson CG. Symptom-Triggered Therapy for Alcohol Withdrawal Syndrome: a Systematic Review and Meta-analysis of Randomized Controlled Trials. J Gen Intern Med. 2019;34:1018-24

Saitz R, Mayo-Smith MF, Roberts MS, et al. Individualized treatment for alcohol withdrawal: a randomized double-blind controlled trial. JAMA 1994;272:519-23

Evidence Level: I

What is the evidence for benzodiazepine programs of more than 7 days duration?
A Cochrane systematic review of 64 trials in a total of 4309 patients (Amato, 2010) included programs of up to 15 days, but made no recommendations on duration.

Amato L, Minozzi S, Vecchi S, et al. Benzodiazepines for alcohol withdrawal. Cochrane Database Syst Rev. 2010, 3 CD005063
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005063.pub3/full

Evidence Level: V

What are the risks involved in treating alcohol withdrawal on an outpatient basis?
A 2017 review stated that outpatient treatment for detoxification can be difficult because patients often experience significant craving due to complex pathways involved in dopaminergic and opioid center dysregulation. Patients may experience obsession and intrusive thoughts through serotonin deficiency. Benzodiazepines do not treat this aspect of detoxification efficiently (Long, 2017).
In a randomised, prospective trial of outpatient vs inpatient treatment in 164 men of low socio-economic status (Hayashida, 1989), no serious medical complications were observed in either group, regardless of whether they completed treatment or not. Alcohol and non-alcohol related outcome measures at 6 months were similar in both groups.
In order to be considered for an outpatient program, patients should exhibit only mild to moderate symptoms of alcohol withdrawal and be suffering from no medical conditions or severe psychiatric disorders that could complicate withdrawal. They should also have no past history of seizures or delirium tremens, and should have access to a reliable support person at home (Chang, 2001; Myrick, 1998).

Chang PH, Steinberg MB. Alcohol withdrawal. Med Clin N Am 2001;85:1191-1212

Hayashida M, Alterman AI, McLellan AT, et al. Comparative effectiveness and costs of inpatient and outpatient detoxification of patients with mild-to-moderate alcohol withdrawal syndrome. N Engl J Med 1989;320:358-65

Myrick H, Anton RE. Treatment of alcohol withdrawal. Alcohol Health Res World 1998;22:38-43

Long D, Long B & Koyfman A. The emergency medicine management of severe alcohol withdrawal. American journal of emergency medicine; 2017;35:1005-11

Evidence Level: II

Mild withdrawal begins 6-8 hours after the last drink, moderate to severe withdrawal ~48 hours after?
In an observational study of 539 episodes of alcohol withdrawal in a general hospital (Foy, 1997), the median time of onset of symptoms was 5 hours, with 90% of reactions beginning within 20 hours. The median time of onset for patients who had complications was 7 hours, compared to 4 hours for those without. Most patients who experienced hallucinations did so in the first 24 hours, and those with delirium, in the first 48 hours.

Foy A, Kay J, Taylor A. The course of alcohol withdrawal in a general hospital. QJM 1997;90:253-61

Not found an answer to your question? Wish to suggest an edit to this document?
Please contact the BCGP Clinical Effectiveness Librarian at bedsideclinicalguidelines@uhnm.nhs.uk

http://qjmed.oxfordjournals.org/content/qjmed/90/4/253.full.pdf

Evidence Level: IV

Non-treatment of alcohol withdrawal carries a 15% mortality rate?
Treatment of alcohol withdrawal has resulted in a reduction of mortality from 15% in the 1960s (Victor, 1966) to <2% by the end of the 1980s (Guthrie, 1989).
Delirium tremens, although occurring in <5% of untreated patients, is responsible for a death rate of 10% - 20%, due mainly to cardiovascular, metabolic, or infectious complications (Chang, 2001; Holbrook, 1999).
Wernicke's encephalopathy, which may develop in 12.5% - 35% of alcoholic patients, has a mortality rate of up to 20% if untreated (Thomson, 2002).

