

OPIOID ADMINISTRATION GUIDELINES

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GENERAL GUIDELINES FOR INTRAVENOUS ADMINISTRATION OF OPIOIDS:

Delivery of an opioid by continuous IV infusion is the **parenteral** route of choice. Continuous infusions have several advantages:

- no waiting between intermittent "PRN" doses for pain relief
- a constant blood level is attained
- if necessary, the blood level can be rapidly increased by giving a bolus injection

In certain patients (e.g. no venous access), continuous SQ infusions via a "butterfly" needle may be useful. The dosages are the same as for continuous IV infusions, however, volume generally must be kept below 10 mL/hr (volume tolerated depends upon the size of the patient).

GENERAL GUIDELINES FOR CONTINUOUS INFUSIONS OF OPIOIDS:

1. Orders must include (use pre-printed order forms):
 - a. concentration of infusion; choose from available standard concentrations as written on pre-printed order forms
 - b. dosage in microgram/kg/hr
 - c. a dose for "breakthrough" pain (see below)
 - d. the patient's weight in kg
2. Opioid infusions must be administered by an accurate infusion pump.
3. All opioids are administered according to the C & W Child and Youth Health Policy NP 008.
4. The recommended dose ranges are appropriate for most patients. Some patients (e.g. intubated patients, those receiving palliative care) may require higher doses.
5. Doses should be lower for patients with hepatic or renal failure.
6. Concurrent administration of sedatives or hypnotics may result in excessive sedation and/or respiratory depression.
7. Oral opioids should not be administered until the opioid infusion is stopped (unless opioid infusion is being weaned).
8. The use of oximetry is highly recommended but should be individualized to each patient.
9. Use adjuvant medications whenever possible to minimize opioid doses and subsequent side effects (see list of adjuvant drugs on page 309).

Note: Acute Pain Service (APS) physicians or nurses are available for consultation if required.

BREAKTHROUGH PAIN:

1. Use the same opioid for breakthrough doses (i.e. PRN morphine boluses with a continuous morphine infusion).
2. With every infusion order, an order for a bolus dose should be written for breakthrough pain. There is a section for "intermittent (bolus) dose" on the pre-printed physician's orders for continuous opioid infusions.

TAPERING AND DISCONTINUING OPIOID INFUSIONS:

1. Patients with acute pain (e.g. post-op) can usually be changed from IV opioid infusions to PO opioid and non-opioid analgesics.
2. Transition to oral analgesics should be started as soon as patient can retain oral fluids and pain is well controlled.
3. Weaning (gradual decrease in infusion rate) is usually necessary only if the infusion has been running for > 5 days, but individual variation is high. For infusions that have been running for greater than 3 weeks wean at a rate of 10% per day.
4. Decreasing the infusion rate by 25% per day will reduce the incidence of withdrawal effects such as jitteriness, yawning, sneezing, decreased feeding, sweating, diarrhea or unusual movements. If withdrawal symptoms occur, the dose needs to be weaned more slowly or adjuvant agents used. Contact the APS for assistance with weaning difficulties.
5. Oral opioid should begin at the same time that weaning begins.
6. Patients should be observed carefully during the transition from IV to PO analgesia for signs of pain and the dosage should be adjusted accordingly.

CONVERSION TO ORAL OPIOIDS:

- If the pain is decreasing (e.g. post-op pain), the patient is comfortable and able to take medications by mouth, a conversion from IV to PO should be done. After doing the conversion from IV dose to PO dose, consider decreasing the PO dose by 20-30% as analgesia requirements decrease. This oral dose can be given PRN.
- If the pain source is constant or increasing consider adjuvant medications and consult the APS.
- The PO to IV conversion ratios are only estimates (see table below). Some patients may require higher or lower doses.

GENERAL PRINCIPLES OF OPIOID CONVERSION

- When switching from one opioid to another, conservative estimates must be used, especially in opioid-tolerant patients (those who have received opioids for approximately 7 days or more).
- The optimal dose of the new opioid should be determined by titration. Cross-tolerance equivalency may or may not occur.

