Treatment of psychiatric aspects of alcohol misuse

PC Naik, LW Brownell

Psychiatric disorders and alcohol misuse often coexist. This article outlines the clinical management of these comorbid disorders. It discusses and suggests therapeutic recommendations.

The immediate management of the acute intoxicated patient involves exclusion of co-existing metabolic disorders, such as hypoglycaemia, physical injuries and infections. The mainstay of treatment is the avoidance of further alcohol consumption and, depending on the level of intoxication, one may need to institute further general supportive measures, such as intravenous rehydration (avoiding the use of glucose to prevent precipitation of Wernicke's encephalopathy). Respiratory and cardiovascular support may be needed if coma occurs. Aspiration of vomit may be avoided by appropriate nursing in the recovery position.

Lheureux and Askenasi (1991) investigated the effects of flumazenil on coma related to acute alcohol intoxication. Eighteen patients were randomly allocated to receive either placebo or flumazenil 1mg. No difference was found between the two groups. Subsequent open administration of higher doses of flumazenil to eleven of these patients resulted in an improvement in five of them. The use of flumazenil in this condition is unlicensed, and clinical experience indicates that such interventions are very rarely indicated. We recommend further evaluation of this treatment. Such treatment could be justified if a patient's life is in danger.

Pathological intoxication

As correctly stated by Dunn and Cook in this issue (see p. 169), the existence of this condition is debatable. If an individual does show evidence of this syndrome, then the patient should be advised to abstain totally from alcohol in the future.

ALCOHOLIC HALLUCINOSIS AND ALCOHOL-INDUCED PSYCHOTIC DISORDER WITH DELUSIONS

The treatment of choice in severe or prolonged cases is neuroleptic medication. Due in part to methodological difficulties, such as the prevalence and heterogeneity of this condition, there are no well-constructed double-blind trials and so the evidence for this intervention is based largely on clinical case reports. There are no guidelines regarding the choice and the dose of neuroleptics. Soyka (1996) recommends the use of high-potency neuroleptics such as haloperidol as the first-line choice, which seems appropriate, as the interaction between alcohol and phenothiazines (e.g. chlorpromazine and thioridazine) is more pronounced.

MANAGEMENT OF WITHDRAWAL SYNDROMES

Alcohol abuse and alcohol dependence are diagnostic categories used for excessive alcohol intake in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM IV; American Psychiatric Association, 1994). Management includes pharmacological, social and psychological support. The last two are important aspects of treatment but are not discussed further in this article. Pharmacological treatment is only required for alcohol dependent individuals.

Setting for treatment

The majority could undergo detoxification as outpatients. However, for obvious clinical reasons, inpatient detoxification is recommended in subjects who are likely to develop severe withdrawal complications (e.g. seizures, delirium tremens), subjects with concurrent severe psychiatric illnesses (e.g. schizophrenia, severe depression), and those with coexisting severe physical illnesses.

Dr PC Naik is Consultant Psychiatrist and Honorary Senior Lecturer and **Dr LW Brownell** is Registrar in Psychiatry, University of Birmingham, Lyndon Resource Centre, Solihull, West Midlands B92 8PW

Correspondence to: Dr PC Naik

Pharmacological treatment

This consists of the use of sedatives and vitamins.

Sedatives: Symptoms of alcohol withdrawal are minimized by using a sedative, which is cross-tolerant with alcohol. Benzodiazepines and chlormethiazole are both equally effective in this respect (Lapierre et al, 1983).

Chlormethiazole can lead to physical dependence. Furthermore, chlormethiazole can be lethal in overdose, especially when taken in combination with alcohol (McInnes, 1987). It should therefore only be used as a second-line drug where close hospital supervision is available, and for a period not longer than 9 days (Association of British Pharmaceutical Industry, 1995).

Benzodiazepines are considered to be the drugs of choice (Institute of Medicine, 1990). There is no consensus regarding which benzodiazepine should be used as first line. Most commonly used ones are chlordiazepoxide and diazepam, which have long half lives and are metabolized to a number of long-acting active metabolites. Diazepam has the advantage of being available for intravenous and rectal administration (the intramuscular route should be avoided, as absorption is erratic). If intramuscular route is essential then lorazepam is the preferred drug. Short-acting benzodiazepines such as oxazepam should be used in subjects with severe liver disease. The following dose regimens are used:

Tapered dose regimen: The initial dose depends on the severity of the withdrawal symptoms but is generally 60–100 mg daily of chlordiazepoxide divided into four doses. The dose should be reduced by 25% every 2 days over the next 7–10 days and then stopped.

