

Pharmacology and Prescribing in Alcohol Misuse.

Abstract

In this article in the series of 'bite sized' pharmacology, we will look at the pharmacological actions of drugs used in the management of alcohol misuse. This article will outline the issues and areas of intervention required in people who misuse alcohol to the detriment of health. It will illustrate the common therapeutic interventions in patients who misuse alcohol and wish to detoxify or reduce their intake. It will then go on to examine the main types of drug used in these interventions and their pharmacodynamic actions. The management will be considered within the NICE guidance and evidence base.

Exercises will be provided to help you apply this knowledge to your prescribing practice.

Alcohol Misuse

According to NHS Choices (2018) Alcohol misuse is the consistent and excessive drinking of alcohol above the low risk limits of 14 units per week. According to the Office for National Statistics release of 2016 figures showed;

- 7,327 alcohol-specific deaths in the UK, a rate of 11.7 deaths/ 100,000 population.
- For the UK, the 2016 alcohol-specific deaths rate continues to remain unchanged since 2013, but is still higher than that observed 15 years ago.
- Since 2001 rates of alcohol-specific deaths among males have been an average of 55% higher than those observed among females.
- Rates of alcohol-specific deaths are highest among those aged 55 to 64 years in 2016.
- Scotland remains the constituent country with the highest rate of alcohol-specific deaths in 2016; yet Scotland has also seen the largest decrease in its rates since they peaked in the early 2000s.

- In England, and for both sexes, alcohol-specific death rates in 2016 were significantly higher in the most deprived local areas when compared with the least deprived local areas.

<https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/drugusealcoholandsmoking/bulletins/opinionsandlifestylesurveyadultdrinkinghabitsingreatbritain/2005to2016>

Pharmacological Action of Alcohol and User Expectation

Alcohol is classed as a general central nervous system depressant. It potentiates the effects of gamma-aminobutyric acid (GABA), the inhibitory central nervous system (CNS) transmitter, in opening chloride channels which are the major inhibitory transmission pathways in the CNS. This is similar to effects seen with benzodiazepines. It also appears to antagonise effects of the excitatory neurotransmitter glutamate through NMDA receptors and promotes the release of endorphins and dopamine, which may go some way explain its pleasurable effects. Rang, Dale, Ritter & Flower (2015)

Alcohol causes relaxation and a feeling of general well-being. It can also promote disinhibited behaviour and has been associated with risk-taking behaviour and impaired judgment. The precise effects vary with the amount taken, the mood of the individual and the environment they are in. It is often said that alcohol will enhance the existing mood whether that be high or low. These effects can be seen with occasional and low level intake but a tolerance (a need for more alcohol to achieve the same effect) can be seen with misuse.

Can we have a picture here relating to alcohol?

Dependency

Alcohol causes physical as well as psychological dependency in some individuals.

Problem drinking can be characterised by

- Drinking more alcohol, or stronger alcohol or for longer

- An inability to reduce intake or stop drinking despite successive attempts
- Memory problems or blackouts
- Absence from work due to drinking behaviour
- Risk taking behaviour or criminal activity
- Withdrawal symptoms from alcohol such as tremor, restlessness, nausea, sweating, palpitations and seizure

Potential harmful effects on health

Excessive consumption of alcohol can cause physical harm in a number of ways. There is a direct toxic effect on tissues such as the brain and liver, an associated poor diet can lead to vitamin deficiency, notably thiamine deficiency that in the long-term causes Wernicke's encephalopathy and Korsakov's syndrome. It can lead to an increased risk of accidents; especially head injury and the general self-neglect which ensues can increase an individual's susceptibility to infection.

Acute adverse effects of alcohol include behavioural disturbance, flushing, hypothermia, diuresis, dehydration, sedation, poor sleep, gastritis, vomiting, oesophageal reflux and haematemesis, hypoglycaemia and arrhythmias. Unconsciousness can occur and death may result from inhalation of vomit.

Regular, high chronic intake can lead to liver damage, gastritis, pancreatitis, hypertension and stroke plus an increased risk of carcinoma. Various psychiatric disorders such as paranoia, depression and anxiety are also common.

The primary goal of drug therapy in management of alcohol misuse is to reduce the likelihood of harm. This is related to the harm that the overuse of alcohol causes as well as any domestic, societal or criminal harm that may arise from the addictive behaviour. The

drugs we use help us manage the patient in the withdrawal from alcohol (or detoxification) stage of their treatment.

Alcohol Withdrawal and its Pharmacological Management

This is a very important area for consideration as it is the area where much of the prescribing in this condition occurs. Persons with significant alcohol dependence will experience withdrawal symptoms which are severe and serious in nature. They may even prove life threatening if not managed appropriately.

They include

- Anxiety
- Tremor
- Restlessness
- Nausea
- Sweating and or fever
- Palpitations and tachycardia
- Seizures
- Delirium tremens

Exercise

Reflect on the common withdrawal symptoms you see in clinical practice and relate these to these to the pharmacological action of alcohol and how withdrawing this produces symptoms and effects.

Pharmacological therapy for assisted alcohol withdrawal is covered in section 1.3 of the NICE Guidance, CG115 (2011) – Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence.