Chang PH, Steinberg MB. Alcohol withdrawal. Med Clin N Am 2001;85:1191-1212

Guthrie SK. The treatment of alcohol withdrawal. Pharmacotherapy 1989;9:131-43

Holbrook AM, Crowther R, Lotter A, et al. Diagnosis and management of acute alcohol withdrawal. CMAJ 1999;160:675-80
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1230114/pdf/cmaj_160_5_675.pdf

Thomson AD, Cook CC, Touquet R, et al. The Royal College of Physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident and emergency department. Alcohol Alcoholism 2002;37:513-21
http://alcalc.oxfordjournals.org/content/37/6/513.long

Victor M. Treatment of alcoholic intoxication and the withdrawal syndrome. Psychosom Med 1966;28:636-50

Evidence Level: V

Glucose (to correct hypoglycaemia) should be deferred until after the first dose of thiamine, to avoid a risk of precipitating Wernicke's encephalopathy?
The evidence for this statement, which reflects standard practice (Thomson, 2002), appears to be largely based on a small series of 4 patients, who developed Wernicke's encephalopathy only after repeated doses of glucose (Watson, 1981). It has been suggested (Hack, 1998) that a severely hypoglycaemic patient should not be denied glucose while awaiting thiamine administration on this evidence, but conversely that thiamine should certainly precede glucose if a fingerstick glucose test shows no serious hypoglycaemia (Marinella, 1998).
A review of case reports (no higher level of evidence could be found) in 2012 (Schabelman et al) concluded that true clinical research about the question of whether or not a glucose load can precipitate acute onset of Wernicke encephalopathy is lacking, and the exact time period for administration of thiamine to prevent worsening or development of Wernicke cannot be determined from the existing literature. Mounting evidence from case reports does seem to show that prolonged glucose supplementation without the addition of thiamine can be a risk factor for the development or worsening of Wernicke encephalopathy.

Hack JB, Hoffman RS. Thiamine before glucose to prevent Wernicke encephalopathy: examining the conventional wisdom. JAMA 1998;279:583

Marinella MA. Thiamine before glucose to prevent Wernicke encephalopathy: examining the conventional wisdom. JAMA 1998;279:583-4

Schabelman E, Kuo D. Glucose before thiamine for Wernicke encephalopathy: a literature review. J Emerg Med. 2012;42:488-94

Thomson AD, Cook CC, Touquet R, et al. The Royal College of Physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident and emergency department. Alcohol Alcoholism 2002;37:513-21
http://alcalc.oxfordjournals.org/content/37/6/513.long

Watson AJ, Walker JF, Tomkin GH, et al. Acute Wernicke's encephalopathy precipitated by glucose loading. Irish J Med Sci 1981;150:301-3

Evidence Level: V

Oral thiamine supplementation is unnecessary following IV treatment?

A Royal College of Physicians report (2001) recommends "Continue vitamin B co strong at a dose of 30mg/day if there are concerns over the patient's diet. Thiamine 50mg q.d.s should also be continued *if* (their italics) there is evidence of cognitive impairment after detoxification is completed." The DoH guidelines (2007) state that "Patients drinking heavily may suffer from vitamin deficiencies and associated health consequences. Providing appropriate supplements may help prevent future problems". No references are offered to back up either statement. It is, however, well recognised that "the repeat A&E attender is unlikely to take oral medication regularly on discharge" (Thompson, 2002).

A questionnaire survey of 427 A&E specialists and psychiatrists (Hope, 1999) revealed wide variation of practice and no consensus on the question of vitamin supplementation for chronic alcohol misusers.

Department of Health, Scottish Office Department of Health, Welsh Office, et al. Drug misuse and dependence: UK guidelines on clinical management. London, Department of Health, 2007
http://www.nta.nhs.uk/uploads/clinical_guidelines_2007.pdf

Hope LC, Cook CC, Thomson AD. A survey of the current clinical practice of psychiatrists and accident and emergency specialists in the United Kingdom concerning vitamin supplementation for chronic alcohol misusers. Alcohol Alcoholism 1999;34:862-7

Royal College of Physicians. Alcohol: can the NHS afford it? Recommendations for a coherent alcohol strategy for hospitals: a report of a working party of the Royal College of Physicians. London: RCP, 2001
http://www.alcohollearningcentre.org.uk/_library/alcoholNHS_afford_it.pdf

Thomson AD, Cook CC, Touquet R, et al. The Royal College of Physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident and emergency department. Alcohol Alcoholism 2002;37:513-21
http://alcalc.oxfordjournals.org/content/37/6/513.long

Evidence Level: V

Last amended August 2019
Last reviewed October 2023