OPIOID CONVERSION TABLE

	Parenteral (mg)	Oral (mg)
Morphine	1	3
Hydromorphone ¹	0.2	1
Fentanyl	0.01	N/A
Codeine ¹	N/A	20-30
Methadone	Consult APS	Consult APS

¹ Hydromorphone and codeine should not be used in patients with a true allergic reaction to morphine.

DOSING GUIDELINES FOR CHILDREN < 3 MONTHS:

Note: *The administration of morphine by continuous infusion in infants < 1 month and the ex-premature infant < 52 weeks PCA is restricted to Critical Care areas. Term post-surgical infants aged 1-3 months may be eligible for monitoring on 3R room 12. Consult Acute Pain Service (APS).*

DOSING GUIDELINES FOR CHILDREN > 3 MONTHS:

Note: *These guidelines do not apply to neonates, ex-premature infants and young infants (< 3 months) as they metabolize morphine (and other opioids) more slowly, they may require modification in dosage and may be at increased risk of apnea.*

A. MORPHINE ADMINISTRATION GUIDELINES:

1. Writing the orders (preprinted order sheets are available and required for all wards outside critical care areas):
 - a. The **initial infusion rate** is 5 - 40 microgram/kg/hr
 - b. Choose from the 3 standard concentrations available based on the patient's weight and fluid requirements.
 - c. **Titrate** infusion rate to control pain. A clinically important change in morphine levels will not occur until about one hour after the change in rate. If a more rapid increase in analgesia is required, give a bolus dose (10-20 microgram/kg/dose) at the same time that the infusion rate is increased.
 - d. If the infusion must be stopped (e.g. to administer an incompatible drug) a bolus dose should be administered to prevent pain from recurring. The size of the bolus dose should reflect the time that the infusion is stopped. For example, if it is stopped for 30 minutes, administer one-half of the hourly infusion rate as a bolus, to be given just after the infusion is stopped.
2. Converting IV morphine to PO (immediate-release morphine tablets or morphine oral liquid):

Morphine is subject to substantial first pass metabolism when given orally, which means that before morphine reaches the systemic circulation a substantial amount is metabolized to inactive or less active compounds. Therefore a higher dose **must** be given orally. For the majority of patients, the conversion ratio from IV to PO is 1:3.

 - a. determine the patient's total daily IV morphine requirements
 - b. multiply this amount by 3 to obtain the daily oral dosage
 - c. Choose the appropriate dosing interval and divide up the daily total:

Dosage Form	Interval	Availability
MOS® (morphine oral solution)	Q4H	1, 5, 10 mg/mL
Morphine immediate-release tablets	Q4H	5 mg
M-Eslon extended release capsules	Q8-12H	10, 15, 30, 100 mg

- d. For on-going pain morphine should be given around the clock rather than PRN.

Example: Converting IV morphine to PO

Manpreet is a 45 kg patient receiving continuous IV morphine at 20 microgram/kg/hr. She will be changed to oral morphine, using immediate release morphine tablets.

Calculate the total daily morphine requirement:

$45 \text{ kg} \times 20 \text{ microgram/kg/hr} \times 24 \text{ hrs} = 21,600 \text{ microgram/day} = 21.6 \text{ mg/day}$ of IV morphine

Convert to oral morphine:

$21.6 \times 3 = 64.8 \text{ mg}$ or oral morphine per day.