Loading dose regimen: The first dose of diazepam is administered when the revised Clinical Institute Withdrawal Assessment for alcohol (CIWA-Ar) score (Sullivan et al, 1989) is between 10 and 20. Diazepam is administered every 1–2 hours until the score falls below 10 and usually no further medication is required (Thorburn, 1994).

Symptom triggered regimen: Chlordiazepoxide is only prescribed in response to the signs and symptoms of alcohol withdrawal. Saitz et al (1994) carried out a randomized, double-blind trial comparing the symptom triggered regimen with the tapered dose regimen. They concluded that the symptom triggered regimen was equally efficacious and decreased both treatment duration and the amount of benzodiazepine used. However, the initial dose of chlordiazepoxide they used in the tapered dose regimen was 200 mg, which is much higher than that used in routine clinical practice, so their results could well be a Type 2 error. Also they excluded those individuals with a history of seizures, those with coexisting medical and psychiatric illnesses and those dependent on drugs. A further limitation of this regimen is that it may not be as feasible to use on a general ward: their study was carried out in a specialized alcohol detoxification unit, where the nurses are more experienced in using the CIWA-Ar scale.

We recommend that the tapered dose regimen should be used in all individuals being detoxified in the community and those in an inpatient setting with a history of seizures, delirium tremens and with coexisting psychiatric and physical illnesses.

Other agents: Carbamazepine (Stuppaceck et al, 1992), clonidine and beta-blockers have been studied and used in the treatment of alcohol withdrawal. None of these have been shown to be significantly superior to benzodiazepines. These agents are not cross-tolerant to alcohol, hence their effectiveness in preventing delirium tremens is questionable. Also they are not licensed for use in alcohol withdrawal.

Vitamins: Vitamin B deficiencies are prevalent in alcohol-dependent individuals. Although data are sparse regarding route, dose and duration of supplements during alcohol withdrawal, the following points are pertinent.

The Committee on Safety of Medicines (1989) reminded doctors that potentially serious allergic adverse reactions might occur during or shortly after the administration of Parentrovite preparations. This product was withdrawn in November 1992. The use of parenteral B complex vitamin preparations has declined, even in cases in which parenteral treatment is considered essential (Hallwood, 1996). Ramayya and Jauhar (1997) concluded that the increasing incidence of Korsakoff's psychosis might be related to the warning of anaphylaxis from the Committee on Safety of Medicines (1989) and the subsequent withdrawal of high-potency parenteral preparations.

Wernicke's encephalopathy, which is caused by thiamine deficiency, carries a significant morbidity and mortality. They should therefore be treated early and adequately. The diagnosis of Wernicke's encephalopathy is missed in a high proportion of cases. Harper (1983) found that only around 20% of cases of Wernicke's encephalopathy diagnosed at autopsy had been suspected in life. The absorption of thiamine in alcohol-dependent individuals is considerably reduced. Oral vitamin B supplementation may therefore not be adequate in preventing and treating Wernicke's encephalopathy. Considering these factors, a sensible approach for the use of vitamins would be as follows:

All alcohol-dependent individuals who are at risk of developing Wernicke's encephalopathy should be treated with parenteral B vitamin complex preparations. This would include those being detoxified as inpatients, and those being detoxified in the community and who have a history of severe malnutrition or are unable to take an adequate diet, but are unwilling to be admitted to hospital. The following precautions must be adhered to:

- Intravenous injections should be administered slowly (over 10 minutes)
- Facilities for treating anaphylaxis should be available when administered.

Data regarding the dosage of parenteral vitamin administration are scanty. The proportion of anaphylactic and serious allergic reactions is significantly greater for intravenous than intramuscular routes. A sensible approach would be to use high intravenous doses in severe cases. Chataway and Hardway (1995) recommend using Pabrinex (intravenous high potency) two ampoule pairs, which may be repeated 8-hourly for 2 days, followed by one ampoule pair intravenously until the patient can tolerate oral thiamine. In less severe cases one pair Pabrinex twice daily, intravenously or intramuscularly, for up to 3 days followed by oral vitamins. In both instances, oral B vitamins (e.g. vitamin B complex strong) should be continued for at least 3 months. Hydration should be maintained and electrolytes should be monitored carefully.

