

P & T News

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PRESCRIBING POST-OPERATIVE OPIOIDS

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As part of the ongoing evaluation of analgesic therapies, the safe and effective use of opioids in the post-operative patient has recently been reviewed by the UIHC Pain Management Service and the Pain Management Section of the Pharmacy and Therapeutics Subcommittee. For the majority of patients, severe pain following surgical procedures can effectively be treated with morphine; however, in certain situations, therapeutic alternatives may be warranted to provide adequate analgesia and/or avoid adverse drug reactions. Some analgesics, such as meperidine, should generally be avoided because of the high incidence of adverse effects. Prescribers should carefully evaluate patient needs and past medical history to select the most appropriate post-operative analgesic therapy.

Guidelines for Prescribing Acute/Post-operative Opioid Analgesics

The following stepped approach to prescribing parenteral opioid analgesics in a post-operative patient has been recommended by the Pain Management Service:

1. Use **morphine** first, as it is effective, familiar and relatively easy to use.
2. Use **hydromorphone** if morphine intolerance is present or pain relief is inadequate despite adjusting the morphine dose. Remember that hydromorphone is 5-6 times more potent than morphine.
3. Use **fentanyl** if:
 - A true morphine allergy is present, or
 - The patient has an intolerance to morphine and hydromorphone, and
 - The patient is in a monitored bed (such as in an ICU or the Burn Unit), or the therapy has been ordered by Palliative Care, Oncology or Pain Management Service prescribers.
4. Use **meperidine** only if:
 - ALL other opioids are ineffective, or
 - ALL other opioids are intolerable.

Trouble Shooting

The following scenarios help to illustrate situations in which the use of an opioid other than morphine might be appropriate.



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Scenario 1: Morphine “allergy.” Immune-mediated allergy to opioids is rare. What is stated as an allergy by the patient may be intolerance (nausea or vomiting) or a histamine-related side effect. All opioids cause histamine release that can lead to itching, flushing, urticaria, or asthma exacerbation. Therefore, careful history taking, documentation and communication of findings related to past adverse reactions are imperative.

First line opioid therapy for acute or post-operative pain should start with morphine. If morphine is not tolerated, hydromorphone, hydrocodone, or oxycodone may be tried, followed by fentanyl and, lastly, meperidine. Fentanyl can be considered in patients with a true allergy to phenanthrenes (like morphine, hydromorphone, or hydrocodone).³

Scenario 2: Morphine is not effective. If the patient is receiving morphine and pain is not controlled, make certain that an appropriate dose is being used. If the dose is too low, adjust the dose using the “Adult Opioid Reference Guide” which can be accessed via the UIHC *Formulary and Handbook* under “pocket cards”. If the higher dose is inadequate or ineffective, consider switching to another analgesic. Follow the guidelines suggested in Scenario 1 above and use the opioid reference guide for dosing conversion.

Scenario 3: Adverse effects are present (patient doesn’t tolerate morphine). If the patient is not tolerating morphine due to side effects, medication can be prescribed to reduce or eliminate the side effects. For example, if morphine is causing constipation, consider a stool softener and/or senna; for severe nausea and vomiting, give an anti-emetic. If the patient is experiencing itching, an antihistamine may be given (except for patients receiving an epidural opioid). If side effects are still intolerable, morphine can be switched to hydromorphone. If the patient cannot tolerate morphine due to a true allergy, switch to a different drug (see above).

Scenario 4: The patient requests or demands meperidine (Demerol®). Individualization of a pain management regimen begins with selection of an appropriate drug. Factors that guide this process include: characteristics of the pain (e.g., duration, intensity, quality), characteristics of the agent (e.g., analgesic ceiling, expected time of onset and duration of analgesia, available routes of administration, dosing interval, side effects, potential for accumulation of toxic metabolites, and potential for addiction), and patient factors (e.g., age, coexisting diseases, other medications, acute pain, response to previous treatments).² There are several reasons why meperidine is discouraged as a first-line agent for post-operative pain, and these are discussed below.

Meperidine

Oral meperidine is not available at the UIHC due to the drug’s poor absorption and safety concerns associated with long-term use. Parenteral use is discouraged due to safety concerns. Use of meperidine can lead to serious side effects including hypotension, syncope, respiratory depression, and seizures.^{1,4} Meperidine has a toxic metabolite, normeperidine, which is renally excreted. Normeperidine is half as potent as meperidine as an analgesic, but is two to three times as potent as a convulsant.^{5,6}

Meperidine use is discouraged in the following patients/situations:

- Patients with renal impairment (creatinine clearance <50 ml/min)
- Elderly patients (>65 years)
- Patients taking monoamine oxidase inhibitors (MAOI) or within 14 days of MAOI use
- Duration more than 48 hours
- Doses > 600mg /day
- Patients with seizure history, or at increased risk of seizures
- Chronic pain
- Patient-Controlled analgesia (PCA) use
- Continuous infusion

Questions about the appropriate use of opioids in the treatment of severe post-operative pain may be directed to the Pain Management Service
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PHARMACY AND THERAPEUTICS SUBCOMMITTEE ACTIONS

DRUGS ADDED TO STOCK

CEFOXITIN

Injection

Cefoxitin injection is a second generation cephalosporin that is frequently used for surgical prophylaxis for abdominal procedures.

