Hydromorphone in palliative care: what the GP needs to know

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Hydromorphone is a useful analgesic in palliative care, particularly when a patient develops intolerable adverse effects from other opioids. It is five to 10 times as potent as morphine, so care must be taken when switching medications.

Most patients with advanced cancer will suffer pain that requires opioid analgesia.[1] The most widely prescribed opioid is morphine, and it has the greatest body of published information to support its use.[2] Although most patients will achieve adequate analgesia with morphine, there is a small but significant number of patients who will suffer intolerable adverse effects without acceptable analgesia.[3]

Hydromorphone (Dilaudid) is a strong opioid that is similar in action to morphine. In selected patients who have developed intolerable adverse effects from other opioids, switching to hydromorphone has been shown to be beneficial. For the benefit of these patients, understanding of the principles and practice of opioid switching is imperative.[4,5]

How does hydromorphone work?

Hydromorphone is a synthetic analogue of morphine and was introduced into clinical practice in the early part of the 20th century.[6] It is believed to mimic the effects of the endogenous opioids by interactions with mu and delta opioid receptors through mechanisms not completely understood.

When is it used?

Since 1985, the World Health Organization has recommended that it is acceptable to use hydromorphone as an alternative to morphine.[7] Since its introduction, it has been widely used in the USA, but only recently introduced into the UK and Australia.

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In palliative care, it is most often prescribed to a patient who is experiencing intolerable side effects from another opioid. In particular, hydromorphone is less likely than morphine to cause pruritus, nausea and vomiting, and sedation.[8,9] Patients with itch secondary to morphine have had reduction or resolution of pruritus after a switch to hydromorphone.[10,11] Similarly, intractable nausea or vomiting may improve when switched to hydromorphone. Also, in clinical experience and observational studies, patients encounter less sedation and fewer neurotoxic effects from hydromorphone compared with morphine.[12,13]

In what forms is it available?

In Australia, hydromorphone is available in a variety of immediate release oral preparations (a 1 mg/mL liquid and 2, 4 and 8 mg tablets) and in ampoules of 2 or 10 mg in 1 mL, 50 mg in 5 mL and 500 mg in 50 mL for parenteral administration.[14] Slow release oral forms are available in the USA and UK, but are not yet available here although they have been approved by the Australian Drug Evaluation Committee.

Considerations in administration

Patients experience analgesia about 30 minutes after oral administration of hydromorphone, and the duration of action is roughly

four hours; there is, however, wide individual variation.[15] Extensive hepatic first-pass metabolism necessitates caution in liver disease. Care needs to be taken in renal disease also, since the major metabolite, hydromorphone-3-gluronide, is renally excreted and accumulation of this metabolite may cause similar neurotoxic side effects to those seen with morphine.[16]

The injectable preparations can be administered in a variety of fashions, including intravenous, intramuscular, subcutaneous and neuroaxial, with the subcutaneous route the most used in palliative care. Hydromorphone is more lipid soluble than morphine, and therefore has a more rapid onset of analgesia after subcutaneous injection; again, pain relief lasts for about four hours.[15]

When switching between oral and parenteral hydromorphone, it is important to adjust the dose to allow for a conversion factor of 2:1 to 3:1; i.e. 2 to 3 mg of oral hydromorphone is equivalent to 1 mg of parenteral hydromorphone.[17]

Switching from morphine to hydromorphone

Before prescribing hydromorphone, or any other opioids, close review of the formal product information is necessary, and whenever opioid switching is being undertaken, discussion with a palliative medicine physician is recommended.

When commencing or switching to hydromorphone, the most important issue is the increased potency of hydromorphone – 1 mg of hydromorphone equals 5 to 10 mg of morphine.[6] The need to acknowledge the potency of hydromorphone cannot be overemphasised.

Usually, morphine is the initial opioid used in palliative care and changing to an alternative opioid is considered when suboptimal analgesia or intolerable side effects occur. It is best to start using a conservative approach, always ensuring adequate breakthrough doses of hydromorphone are prescribed, closely monitoring the patient and ascertaining how much breakthrough analgesia is used.[18] The correct dose of rescue or breakthrough analgesia is not clearly defined, but the European Association for Palliative Care advocates the equivalent of the fourth hourly regular dose on an 'as needed' basis.[2] Always, individual titration is imperative.

Adverse effects

Hydromorphone and morphine have similar adverse effects, with the exceptions that hydromorphone is less likely to cause pruritus, nausea and vomiting, and sedation.[8,9]

Although hydromorphone causes less nausea and vomiting than morphine, it has the same effect of disordered gastrointestinal motility as morphine. Hence, some patients using hydromorphone will experience nausea, and all will become constipated if precautions are not taken. (The reason why this drug usually causes less nausea and vomiting is unclear. It is probably due to a combination of decreased accumulation of metabolites, incomplete cross-tolerance allowing a better mixture of analgesic and toxic effects, and increased potency of hydromorphone allowing decreased doses of opioid to be administered.)

Usually, neurotoxicity and sedation are less frequent in patients using hydromorphone than in those using morphine, but the sedative side effects are highly individually variable. In patients with renal or liver impairment, there is increased likelihood of morphine neurotoxicity, but the data to support the clinical safety of hydromorphone in these patients are limited and mixed. It is therefore necessary to exercise extreme caution in patients with renal or hepatic disease, including starting with reduced doses and keeping patients under close supervision.

Similar to morphine, high concentration hydromorphone subcutaneous infusions may cause erythema and swelling at the injection site. Hydromorphone may also cause orthostatic hypotension due to peripheral arteriolar and venous dilatation. This adverse effect reinforces the need for care when prescribing medications in the presence of extreme frailty and intercurrent illness, typical characteristics of palliative medicine patients.

Tolerance may occur with repeated use of opioids. However, it is very rare in palliative medicine that increasing doses of opioids are needed because of tolerance. It is more likely that increased requirement of analgesia represents progression of disease, and alterations to treatment must be made appropriately. Tolerance develops to most side effects of opioids, with the exception of constipation.[19,20]

As with morphine, hydromorphone can cause respiratory depression and extreme caution must be exercised when other centrally acting medications are prescribed in combination with hydromorphone.[21]

Summary

Hydromorphone is a relatively safe, effective and potent opioid that is a useful addition to the range of analgesics available, when used with knowledge and care. In some instances it may be preferable to morphine, with a decreased incidence of sedation, nausea and vomiting, and pruritus. However, hydromorphone has other opioid side effects, very similar to those of morphine, and it must be used with care in patients with renal or liver disease.

Hydromorphone is currently only available in immediate release oral and parenteral forms. Unfortunately, at times the supply of some of these preparations has been difficult. Before starting hydromorphone, availability should be checked with the dispensing pharmacist. MT

A list of references is available on request to the editorial office.

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