Round this down to 60 mg per day and divide by 6 to determine 4 hourly dose (10 mg PO Q4H). If the pain model is decreasing (ie post-surgical) the dose may be decreased by 30% (eg 6 mg PO Q4H)

Extended release morphine:

For ongoing pain, morphine PO may also be given as extended-release capsule (M-Eslon). Divide the total daily oral dose of 60 mg by 2 to determine the 12 hourly dose (30 mg PO Q12H)

- e. Breakthrough doses should be ordered, using immediate release dosage forms (oral solution or tablets). The usual dose is 1/24th of the daily morphine dose Q1H PRN or 1/12th of the daily dose Q2H PRN. Higher or lower breakthrough doses may be needed, depending on patient response.
- f. If two or more breakthrough doses are required per day, the total amount of morphine administered daily should be increased by this amount. (See section on breakthrough pain above).
- g. Do not adjust a long-acting morphine (e.g. M-Eslon®) dosage more frequently than every 24 hours. Use breakthrough doses of short-acting morphine to treat pain while the long acting form is being titrated.

B. HYDROMORPHONE INFUSION GUIDELINES

(Preprinted order sheets are available and required for all wards outside critical care areas)

- Hydromorphone infusions are managed by the APS only (except in critical care areas)
- Hydromorphone is more potent than morphine (5 times) but is not a better analgesic when equi-analgesic doses are given.
- The side effects of hydromorphone are similar to morphine, but may differ from patient to patient. For example, those patients who experience intolerable side effects with IV morphine (e.g. dysphoria, pruritis, vomiting) may tolerate hydromorphone. The reverse also applies (ie those intolerant of hydromorphone may tolerate morphine).
- Hydromorphone is NOT to be used if the patient has an anaphylactoid type of allergy to morphine.
- Hydromorphone is a more suitable agent for patients with renal impairment and there is no accumulation of metabolites.

1. Using the pre-printed orders:

- a. The initial IV infusion rate of hydromorphone is 1 – 8 microgram/kg/hr
- b. Choose from the 3 standard concentrations available based on patient's weight and fluid requirements.
- c. **Titrate** infusion rate to control pain. A clinically important change in hydromorphone levels will not occur until about 20 minutes after the change in rate.
- d. With every hydromorphone infusion and order should be written for **breakthrough** pain. This dose is 2-4 mcg/kg, to be given every 30 minutes PRN.
- e. If the infusion must be stopped (e.g. to administer an incompatible drug) a bolus dose should be given. The size of the bolus dose should reflect the time that the infusion is stopped. For example, if it is stopped for 30 minutes, administer one-half of the hourly infusion rate as a bolus, just after the infusion is stopped.

2. Converting IV hydromorphone to PO

The bioavailability of an oral dose of hydromorphone is about 20%, therefore a higher dose must be given orally. For the majority of patients, the conversion ratio from IV to PO is 1:5

- a. Determine the patient's total daily IV hydromorphone requirements.
- b. Multiply this amount by 5 to obtain the daily oral dosage.
- c. Choose the appropriate dosing interval and divide up the daily total.

Dosage form	Interval	Availability
Hydromorphone oral solution	Q4H	1 mg/mL
Hydromorphone tablets	Q4H	1, 2, 4, 8 mg
Hydromorphone sustained release capsules (Hydromorph Contin)	Q12H	3, 6, 12, 24, 30 mg

- d. To maintain pain relief, oral hydromorphone should be given around the clock, not PRN in cases of sustained or increasing pain
- d. Breakthrough doses should be ordered, using immediate release dosage forms (oral solution or tablets). The usual dose is 1/24th of the daily hydromorphone dose Q1H PRN or 1/12th of the daily dose Q2H PRN. Higher or lower breakthrough doses may be needed, depending on patient response.

Example: Converting IV hydromorphone to oral:

Sophie is a 20 kg patient receiving continuous infusion IV hydromorphone at 2 microgram/kg/hr. She will be changed to oral hydromorphone.

Calculate the total daily hydromorphone requirement:

$20 \text{ kg} \times 2 \text{ microgram/kg/hr} \times 24 \text{ hrs} = 960 \text{ microgram/day}$ of IV hydromorphone

Convert to oral hydromorphone:

$960 \times 5 = 4800$ microgram (4.8 milligrams) of PO hydromorphone per day. Divide this amount by 6 and prescribe hydromorphone 800 mcg PO Q4H. If the pain model is decreasing (eg post surgery) than the dose can be decreased by 30% (ie 560 mcg PO Q4H).

