08 - Relapse prevention

Relapse prevention

Addictions and substance misuse CHAPTER 4 Relapse prevention There is no place for the continued use of benzodiazepines beyond treatment of the acute alcohol withdrawal syndrome. Acamprosate and supervised disulfiram are licensed in some countries for the treatment of alcohol dependence and may be offered in combination with psychosocial treatment.2 Treatment should be initiated by a specialist service. After 12 weeks, transfer of the prescribing to primary care may be appropriate, although specialist care may continue. Naltrexone is also recommended as an adjunct in the treatment of moderate and severe alcohol dependence.2 As it does not have marketing authorisation for the treatment of alcohol dependence in some countries, informed consent should be sought and documented prior to commencing treatment. A large number of new and repurposed agents are undergoing evaluation for the treatment of alcohol use disorder (AUD).21,22 Acamprosate Acamprosate is a synthetic taurine analogue that acts as a functional glutamatergic N-methyl-D-aspartate (NMDA) antagonist and also increases gamma-aminobutyric acid (GABA) function. The number needed to treat (NNT) for the maintenance of abstinence has been calculated as 9–11.9 Acamprosate should be initiated as soon as possible after abstinence has been achieved although the British Association for Psychopharmacology consensus guidelines11 recommend that acamprosate should be started during detoxification because of its potential neuroprotective effect. In the UK, NICE2 recommends that acamprosate should be continued for up to 6 months, with regular (monthly) supervision (Box 4.1). The summary of product characteristics (SPC) recommends that it is given for 1 year. Box 4.1 Acamprosate: NICE Clinical guideline 115 (2011)2,23 Acamprosate should be offered for relapse prevention in moderately to severely dependent drinkers, in combination with psychosocial treatment. It should be prescribed for up to 6 months, or longer for those who perceive benefit and wish to continue taking it. The dose is 1998mg daily (666mg three times per day) for individuals over 60kg. For those under 60kg, the dose is 1332mg daily. Treatment should be stopped in those who continue to drink for 4–6 weeks after starting the drug. Table 4.7 Treatment of somatic symptoms. Symptom Recommended treatment Dehydration Ensure adequate fluid intake in order to maintain hydration and electrolyte balance; dehydration can precipitate life-threatening cardiac arrhythmia Pain Paracetamol (acetaminophen) Nausea and vomiting Metoclopramide 10mg or prochlorperazine 5mg 4–6 hourly Diarrhoea Diphenoxylate and atropine (Lomotil) or loperamide Skin itching Occurs commonly and not only in individuals with alcoholic liver disease: use oral antihistamines

490 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 4 Acamprosate is relatively well tolerated. Adverse effects include diarrhoea, abdominal pain, nausea, vomiting and pruritis.2 It is contraindicated in severe renal or hepatic impairment, thus baseline liver and kidney function tests should be performed before commencing treatment. Acamprosate should be avoided in individuals

who are pregnant or breastfeeding. Naltrexone Opioid blockade prevents increased dopaminergic activity after the consumption of alcohol, thus reducing its rewarding effects. Naltrexone, a non--selective opioid receptor antagonist, significantly reduces relapse to heavy drinking.2,24 Although early trials used a dose of 50mg/day, later US studies have used 100mg/day. In the UK the usual dose is 50mg/day with a trial dose of 25mg for 2 days to evaluate for adverse effects (Box 4.2). Naltrexone is well tolerated but adverse effects include nausea (especially in the early stages of treatment), headache, abdominal pain, reduced appetite and tiredness. A comprehensive medical assessment should be carried out prior to commencing naltrexone, together with baseline renal and liver function tests. Naltrexone can be started when patients are still drinking or during medically assisted withdrawal. There is no clear evidence as to the optimal duration of treatment but 6 months appears to be an appropriate period with follow-up, including monitoring liver function.9 Patients on naltrexone should not be given opioid agonist drugs for analgesia, non-opioid analgesics should be used instead. In the event that opioid analgesia is necessary, it can be instituted 48–72 hours after cessation of naltrexone. Hepatotoxicity has been described with high doses of naltrexone, so use should probably be avoided in acute liver failure.25 Long-acting injectable naltrexone has been developed to improve compliance.26 Adverse effects are similar to those seen with the oral preparation.27 In the UK, NICE concluded that the initial evidence was encouraging but not enough to support routine use. Nalmefene Nalmefene is also an opioid antagonist, recommended by NICE as an option for reducing alcohol consumption in people with alcohol dependence.2,24 It has been shown in one meta-analysis to be superior to naltrexone in reducing heavy drinking.28 Box 4.2 Naltrexone: NICE Clinical guideline 115 (2011)2,24 Naltrexone (50mg/day) should be offered for relapse prevention in moderately to severely dependent drinkers in combination with psychosocial treatment. It should be prescribed for up to 6 months, or longer for those who perceive benefit and wish to continue taking it. Treatment should be stopped in those who continue to drink for 4–6 weeks after starting the drug or in those who feel unwell while taking it.

Addictions and substance misuse CHAPTER 4 However, use of nalmefene remains controversial, with another meta-analysis suggesting that nalmefene had only limited efficacy in reducing alcohol consumption and that its value in treating alcohol addiction and relapse prevention is not fully established.29 Nalmefene’s efficacy is better than placebo30 but its place in therapy has yet to be established. Disulfiram (Antabuse) Disulfiram is a second-line treatment for those with moderate or severe alcohol dependence who have successfully completed withdrawal and want to maintain abstinence.31 It acts by inhibiting the enzyme aldehyde dehydrogenase, thus preventing complete metabolism of alcohol in the liver. This results in an accumulation of the toxic intermediate product, acetaldehyde, which causes the alcohol–disulfiram reaction, acting as a deterrent for further alcohol use (Table 4.8). Supervised medication optimises compliance and contributes to effectiveness. The intensity of the intolerance reaction is dose-dependent, with regard to both the amount of alcohol consumed and the dose of disulfiram. However, it is thought that much of the therapeutic effect is mediated by the mental anticipation of the aversive reaction, rather than the pharmacological action itself. Sudden death can occur but is more prevalent at disulfiram doses above 1000mg.31 With this in mind, the value of prescribing higher doses of disulfiram must be carefully considered. The first dose is usually 800mg, reducing to 100–200mg daily for maintenance. In comorbid alcohol and cocaine dependence doses of 500mg daily have been given. Halitosis is a common adverse effect. If there is a sudden onset of jaundice (signalling the rare complication of hepatotoxicity), the patient should stop the drug and seek urgent medical attention. The evidence for disulfiram is weaker than for acamprosate and naltrexone2 although its

effect size may be greater.32 In the UK, NICE recommends its use ‘as a second-line option for moderate to severe alcohol dependence for patients who are not suitable for acamprosate or naltrexone or have a specified preference for disulfiram and who aim to stay abstinent from alcohol’ (Box 4.3).2 Table 4.8 The alcohol–disulfiram reaction. Mild alcohol–disulfiram reaction Severe alcohol–disulfiram reaction Contraindications Facial flushing Sweating Nausea Hyperventilation Dyspnea Tachycardia Hypotenision Acute heart failure Myocardial infarction Arrhythmias Bradycardia Respiratory depression Severe hypotension Ingestion of alcohol within the previous 24 hours Cardiac failure Coronary artery disease Hypertension Cerebrovascular disease Pregnancy Breastfeeding Liver disease Peripheral neuropathy Severe mental illness

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