All individuals being detoxified in the community should be treated with high oral doses of vitamins. In healthy volunteers around 5 mg of thiamine is absorbed from an oral dose of 10 mg, and the amount absorbed does not increase with bigger doses (Thomson et al, 1970). The recommended daily dietary intake of thiamine is 1–1.3 mg and 0.7 mg for healthy men and women respectively. For a number of reasons, absorption is reduced in alcohol-dependent individuals. Therefore, for subjects with mild deficiency states, a suitable preparation and regimen is compound vitamin B strong tablets one to two tablets daily. This would provide thiamine 15–30 mg daily. It would be advisable for vitamin supplementation to be continued, especially in those with inadequate diets.

Treatment of withdrawal seizures: Seizures usually respond to treatment with diazepam or chlormethiazole. There is no clear evidence to justify the routine use of carbamazepine, phenytoin and sodium valproate in the prevention or treatment of withdrawal seizures.

ALCOHOLIC BRAIN DAMAGE

Alcoholic dementia

The mainstay of treatment for dementia of any aetiology remains psychosocially based. There is now a greater emphasis on biological treatments of specific forms of dementia, notably anticholinesterase drugs such as donepezil in Alzheimer's disease. McEntee and Mair (1990) have suggested a role for neurotransmitter systems (such as dopaminergic, noradrenergic and serotonergic) in alcoholic dementia, and for potential treatments targeting these systems. To date, however, there has been little evidence to suggest a particular role for a specific biological treatment for dementia in alcoholism.

Strategies such as relapse prevention to help individuals abstain from alcohol should be employed, as there is evidence that both radiological abnormalities of alcoholic dementia and cognitive functioning may partially recover with abstinence over time (Jacobson, 1988).

Wernicke's encephalopathy and Korsakoff's syndrome

The management of Wernicke's encephalopathy is described above. There is less evidence to support the benefits of the administration of thiamine to patients with established Korsakoff's psychosis, although it is common practice to give such patients oral supplements.

Martin et al (1989) concluded that the use of fluvoxamine was beneficial in doses of 100–200 mg per day in improving episodic memory in Korsakoff's syndrome. However, this study involved only 10 subjects and so this potential treatment requires further investigation.

PSYCHIATRIC SYNDROMES AND ALCOHOL

Schizophrenia

Despite the high co-morbidity of alcohol dependence and schizophrenia, there is little research in this area. One of the first goals in management must be the education of the patient, encouraging abstinence from alcohol. These individuals also require treatment of the psychotic illness with neuroleptic medication, as discussed above. In individuals in whom adherence with medication is poor, it may be appropriate to consider treatment with long-acting depot neuroleptic preparations.

It is necessary to consider the interactions of neuroleptics with alcohol, and to advise patients of these risks. Alcohol can worsen the extrapyramidal side-effects of antipsychotic medications, and alcoholism predisposes the patient to the development of tardive dyskinesia. In such individuals it

may therefore be sensible to consider the use of newer atypical antipsychotic drugs such as clozapine, where these effects may be less pronounced.

In the management of alcohol misuse, the usual psychological, social and pharmacological approaches may be employed. But disulfiram should be avoided, as this compound may inhibit the enzyme dopamine beta-hydroxylase and hence worsen psychosis, although reports of this are extremely rare.

Hypomania

Treatment could be considered for the acute phase and long-term prophylaxis of the disorder. In the acute phase, the use of antipsychotics, as described above, would be an appropriate intervention. There are no long-term outcome studies evaluating the use of mood stabilizers such as lithium and carbamazepine in alcoholic hypomanics. Hence there are no clear guidelines regarding the prophylaxis of bipolar affective disorder in these individuals. It would seem to make good clinical sense to prescribe either lithium or carbamazepine in patients who have had two manic episodes or one severe manic episode.

When considering using lithium, it would be necessary to obtain a baseline creatinine clearance, urea, electrolytes, thyroid function tests and liver function tests. Urea, creatinine, electrolytes, thyroid function tests and lithium levels should be monitored every 3 months. One should aim for a lithium level of 0.5–1mmol/litre. Fawcett et al (1987) concluded that lithium led to a reduction of alcohol intake in alcoholics. Other studies (Dorus et al, 1989), however, have failed to replicate these findings.

Carbamazepine is a good alternative mood-stabilizing agent, but it should be used with caution in alcoholics as they may have hepatic impairment. Mueller et al (1997) carried out a double-blind placebo-controlled study in 29 alcoholics, and showed some treatment effects tending to favour the treatment group. As this was a small pilot study and the results did not reach statistical significance, further investigation is required.