Convert to controlled release hydromorphone:

For ongoing pain, hydromorphone may also be given as controlled release capsule. Divide the total daily PO dose by 2 and prescribe hydromorphone controlled release 3 mg PO Q12H (dose rounded up—this may not always be appropriate)

3. Converting from continuous IV morphine to continuous IV hydromorphone.

As noted under “Opioid conversion table”, the ratio is as follows:

1 mg morphine = 0.2 mg hydromorphone.

Example: Changing from morphine to hydromorphone:

Oscar is a 30 kg patient receiving morphine by continuous infusion at 40 microgram/kg/hr. His pain management is good but pruritis is intolerable and unresponsive to current antipruritic therapy. It is not appropriate to decrease his opioid dose or to add non-opioid adjuvants. It is decided to change to hydromorphone. He has been on the morphine infusion at 40 microgram/kg/hr for 36 hours.

Converting morphine requirement to hydromorphone:

1 microgram of morphine = 0.2 micrograms hydromorphone, so 40 microgram/kg/hr of morphine = 8 microgram/kg/hr of hydromorphone (conversions are approximate).

Calculating the hydromorphone dose:

$30 \text{ kg} \times 0.2 = 6 \text{ mg}$ in 100 mL of normal saline. Each mL/hr delivers 2 micrograms/kg/hr

Start the hydromorphone infusion at 4 mL/hr (= 8 microgram/kg/hr), with a breakthrough dose and titrate to achieve OPTIMAL pain control with MINIMAL side effects.

C. FENTANYL ADMINISTRATION GUIDELINES

- Fentanyl may be used if a true allergic reaction to morphine has occurred. The routine use of fentanyl is not recommended due to the extremely rapid onset of action and narrow therapeutic index. Fentanyl infusions are managed by the APS only (except in critical care areas)

Using the pre-printed orders

(Preprinted order sheets are available and required for all wards outside critical care areas)

- a. Fentanyl infusions will be prepared in a standard concentration of 25 mcg/mL.
- b. The initial infusion rate should be 1 - 4 mcg/kg/hr
- c. Rescue intermittent (bolus) doses are not allowed with continuous fentanyl infusions. The risk of respiratory depression is high.

Converting from morphine IV to fentanyl

Conversion from IV morphine to fentanyl is not a simple conversion. Equi-analgesic doses are based on single doses and therefore do not apply to infusions. The Acute Pain Service should be consulted for assistance with this conversion.

MANAGING ADVERSE EFFECTS OF OPIOIDS:

- Frequent and significant adverse effects are common with opioid use.
- Adverse effects (except allergy) are dose-related and may be relieved by simply lowering the opioid dose. If appropriate, decrease the opioid dose by 10-25%, and observe the effect.
- Lowering the opioid dose may be achieved by using non-opioid adjuvants (see table at end of chapter).
- Tolerance to adverse effects (except constipation) will occur over days to weeks of ongoing opioid use.
- Anticipate side effects and provide PRN orders to manage these effects.
- If other measures fail, try an alternate opioid or use the oral route instead of the IV route.

A. Constipation

- Expected in most patients on opioids for more than 3 to 5 days.
- Not usually a problem in acute post-operative patients with short term use of opioids.
- If ongoing therapy is anticipated, pre-emptively prescribe stool softeners (eg docusate 5 mg/kg/24 hr given once daily or divided BID).
- If docusate is ineffective, senna glycosides or bisacodyl may be added

B. Nausea and vomiting

- Occurs in up to 50% of post-op patients and is multifactorial (anesthetic agent used, site of surgery, etc)
- Some patients may benefit from the prophylactic use of anti-emetics:
dimenhydrinate 0.5-1 mg/kg/dose IV/PO/PR Q6H
metoclopramide 0.1-0.2 mg/kg/dose IV/PO Q6H
ondansetron 0.1 mg/kg/dose IV/PO Q8H