PREGABALIN

Capsule: 75 mg, 100 mg, 150 mg, 200 mg, 300 mg

Pregabalin (Lyrica® - Pfizer) is indicated for the management of neuropathic pain, and as adjunctive therapy for adult patients with partial onset seizures.

Note: The prescribing of pregabalin is restricted to Neurology, Pain Medicine, and Endocrinology.

TIGECYCLINE

Injection

Tigecycline injection (Tygacil® - Wyeth) is a tetracycline derivative with bacterostatic activity. It has no activity against *Pseudomonas* or *Proteus*.

Note: The prescribing of tigecycline is restricted to Infectious Diseases approval.

DRUGS DELETED FROM STOCK

CLOTRIMAZOLE VAGINAL TABLETS

Discontinued by the manufacturer. Terconazole vaginal suppositories and cream are available.

DRUGS DELETED FROM STOCK (Cont'd)

GEFITINIB TABLETS (IRESSA®)

No longer commercially available; only available from the manufacturer through the Iressa® Access Program.

MINOCYCLINE INJECTION

Discontinued by the manufacturer.

STREPTOKINASE INJECTION

Discontinued by the manufacturer. Alteplase injection is available.

ADDITIONAL ACTIONS

DARBEPOETIN ALFA INJECTION (ARANESP®)

A 300 mcg per 0.6 ml syringe has been added to stock.

MESALAMINE 1 gm RECTAL SUPPOSITORIES

Replaces the 500 mg strength that was discontinued by the manufacturer.

SAQUINAVIR (INVIRASE®)

A 500 mg tablet was added to stock.

Note: The cost following each monograph is the inpatient acquisition cost.

For information regarding newly marketed drugs, drug-drug interactions, foreign drug identification, adverse drug reactions, alternative medications or other medication-related questions, contact the
DRUG INFORMATION CENTER.

The Center is open Monday through Friday from 8:00 a.m. - 12:30 p.m. and 1:00 p.m. - 4:30 p.m. (except holidays).

**ADVERSE DRUG
REACTION?**

**CALL THE DRUG
INFORMATION
CENTER**

THE APPROPRIATE USE OF INJECTABLE LEVOTHYROXINE

Elizabeth A. Beltz, PharmD

Oral levothyroxine is commonly used to treat hypothyroidism. Levothyroxine provides L-thyroxine (T_4) which is deiodinated to L-triiodothyronine (T_3). Levothyroxine sodium for injection is indicated for situations where a rapid onset of effect is desired (myxedema coma or crisis) or in patients in whom the oral route is precluded for long periods of time.¹ Levothyroxine should be given by the intravenous (IV) route for myxedema coma or crisis. It may be given either IV or intramuscularly in situations where a rapid onset of action is not critical.¹

Pharmacokinetic Properties

Frequently, orders are written to administer levothyroxine intravenously in patients who cannot ingest substances by the enteral route (or are NPO) for a short period of time. **Because levothyroxine has a half-life of approximately 7 days, it is usually unnecessary to change an oral dose to intravenous unless the patient has been NPO for more than one week.**¹⁻⁴ In fact, no adverse outcomes have been noted in hypothyroid patients undergoing surgery or cardiac catheterization without thyroid replacement.^{5,6} Because oral levothyroxine has a bioavailability of only 50-75%, **when it is necessary to switch the patient to parenteral levothyroxine, the dose should be approximately 50% of the patient's oral maintenance dose.**^{1,2}

Cardiovascular Risks

Judicious use of intravenous levothyroxine is indicated because of potential cardiovascular risks. Patients with cardiovascular diseases should be monitored closely. Generally, the effect of intravenous levothyroxine is not seen before six to eight hours after administration. This delay is related to the time required for T_4 to be converted to T_3 . However, one author has reported a case of cardiac arrest following an intravenous dose of 300 micrograms of levothyroxine sodium.⁶ This occurred approximately 15 minutes after the infusion. The authors felt that an immediate effect from levothyroxine was unlikely, but because of reports of large doses of levothyroxine augmenting the calorogenic effect of norepinephrine within minutes, they felt that a direct and rapid effect on the myocardium was possible. Therefore, even for the management of myxedema coma or crisis, initial intravenous doses should not exceed 0.2 mcg/Kg body weight.

Product Stability

Intravenous levothyroxine has very limited stability (i.e., short expiration dating) after it has been prepared for administration. Once reconstituted, the medication must be used immediately. Therefore, the nurse must notify the Pharmacy at the time the dose is to be given so that it can be prepared at that time.

Summary

In summary, intravenous levothyroxine should be reserved for use in myxedema coma or crisis where a rapid onset of effect is desired. It may also be used in patients unable to take the oral form (either by mouth or through a gastrointestinal tube) for more than 7 days. If the intravenous form is used, the dose should be 50% that of the patient's previous maintenance dose because of the decreased bioavailability of the oral formulation.

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