

encapsulate

Welcome to 'encapsulate'

The seventh edition of **encapsulate** looks at the disadvantages of using Pethidine, and recommended alternatives in the treatment of acute pain. We also look at the need to always consider alcohol consumption when prescribing medications and counselling patients due to dangerous medication interactions with alcohol.

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Pethidine

Pethidine is a synthetic opioid agonist. It is indicated for the treatment of moderate to severe acute pain not responsive to non-opioid analgesics, as preoperative medication, as an analgesic adjunct during general anaesthesia and for obstetric analgesia.

According to the Therapeutic Guidelines and the Australian Medicines Handbook, the use of pethidine is not recommended (especially if multiple doses are needed) and should be avoided. This is because there is little evidence to suggest it is better than other opioid analgesics and has several significant disadvantages, including:

- Short duration of action. (Pethidine has a half life of 3-5 hours and useful analgesia lasts 2-4 hours after parenteral administration)
- Higher potential for abuse. (Pethidine is the opioid drug abusers most commonly seek and the opioid most commonly abused by health professionals. ¹)
- Increased potential for serious drug interactions including MAOI, SSRIs and other medications which effect serotonin levels. These interactions may result in serotonin syndrome.

- Accumulation of the active neurotoxic metabolite norpethidine. Norpethidine:
 - Is twice as potent as a convulsive agent while having half the analgesic activity of pethidine.
 - Has a longer elimination half life (8-21 hours) and can therefore accumulate putting the patient at risk of hyper-excitability, tremors, myolonus and seizures.
 - Has an increased half-life in patients over 60 years of age, neonates and those with renal impairment.
- Other side effects are similar to those of morphine (bronchospasm, increased biliary pressure)

In theory, if a patient requires opiate analgesic therapy, any opioid could be used provided appropriate dose titration is undertaken to meet individual patient pain requirements while minimising adverse effects. However, morphine is the preferred opioid analgesic because of familiarity; availability of several different strengths/dose forms and cost. ²

If a patient cannot tolerate the adverse effects of morphine or morphine is contraindicated other opioid analgesics can be considered. According to the Therapeutic Guidelines, intravenous fentanyl is an alternative to intravenous morphine in the treatment of acute pain.

Despite its limitations and the recommendations against its use, pethidine continues to be prescribed. When pethidine is used for acute pain, it should not be used for more than 72 hours. Pethidine should never be used for the treatment of long term or chronic pain relief.

References:

1. Kaye K.I. et al, *Pethidine in emergency departments: promoting evidence-based prescribing*, *Medical Journal of Australia (MJA)* 2005; 183(3): 129-133.
2. *Australian Medicines Handbook* 2008

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Medication Interactions with Alcohol

Alcohol has the potential to interact with a number over the counter and prescription medicines. These include: non-opioid and opioid analgesics; sedatives; hypnotics; antipsychotics; antidepressants; antiepileptics; antihistamines; cardiovascular medication; and anti-diabetic medication.

There are various mechanisms by which alcohol can interact with these medicines.

Alcohol can alter the way medicines work. Many medicines are known to cause drowsiness. Consuming alcohol while taking these medicines may potentiate this drowsiness. An example is the interaction between opioid analgesics and alcohol.

Other interactions occur due to the mechanism for alcohol breakdown and removal from the body. Alcohol, and many other medicines, are metabolised in the liver by cytochrome P450 (CYP) enzymes. A single drink can inhibit a medicine's metabolism by competing for the same CYP enzymes. This may increase the medicines availability in the body, resulting in an increased therapeutic effect and risk of side effects. An example is the interaction between warfarin and alcohol. Plasma warfarin levels may be increased resulting in an increased anticoagulant effect and risk of bleeding.

Chronic alcohol consumption can increase the levels of certain CYP3A enzymes. This may increase the rate of metabolism for many medicines, resulting in a decreased therapeutic effect. Warfarin and alcohol also interact in this way. Long term alcohol consumption increases the metabolism of warfarin, decreasing plasma warfarin levels and anticoagulant effect.

Alcohol related enzyme induction can also cause the breakdown of medicines into toxic chemicals that damage the liver and other

body organs. For example, liver damage from toxic metabolites of paracetamol may occur at therapeutic doses of 1g every 4 hours.

Alcohol related enzyme induction can take several weeks to return to 'normal' or pre-drinking levels after drinking is stopped. This is a major consideration, particularly for medicines with a narrow therapeutic index.

In some cases, the mechanism of interaction is unclear, e.g. duloxetine (Cymbalta®). Duloxetine is contraindicated for heavy drinkers as it is reported to worsen pre-existing hepatic impairment. Plasma concentration levels of duloxetine are also elevated in individuals with hepatic impairment, which is sometimes related to alcohol consumption.

The above examples are a small subset of the many and varied medication interactions with alcohol. Healthcare professionals should be aware of the medications that interact with alcohol and implications for their patients. Pharmacists and approved drug references are a good source of information.

Consumption of alcohol in the community is widespread making it important for healthcare professionals to ask patients about their usual alcohol consumption when prescribing/supplying a new medicine or stopping an existing medicine. Patient counselling must always include potential interactions and how to avoid them.

References

1. McIntyre RS, Panjwani ZD, Nguyen HT. The hepatic safety profile of duloxetine: a review. *Expert Opin Drug Metab Toxicol* 2008;4:281-5.
2. Weathermon, R, Crabb, DW, *Alcohol and Medication Interactions* Vol. 23, No. 1, 1999

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