Prescribing Considerations Associated with HYDROmorphine Injection

(The following information has been excerpted directly from the package inserts for HYDROmorphine and is intended to provide information and guidance in the appropriate prescribing of HYDROmorphine.)

Dosage and Administration

Dilaudid® injection: The usual starting dose is 1 mg to 2 mg subcutaneously or intramuscularly every two to three hours as necessary. The dose should be adjusted according to the severity of pain, as well as the patient’s underlying disease state and age.

[New information] Should intravenous administration be necessary, the injection should be given slowly, over at least two to three minutes. The usual starting dose is 0.2 to 1 mg.

Risk of medication errors: Morphine does not convert to HYDROmorphine on a milligram per milligram basis.

Clinical Pharmacology

HYDROmorphine hydrochloride is a pure opioid agonist with the principal therapeutic activity of analgesia. Opioid analgesics also suppress the cough reflex and may cause respiratory depression, mood changes, mental clouding, euphoria, dysphoria, nausea, vomiting, constipation, and electroencephalographic changes.

Central Nervous System

Specific central nervous system (CNS) opiate receptors have been identified, and opioids are believed to express their pharmacological effects by combining with these receptors. HYDROmorphine depresses the cough reflex by direct effect on the cough center in the medulla. HYDROmorphine produces respiratory depression by direct effect on brain stem respiratory centers. The mechanism of respiratory depression also involves a reduction in the responsiveness of the brain stem respiratory centers to increases in carbon dioxide tension. HYDROmorphine causes miosis. Pinpoint pupils are a common sign of opioid overdose but are not pathognomonic.

Cardiovascular System

HYDROmorphine may produce hypotension as a result of either peripheral vasodilation, release of histamine, or both. Other manifestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, and red eyes.

Gastrointestinal Tract and Other Smooth Muscle

Gastric, biliary, and pancreatic secretions are decreased by opioids such as HYDROmorphine. HYDROmorphine causes a reduction in motility associated with an increase in tone in the gastric antrum and duodenum. Digestion of food in the small intestine is delayed, and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, and tone may be increased to the point of spasm. The end result is constipation.

Pharmacokinetics and Metabolism: Special Populations

Hepatic Impairment

After oral administration of HYDROmorphine at a single oral 4 mg dose (2 mg Dilaudid IR Tablets), mean exposure to HYDROmorphine (Cmax and AUC) is increased four-fold in patients with moderate (Child-Pugh Group B) hepatic impairment compared with subjects with normal hepatic function. Due to increased exposure of HYDROmorphine, patients with moderate hepatic impairment should be started at a lower dose and closely monitored during dose titration.

Renal Impairment

After oral administration of HYDROmorphine at a single oral 4 mg dose (2 mg Dilaudid IR Tablets), mean exposure to HYDROmorphine (Cmax and AUC) is increased in patients with impaired renal function by two-fold in moderate (CLcr = 40 mL/min to 60 mL/min) and three-fold in severe (CLcr < 30 mL/min) renal impairment compared with normal subjects (CLcr > 80 mL/min).

In addition, in patients with severe renal impairment, HYDROmorphine appeared to be more slowly eliminated with longer terminal elimination half-life (40 hours) compared to patients with normal renal function (15 hours). Patients with moderate renal impairment should be started on a lower dose. Starting doses for patients with severe renal impairment should be even lower. Patients with renal impairment should be closely monitored during dose titration.

Warnings

Respiratory Depression

Respiratory depression is the chief hazard of HYDROmorphine. Respiratory depression occurs most frequently in overdose situations, in the elderly, in the debilitated, and in those suffering from conditions accompanied by hypoxia or hypercapnia when even moderate therapeutic doses may dangerously decrease pulmonary ventilation.
HYDROMorphone should be used with extreme caution in patients with chronic obstructive pulmonary disease or cor pulmonale or patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression. In such patients, even usual therapeutic doses of opioid analgesics may decrease respiratory drive while simultaneously increasing airway resistance to the point of apnea.

**Hypotensive Effect**

Opioid analgesics, including HYDROMorphone, may cause severe hypotension in an individual whose ability to maintain his or her blood pressure has already been compromised by a depleted blood volume or a concurrent administration of drugs such as phenothiazines or general anesthetics. HYDROMorphone may produce orthostatic hypotension in ambulatory patients.

**Precautions**

**Special Risk Patients**

HYDROMorphone should be given with caution, and the initial dose should be reduced in the elderly or debilitated and those with severe impairment of hepatic, pulmonary or renal function; myxedema or hypothyroidism; adrenocortical insufficiency (e.g., Addison Disease); CNS depression or coma; toxic psychoses; prostatic hypertrophy or urethral stricture; gall bladder disease; acute alcoholism; delirium tremens; or kyphoscoliosis or following gastrointestinal surgery.

The administration of opioid analgesics, including HYDROMorphone, may obscure the diagnosis or clinical course in patients with acute abdominal conditions and may aggravate preexisting convulsions in patients with convulsive disorders.

Opioid administration at very high doses is associated with seizures and myoclonus in a variety of diseases where pain control is the primary focus.

**Drug Interactions with other CNS Depressants**

The concomitant use of other CNS depressants including sedatives or hypnotics, general anesthetics, phenothiazines, tranquilizers, and alcohol may produce additive depressant effects. Respiratory depression, hypotension, and profound sedation or coma may occur. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

**Adverse Reactions**

The major hazards of HYDROMorphone include respiratory depression and apnea. To a lesser degree, circulatory depression, respiratory arrest, shock, and cardiac arrest have occurred.

The most frequently observed adverse effects are lightheadedness, dizziness, sedation, nausea, vomiting, sweating, flushing, dysphoria, euphoria, dry mouth, and pruritus. These effects seem to be more prominent in ambulatory patients and in those not experiencing severe pain.

**Overdosage**

Serious overdosage with HYDROMorphone is characterized by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and sometimes bradycardia and hypotension. In serious overdosage, particularly following intravenous injection, apnea, circulatory collapse, cardiac arrest, and death may occur.

In the treatment of overdosage, primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. Supportive measures (e.g., oxygen, vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated.

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**Sources:**


More information is available online at http://www.patientsafetyauthority.org.

This handout accompanies

Adverse drug events with HYDROMorphone: how preventable are they?

Pa Patient Saf Advis [online] 2010 Sep [cited 2010 Sep 1].

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