Depression

There is a complex interaction between depression and alcohol, alcohol being used by depressed patients to self-medicate their symptoms and also being a mood depressant. Diagnosis of the primary disorder is therefore difficult in the presence of ongoing alcohol intake, and it is advisable to wait for 3–6 weeks after detoxification before attempting treatment with antidepressants. When a decision to use such medication is made, the choice of drug will be influenced by the risk of further alcohol abuse. Monoamine oxidase inhibitors are contraindicated as a result of their dangerous interactions with alcohol. Tricyclic antidepressants can be useful, although they may produce excessive sedation if taken with alcohol and are dangerous in overdose, thus they should be used cautiously. The drugs of choice are selective serotonin-reuptake inhibitors as they are safer and may also produce an independent reduction in alcohol intake at high doses.

Anxiety disorders

Treatment of this co-morbid disorder should ideally be instituted when individuals have become abstinent. Such treatment consists of psychological (e.g. anxiety management, cognitive–behavioural therapy) and pharmacological interventions. The use of benzodiazepines should be avoided, but selective serotonin-reuptake inhibitors (e.g. citalopram, paroxetine) could be used.

PERSONALITY FACTORS

There is little evidence regarding management of personality disorders in combination with alcoholism. Treatment would be of the main underlying condition. The management of personality disorders consists of supportive psychotherapy, crisis intervention, group therapy (e.g. in therapeutic community) and the use of low-dose neuroleptics for short periods of time.

BEHAVIOURAL SYNDROMES AND ALCOHOL

Eating disorders

There is very little research evidence in this area. Treatment would be of the underlying eating disorder in combination with that of the alcohol misuse.

Morbid jealousy

The treatment of this condition must follow a careful assessment of the mental state and social circumstances. In particular, careful attention must be paid to the assessment of risk to the patient's partner or their suspected lover. In cases where the risk to others is apparent, it may be appropriate to warn those at risk of the situation. If ideas of jealousy are delusional in intensity, treatment with an antipsychotic drug, in addition to abstinence from alcohol will be indicated. Treatment may be best administered on an inpatient basis.

ALCOHOL DEPENDENCE

The principle of treatment of alcohol dependence is the adoption of a biopsychosocial model. Social and psychological aspects of treatment will not be further discussed here.

Pharmacological treatments are sometimes used in order to maintain abstinence. Disulfiram is an aldehyde dehydrogenase inhibitor, which acts as a deterrent against further alcohol consumption by producing an artificially high level of plasma acetaldehyde after alcohol ingestion, resulting in a variety of unpleasant symptoms. The enzyme inhibition is irreversible, so that the effects continue for several days after cessation of the drug. Disulfiram is administered daily, as a single oral dose of 200 mg. Fuller et al (1986) investigated the effectiveness of treatment with disulfiram in reducing relapse in abstinent alcoholics, and demonstrated a significant relationship between adherence with the medication and complete abstinence at follow-up. Azrin et al (1982) studied 43 alcoholics for 6 months and demonstrated that supervision of the administration of the drug was effective in improving compliance and in improving outcome.

Drugs said to reduce craving for alcohol and thereby reducing relapse in abstinent alcoholics have recently become more popular. One of the first classes of drugs to be investigated was the selective serotonin-reuptake inhibitors, which have been discussed above. More recently, the gamma-amino-butyric acid (GABA) analogue acamprosate has been studied. Lhuintre et al (1990) and Whitworth et al (1996) have demonstrated an improved outcome in alcoholics who have been detoxified. This drug is recommended for use in abstinent alcoholics who crave alcohol, are motivated, anxious and have good social support.

CONCLUSIONS

Despite a high prevalence and a complicated relationship between psychiatric disorders and alcoholism, there is a paucity of research in this area. It is recommended that further research be carried out in this important but relatively neglected area, in order that clinicians may be able to practice evidence-based medicine. Treatment must consist not only of that of the psychiatric disorder, but also of the alcohol misuse. HM

Association of British Pharmaceutical Industry (1995) *ABPI Data Compendium.* Datapharm Publications Ltd, London

American Psychiatric Association (1994) *Diagnostic and Statistical Manual for Mental Disorders.* 4th edn (DSM-IV). APA: Washington DC

Azrin NH, Sisson RW, Meyers R, Godley M (1982) Alcoholism treatment by disulfiram and community reinforcement therapy. *J Behavioural Ther Experimental Psychiatry* **13:** 105–12

Chataway J, Hardman E (1995) Thiamine in Wernicke's syndrome-how much and how long? *Postgrad Med J* **71:** 249

Committee on Safety of Medicines (1989) Parentrovite and allergic reactions. *Curr Prob* **24:** 1

Dorus W, Ostrow DG, Anton R et al (1989) Lithium treatment of depressed and non-depressed alcoholics. *JAMA* **262:** 1646–52