Chlordiazepoxide- this is a long acting benzodiazepine drug which is used in assisted withdrawal from alcohol. It has classical benzodiazepine effects mediated through its effect on GABA, which reduces neuronal excitability. It is helpful in symptom control as it can suppress many of the symptoms we saw above but particularly useful in prevention of seizures. It can be used in varying doses dependent on severity of dependence and response. In some patients diazepam may be used and it acts in a similar fashion. Choice is often dictated by local protocols and may be influenced if hepatic impairment when the use of lorazepam, which relies less on hepatic metabolism, is a safer option. Patients should be supervised through their withdrawal for possible cross tolerance of benzodiazepines with alcohol.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, explore the range of benzodiazepines and their indications.

Reconcile this with your local policy on prescribing in alcohol withdrawal and NICE

Guidance

Clomethiazole- this is a barbiturate type drug that is useful in assisted withdrawal from alcohol. It can relieve or suppress the symptoms associated with withdrawal which related to central withdrawal actions and has an effect on GABA receptor action, producing anticonvulsant and anxiolytic effects. It is for short term use only and should only be used in monitored inpatient settings and where the patient has no access to alcohol, as there is a risk of overdose and misuse. It is contraindicated in patients who continue to drink and should be used with extreme caution and at lower doses in hepatic impairment due to the risk of coma.

Thiamine- this essential nutrient is depleted in people with chronic long term alcohol misuse. Thiamine deficiency is associated with an increased incidence of Wernicke's encephalopathy and Wernicke- Korsakoff psychosis. Replacement of this deficiency by supplement can lessen the impact of either of these alcoholic brain diseases and is an essential component of assisted withdrawal. Doses vary dependant on the severity of deficiency and are usually administered orally although parenteral formulations are available. .

Drugs can continue to be used after successful withdrawal has been achieved to support the patients health and maintain abstinence or try to prevent relapse.

Acamprosate- Acamprosate is useful for patients who have withdrawn from alcohol and it can prevent relapse. Treatment should commence as soon as abstinence has been achieved and continue for up to one year. It should be used with caution in hepatic impairment and avoided completely if this is severe in nature. Its mode of action is proposed to be at NMDA and GABA receptors and can reduce the craving for alcohol. Used alone it had limited effectiveness and should be combined with psychological support (Robertson 2016).

Disulfiram- this drug is given to help achieve and maintain abstinence. When taken, if alcohol is imbibed while on this drug and extreme and unpleasant reaction occurs. It creates an acute sensitivity to alcohol by inhibition of the enzyme acetaldehyde dehydrogenase which metabolises the primary metabolite of alcohol- acetaldehyde- to a harmless chemical, this thereby reduces normal alcohol metabolism by the liver and leads to an accumulation of acetaldehyde giving the patient unpleasant and hangover like effects. It is for this reason it is sometimes referred to as aversion therapy. Symptoms occur within 10-20 minutes of consuming alcohol and are brought about by the accumulation of acetaldehyde which

provokes flushing, headache, palpitations, nausea and vomiting. It is only effective if taken on a daily basis (Robertson 2016).

Naltrexone- Naltrexone- this drug is an opioid receptor antagonist found to have benefit in prevention of relapse after successful alcohol withdrawal. It has been shown to decrease the amount and frequency of drinking (SAMHSA 2016). Care should be taken when prescribing for patients on opioid based analgesia as it can reduce the effectiveness of these painkillers (NICE 2011).

Hepatic Impairment in Alcohol Misuse

Hepatic impairment is a factor to consider when prescribing for this group of patients.

Cirrhosis or liver disease caused by alcohol misuse reduced hepatic function and the body's ability to eliminate drugs. Guidance in the BNF and other drug choice support policies should be followed and liver function tests carried out and monitored regularly throughout treatment.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out the usual doses of the drugs above that you are most likely to prescribe in practice. Relate any issues with potential hepatic impairment for patients with alcoholic liver disease and how this would impact on your prescribing practice.

Can we have a photo of a BNF here please?

References & Further Reading

Barber and Robertson (2015) Essentials of Pharmacology for Nurses 3rd Edition McGraw Hill London

BNF Online via NICE <https://bnf.nice.org.uk/>

Electronic Medicines Compendium <https://www.medicines.org.uk/emc>

NHS Choices- <https://www.nhs.uk/conditions/alcohol-misuse/>

NICE CG115 (2011) Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence.

<https://www.nice.org.uk/guidance/cg115/chapter/1-Guidance#interventions-for-alcohol-misuse>

Office for National Statistics Bulletin- Alcohol-specific deaths in the UK

<https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/causesofdeath/bulletins/alcoholrelateddeathsintheunitedkingdom/registeredin2016>

Rang, H.P., Ritter. J.M., Flower. R.J. and Henderson, G. (2015) Rang and Dales Pharmacology 8th ed. Churchill Livingstone. London.

Robertson, D (2016) Essentials of Medicines Management for Mental Health Nurses, McGraw Hill, London

Substance Abuse and mental Health Services Administration (2016) *Naltrexone* retrieved from <https://www.samhsa.gov/medication-assisted-treatment/treatment/naltrexone>