# Hydromorphone: A cost-effective alternative to the use of oxymorphone

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Hydromorphone (Dilaudid, Knoll Pharma, Markham, Ontario) is an opioid analgesic that has been in use in human anesthesia and pain management for some time. Its action is similar to that of morphine and oxymorphone, both in primary and side effects. We have recently instituted the use of this low-cost alternative to oxymorphone in our clinical practice at the Ontario Veterinary College (OVC). Hydromorphone can be used as a premedication, alone or in combination with tranquilizers or sedatives; as part of an induction regime for high-risk patients; and as an analgesic in the perianesthetic period.

## Pharmacology

Hydromorphone is a hydrogenated ketone derivative of morphine and is formulated as a hydrochloride without preservatives. It is an opioid analgesic and, as such, it demonstrates many of the effects characteristic of this class of drugs. Its action is most similar to that of morphine. It is roughly 5 times more potent than morphine and equal in potency to oxymorphone. As with other pure agonists, there is no ceiling to the analgesic effects of hydromorphone. Thus, animals demonstrating severe pain that is refractory to a single dose of hydromorphone may be more likely to experience relief from pain when the dose is increased.

The half-life of hydromorphone in humans is 2.65 ± 0.88 h. A large volume of distribution indicates extensive tissue distribution. While the onset of action of hydromorphone in humans may be slightly shorter than that of morphine, this does not appear to be the case in small animal patients. The elimination of hydromorphone is primarily by liver metabolism. As with morphine and its metabolites, excitatory responses following the administration of hydromorphone appear to be related to one of its metabolites, hydromorphone-3-glucuronide. This glucuronide metabolite is excreted along with minor quantities of the parent compound and other metabolites produced by reduction.

## Premedication

We commonly use a dose of 0.1 mg/kg body weight (BW) for premedication prior to moderately painful procedures. Hydromorphone (0.1 mg/kg BW) can be combined with acepromazine (0.02–0.05 mg/kg BW in dogs and 0.05–0.2 mg/kg BW in cats) for use in young, healthy patients. The use of acepromazine in combination with hydromorphone produces excellent sedation and chemical restraint. Normally, effective, at times profound, sedation is produced following the administration of hydromorphone alone (0.1 mg/kg BW), in cases where the use of acepromazine as part of the premedication regime is contraindicated.

## Chemical restraint

Our personal preference for aggressive or fractious dogs is a combination of acepromazine (0.05 mg/kg BW) + hydromorphone (0.1–0.2 mg/kg BW) given IM. In our experience, this combination produces sedation that is comparable with, if not better than, that achieved with either fentanyl citrate/droperidol or an acepromazine (0.05 mg/kg BW)/morphine (1.0 mg/kg BW) combination. An added advantage to the use of this combination is the small volume of the injectant required, which makes rapid injection possible.

The excellent chemical restraint and analgesia produced by this combination can be very useful for carrying out joint taps, hip radiographs, and other procedures that the practitioner may normally attempt to perform with only sedation or tranquilization. This combination may be administered IV; however, our experience has shown that a period of up to 15 min may still be required for the maximum effect to occur, even following IV administration. In very aggressive and excited dogs that demonstrate inadequate sedation following IM administration of this combination, an additional wait of 15 min may produce the required level of sedation and negate the need for the administration of a supplemental dose. Reversal of the sedation produced by this combination will be required more frequently than it is following the administration of acepromazine/butorphanol combinations.

Heavily sedated dogs may ventilate poorly (shallow rapid ventilation). The resultant carbon dioxide retention and its effect on the oxygenation of a dog breathing only room air can be countered by the administration of supplemental oxygen by facemask. The use of pulse oximetry is indicated in cases where poor oxygenation is of particular concern.

## Induction

In critical patients that may not tolerate the cardiovascular depression of commonly used injectable induction

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agents, general anesthesia can be induced by using a combination of hydromorphone (0.05–0.2 mg/kg BW given slowly, IV, to effect) followed by diazepam (0.02 mg/kg BW, IV). Precipitation will occur if these 2 drugs are mixed in the same syringe. Following the administration of this combination, endotracheal intubation may be possible. In the event that intubation is not possible, a greater depth of anesthesia can be obtained by delivery of an inhalant by facemask.

Animals induced with this combination will likely require positive pressure ventilation due to the depression produced by such a high dose of hydromorphone. Induction with this combination also produces a significant reduction in the concentration of inhalant required to maintain anesthesia. This reduction in inhalant concentration will provide some relief from the inhalant-induced cardiovascular depression. Bradycardia can occur following the administration of hydromorphone and should be treated with either glycopyrrolate (0.01–0.02 mg/kg BW, IV) or atropine (0.02–0.04 mg/kg BW, IV). The treatment of opioid-induced bradycardia with an anticholinergic has been shown to result in improved oxygen delivery and cardiac output (1,2).

The use of hydromorphone has not been evaluated in patients demonstrating hypovolemia or other critical states. In these cases, oxymorphone is the preferred opioid, since evidence confirming its safety in hypovolemic dogs has been presented (3). However, hydromorphone may still be used for intraoperative analgesia following induction with diazepam/ketamine or isoflurane (facemask).