Fawcett J, Clark DC, Aagesen CA et al (1987) A double-blind, placebo-controlled trial of lithium carbonate therapy for alcoholism. *Arch Gen Psychiatry* **44:** 248–56

Fuller RK, Branchey L, Brightwell DR et al (1986) Disulfiram treatment of alcoholism: a Veterans Administration cooperative study. *JAMA* **256:** 1449–55

Hallwood P (1996) High Potency parenteral B complex vitamin preparation is still available. *Br Med J* **312:** 1226

Harper C (1983) The incidence of Wernicke's encephalopathy in Australia – a neuro pathological study of 131 cases. *J Neurol Neurosurg Psychiatry* **46:** 593–8

Institute of Medicine (1990) *Prevention and Treatment of Alcohol Problems.* National Academy Press: Washington DC: 268–9

Jacobson RR (1988) Cerebral damage in alcohol dependence. *Curr Opin Psychiatry* **1:** 323–4

Lapierre YD, Bulmer DR, Oyewumi ML et al (1983) Comparison of chlormethiazole (Heminevrin) and Chlordiazepoxide (Librium) in the treatment of acute alcohol withdrawal. *Neuropsychology* **10:** 127–30

Lheureux P, Askenasi R (1991) Efficacy of flumazenil in acute alcohol intoxication: a double blind placebo controlled evaluation. *Human Experiment Toxicol* **10:** 235–9

Lhuintre JP, Moore N, Tran G et al (1990) Acamprosate appears to reduce alcohol intake in weaned alcoholics. *Alcohol Alcoholism* **25:** 613–22

McEntee WJ, Mair RG (1990) The Korsakoff syndrome: a neurochemical perspective. *Trends Neurosci* **13:** 340–4

McInnes GT (1987) Chlormethiazole and alcohol: a lethal cocktail. *Br Med J* **294:** 592

Martin PR, Adinoff B, Eckardt MJ et al (1989) Effective pharmacotherapy of alcoholic amnestic disorder with fluvoxamine. *Arch Gen Psychiatry* **46:** 617–21

Mueller TI, Stout RL, Rudden S et al (1997) A double-blind, placebo-controlled pilot study of carbamazepine for the treatment of alcohol dependence. *Alcoholism Clin Experiment Res* **21:** 86–92

Ramayya A, Jauhar P (1997) Increasing incidence of Korsakoff's psychosis in the east end of Glasgow. *Alcohol Alcoholism* **32:** 281–5

Saitz R, Mayo-Smith MF, Roberts MS et al (1994) Individualised treatment for alcohol withdrawal: a randomised double blind controlled trial. *JAMA* **272:** 519–23

Soyka M (1996) Alcohol induced hallucinosis. Clinical aspects, pathophysiology and therapy. *Nervenarzt* **67:** 891–5

Stuppaceck CH, Pycha R, Miller C et al (1992) Carbamazepine *vs* oxazepam in the treatment of alcohol withdrawal: a double-blind study. *Alcohol Alcoholism* **27:** 153–8

Sullivan JT, Sykora K, Scneiderman J et al (1989) Assessment of alcohol withdrawal; the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *Br J Addict* **84:** 1353–7

Thomson AD, Baker H, Leevy CH (1970) Patterns of 35 S-thiamine hydrochloride absorption in the malnourished alcoholic patient. *J Lab Clin Med* **76:** 34–45

Thorburn AW (1994) Alcohol withdrawal: individualising therapy. *Pharmaceut J* **253:** 520

Whitworth AB, Fischer F, Lesch OM et al (1996) Comparison of acamprosate and placebo in long-term treatment of alcohol dependence. *Lancet* **347:** 1438–42

KEY POINTS

- Psychotic disorders in the context of alcohol misuse should be treated with neuroleptics.
- Long-acting benzodiazepines (e.g. chlordiazepoxide) are the drugs of choice in the withdrawal syndrome. Short-acting benzodiazepines (e.g. oxazepam) should be used in individuals with severe liver disease.
- Those individuals being detoxified in an inpatient setting and in the community with a history of severe malnutrition should be treated with parenteral B vitamin complex preparations.
- Oral vitamin B complex in adequate doses should be prescribed to all individuals undergoing detoxification.
- Seizures usually respond to treatment with diazepam or chlormethiazole. There is no evidence that antiepileptics (e.g. carbamazepine) are beneficial in the prevention or treatment of withdrawal seizures.
- Psychosocial interventions are the mainstay of treatment for alcoholic dementia.
- A period of abstinence is necessary before a certain diagnosis of primary depression or anxiety can be made.