C. Pruritis

- Is common and occurs in up to 30% of patients.
- The following drugs may be useful:
diphenhydramine 0.5 mg/kg/dose PO/IV Q6H
naloxone 0.5 – 1 microgram/kg/dose IV Q4-6H
naloxone 1 microgram/kg/hr by infusion only after previous steps have failed
- switching to a different opioid may be effective

D. Respiratory Depression

- Respiratory depression may be due to a single agent (opioid) or multifactorial (other sedatives such as benzodiazepines).
- Increasing sedation may also be due to co-morbidities such as increasing respiratory failure, sepsis, intracranial disorder.
- The cause of respiratory depression should be determined as it may not be medication related.
- The initial treatments of increasing sedation, decreased respiratory effort and rate, and hypoxemia are:
Stop opioid and other sedative medications.
High flow 100% oxygen, airway support and call Code if necessary
Naloxone 0.01 mg/kg/dose IV bolus Q 1 minute until respiratory effort is adequate. Double each subsequent dose until response. (Note that naloxone will reverse respiratory depression and analgesia).
- Naloxone has a short duration of action (about 60 minutes) so repeat doses may be required.
- Patient should receive additional monitoring for at least 4 hours after the event and during re-introduction of opioid analgesia. (see Nursing Policies and Procedures).
- All aspects of medication administration should be reviewed to assess the possibility of medication error. The original opioid infusion should be discarded and a new infusion prepared if the opioid is to be continued.

E. Altered mental status

- Described as mental confusion, clouded consciousness, delirium, hallucinations, paranoia, unusual dreams
- Evaluate underlying cause; rule out physiologic causes.
- Evaluate medications; eliminate CNS acting drugs (eg steroids) as symptoms allow.
- If analgesia is satisfactory, add adjuvants to enable a reduction in opioid dose by 25%
- Try another opioid.

F. Sedation

- Determine whether sedation is due to opioid, increase monitoring and rule out medication error.
- If analgesia is satisfactory, attempt to reduce opioid dose by 10-25%.
- Eliminate non-essential CNS depressant medications.
- Excessive sedation is a symptom of clinically significant opioid-induced respiratory depression.

G. Allergy

- True allergic or anaphylactic reactions are rare.
- Urticaria, wheal formation, pruritus and sneezing are common reactions usually secondary to opioid induced histamine release (pseudoallergic reactions).
- Opioids such as morphine and hydromorphone can cause histamine release in usual clinical doses.
- Antihistamines (eg diphenhydramine) can alleviate symptoms caused by histamine release.
- For true allergy an opioid from a synthetic source (fentanyl or analogs) should be substituted.

H. Urinary Retention

- common in pediatric patients
- can be problematic when urinary catheters are removed
- it is desirable to remove urinary catheters as soon as possible to reduce infection risk
- urinary retention is much worse with IV opioids than PO opioids so early conversion to PO analgesia is desirable

ADJUVANT DRUGS

Opioids are very effective analgesics, but some types of pain (e.g. bone, neuropathic) respond better to adjuvant drugs

These drugs are usually given IN ADDITION to opioids and may be effective in lowering opioid requirements. Reassess the opioid dose after the introduction of an adjuvant drug, as less opioid may be required.

Drug	Dosage	Comments
Acetaminophen	Up to 75 mg/kg/day PO div. Q4-6H. Up to 80 mg/kg/day rectally divided Q6H	May reduce opioid requirement by 20-30%. Use caution with long term use in malnourished, dehydrated patients or with hepatorenal disease.
NSAIDs (ketoralac, ibuprofen, naproxen)	Refer to monographs in yellow dosing section of this handbook	

Other adjuvant drugs that may be considered:

- amitriptyline
- carbamazepine
- clonidine
- dexamethasone
- dexmedetomidine
- gabapentin
- paroxetine
- pregabalin
- tramadol

Consult the APS for guidance.