## Analgesia

Hydromorphone provides effective intra- and postoperative analgesia. The dose range is between 0.05 mg/kg BW and 0.2 mg/kg BW. Animals demonstrating more severe pain will require the higher dose. In our practice, we most commonly use a dose of 0.1 mg/kg BW. The duration of effect is approximately 4–6 h. Caution should be exercised, though, in redosing animals at the end of long surgeries. Excitement due to excessive opioid administration or longer recoveries have been noted more frequently when the redosing interval during or immediately following surgery is based on a 4-hour duration of action for hydromorphone.

As is the practice with oxymorphone, hydromorphone can be given rapidly, IV, when either supplemental intra- or postoperative analgesia is required. Neither hydromorphone nor oxymorphone produces the histamine-mediated vasodilation and consequent hypotension that is seen following rapid IV administration of morphine. Although some investigations indicate that histamine release occurs following the IV administration of hydromorphone (4), this comparatively mild effect does not appear to make IV administration a contraindication.

## Other routes of administration

In our clinical practice, we have administered hydromorphone epidurally, alone and in combination with bupivicaine. Hydromorphone has been shown to be stable for 72 h when mixed with bupivicaine. The dose of hydromorphone that we use for epidural administration is 0.03–0.1 mg/kg BW. The effect obtained following epidural administration appears to be comparable to that seen with morphine. Blood levels of hydromorphone increase rapidly following epidural administration and can produce systemic effects within 5 to 15 min of administration (5). The lowest dose of hydromorphone that appears to be effective epidurally is lower than that used systemically for moderate to severely painful procedures and, thus, may not create significant side effects following systemic absorption.

## Side effects

Side effects from hydromorphone are almost identical to those observed following the administration of morphine. One should expect central nervous system depression. Central nervous system depression is often a desirable sedative side effect of opioid administration. Occasionally, however, the degree of sedation associated with pain relief may be greater than that desired. Excitement can result following the administration of hydromorphone when an imbalance exists between the analgesic requirements of the animal and the administered dose. Reversal of either opioid-induced excitement or excessive depression can be obtained by using butorphanol (0.1–0.2 mg/kg BW, IV) or naloxone (0.004 mg/kg BW, IV), slowly titrated to effect.

Respiratory depression (a depressed ventilatory response to carbon dioxide) can occur, particularly during general anesthesia. This depression is more profound when hydromorphone is administered in higher doses. The occurrence of mild to moderate respiratory depression following the administration of hydromorphone is not necessarily a contraindication to its use. As mentioned previously, the ability of hydromorphone to produce significant respiratory depression (as with most pure agonists) emphasizes the need for monitoring hemoglobin saturation with a pulse oximeter, particularly in the animal that is breathing room air. Other effects on the respiratory system include panting and cough suppression. Panting occurs as frequently as it does with oxymorphone and morphine. Hydromorphone is an effective cough suppressant and is suitable for use in brachycephalic breeds when longer periods of endotracheal intubation during the anesthetic recovery period are required.

Hydromorphone will produce bradycardia due to enhanced vagal tone. This bradycardia occurs as frequently as it does following the administration of either oxymorphone or morphine. Histamine release following hydromorphone administration does not appear to be significant; however, the critically ill patient may not tolerate even slight reductions in cardiovascular performance that may occur with this potential side effect. Hydromorphone will induce vomiting with the same frequency as occurs following a dose of 1.0 mg/kg BW of morphine. Because of this effect, the use of hydromorphone is contraindicated in the preanesthetic period or as part of an induction protocol in cases of suspect gastric dilation, volvulus, or other intestinal obstruction. Defecation may occur immediately following the administration of hydromorphone. Constipation will likely only be a concern with chronic use in small

animals. Urinary retention has been reported in humans following epidural administration of hydromorphone and would be a potential concern in dogs that received hydromorphone by this route. In patients in which this may be of concern, gentle bladder expression will normally reduce the discomfort associated with bladder distension.

## Licensing

Hydromorphone is not licensed for use in any nonhuman species. The basis for our clinical use of this drug comes largely from applying administration techniques and protocols used in humans to animals. Hydromorphone is very similar to both morphine and oxymorphone. This fact, combined with our observations of its use without any significant adverse effects in our clinical practice at the OVC, provides us with the confidence to recommend its use in primary care facilities as an economic alternative to oxymorphone.

## Acquisition

Hydromorphone is available in Canada as an analgesic for humans. It is not available through veterinary supply companies. Since veterinarians must purchase it through pharmaceutical suppliers, we recommend checking with your local pharmacy to explore the cost of obtaining hydromorphone. Hydromorphone is supplied in several concentrations: 2.0 mg/mL, 10 mg/mL, and 50 mg/mL. We use the 10 mg/mL formulation, as this allows us to administer a small volume while still maintaining accuracy in dispensing the required dose.

## Doing the math

At the time of writing, a 1.0 mL (10 mg/mL) vial of hydromorphone can be obtained for $3.52. A 10 mL (1.5 mg/mL) multidose vial of oxymorphone currently costs $40.21. At these prices, the cost for treating a 30 kg dog once at a 0.1 mg/kg BW dose rate, would be $8.04 with oxymorphone and $1.07 with hydromorphone.

## References


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