

PHARMACOLOGICAL APPROACH TO PAIN MANAGEMENT

Good Prescription Practices:

Effective analgesia (through standardised logical prescription):

- By the Ladder (WHO Analgesic Ladder - see below)
- By the Clock Strictly for baseline analgesia
 - Serve on time and regularly
 - Prescribe strictly if immediate post surgery or if there is a persistent pain stimulus
- By the Child: age-specific weight-based dosing
- By the Appropriate route
 - Prescribe IV pain reliever if patient is NBM (note that IV Ibuprofen is also available for children in KKH)
 - Prescribe IV for rapid onset if pain is severe and dynamic
- By Patient's Request (PRN rescue for unexpected pain)
- By Risk Status (constraints of age, disease, post-op status requiring dose reduction or route restrictions)
- Select a drug based on potency to match pain intensity. Include an opiate if moderate to severe pain exists (escalate as per the WHO Ladder, using Multi-modal Therapy & Analgesics round the clock (strictly served) to maintain within the "Analgesic Corridor")
- Appreciate that Pain is dynamic, not static. Proactive treatment dictates provision of PRN analgesics for breakthrough/incident pain. Appreciate that pain is strongly influenced by anxiety

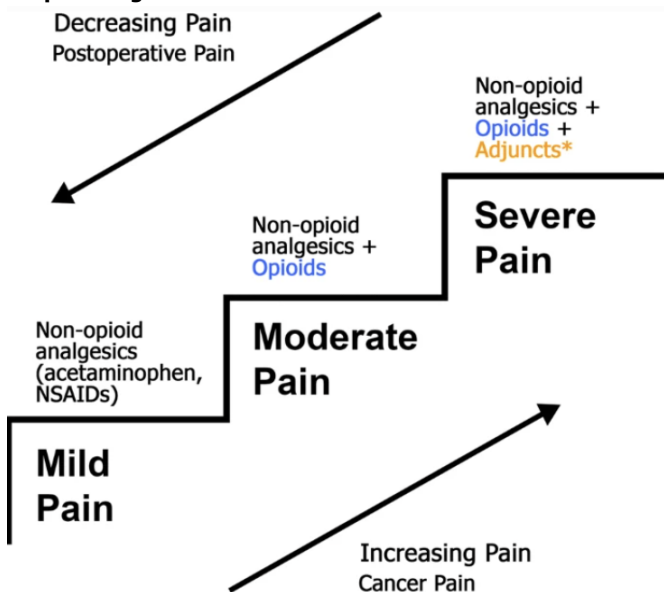
Safety

- Individualise doses on a per kg body weight basis
- Be aware of the maximum allowable single dose limit
- Stay within recommended 24h daily dose limit
- Limit duration of prescription to 3-7 days & reassess
- Daily CLMM review & with adjustments for age, disease, risk profile & response to therapy
- When pain is more than what is expected for the patient, think of alternative causes of pain e.g. compartment syndrome, pressure necrosis or surgical complications

Analgesic Modalities managed in the wards:

- Simple Analgesia : Paracetamol and NSAIDS (enteral or parenteral)
- Specialized Analgesia :
 - o Oral opioids
 - o IV Morphine infusions
 - o Patient Controlled Analgesia (PCA) / Nurse Controlled Analgesia (NCA)
 - o Continuous Epidural / Caudal Infusions or Regional /Plexus Blocks
 - o Continuous Wound Infusion

Simple Analgesia: Where to start



Modified WHO pain ladder figure ([Gai et al. 2020](#))

For patients more than 6 months	For patients 1 to 6 months	For patients less than 1 month
<ul style="list-style-type: none"> The first line: Paracetamol PO/IV 15 mg per kg Q6H maximum of 1 g Q6H <i>strictly given, reassess thereafter.</i> IV for patients who are NBM/ rectal route is not feasible Prescribe for 7 days, reassess thereafter. 	<ul style="list-style-type: none"> The first line: Paracetamol PO/IV 10 mg per kg Q6H <i>strictly given, reassess thereafter.</i> IV for patients who are NBM/ rectal route is not feasible Prescribe for 7 days, reassess thereafter. 	<ul style="list-style-type: none"> The first line: Paracetamol PO/IV 7.5 mg per kg Q6H <i>strictly given, reassess thereafter.</i> IV for patients who are NBM/ rectal route is not feasible Prescribe for 7 days, reassess thereafter.
<ul style="list-style-type: none"> If the patient is still in pain and/or pain is anticipated to require more than Paracetamol for intervention. No contraindication to NSAIDs (e.g. asthma): add Ibuprofen PO/IV 5-10 mg/kg Q8H maximum 40 	<ul style="list-style-type: none"> If the patient is still in pain and/or pain is anticipated to require more than Paracetamol for intervention. Add the following: For <i>patients on regular diet and no gastro-intestinal issues,</i> 	<ul style="list-style-type: none"> If the patient is still in pain and/or pain is anticipated to require more than Paracetamol for intervention. Add the following: For patients on regular diet and no gastro-intestinal issues, consider the

<p>mg/kg/day, 400mg/dose strictly or PRN, reassess thereafter</p> <ul style="list-style-type: none"> • IV for patients who are NBM/ rectal route is not feasible • Consider adding PPI/antacids as indicated. • Prescribe for 3 days, reassess thereafter. 	<p><i>consider the following after discussion with senior doctor:</i></p> <p>Morphine syrup 0.2-0.3 mg/kg/dose Q6H (strictly or PRN)</p> <p><u>or</u> (NO opioid duplication)</p>	<p><i>following after discussion with senior doctor:</i></p> <p>Morphine syrup 0.1-0.2 mg/kg/dose Q6H (strictly or PRN)</p> <p><u>or</u> (NO opioid duplication)</p>
<ul style="list-style-type: none"> • If the patient is still in pain and/or pain is anticipated to require more than Paracetamol and Ibuprofen for intervention. Add the following: • For patients on regular diet and no gastro-intestinal issues, start consider the following after discussion with senior doctor: <p>Morphine syrup 0.2-0.3 mg/kg/dose (Maximum 10 mg/dose) Q6H (strictly or PRN)</p>	<p>Oxycodone 0.1-0.2 mg/kg/dose Q6H (strictly or PRN)</p> <ul style="list-style-type: none"> • Prescribe for 3 days, reassess thereafter. 	<p>Oxycodone 0.05-0.1 mg/kg/dose Q6H (strictly or PRN)</p> <ul style="list-style-type: none"> • Prescribe for 3 days, reassess thereafter.

<p><u>or</u> (NO opioid duplication)</p> <p>Oxycodone 0.1-0.2 mg/kg/dose (Maximum 10 mg/dose) Q6H (strictly or PRN)</p> <ul style="list-style-type: none"> Prescribe for 3 days, reassess thereafter. 		
<p>If the patient is still in pain please refer to Children's Pain Service</p>		
<p>Always order anti emetics (PRN or strictly) whenever opioids are on board for high risks patients (e.g. Ondansetron 0.1 mg/kg maximum 8 mg Q8H.)</p> <p>Address other side effects, and provide adequate monitoring when deemed necessary (particularly when a patient is on opioids).</p>		

Paracetamol

Paracetamol is effective for moderately severe pain and decreases opioid requirements after minor and major surgery in children. Safe dosing of paracetamol requires consideration of the age and body weight of the child and the duration of therapy.

Age	Route	Dose
Below 1 month	IV/PO	7.5 mg/kg/dose Q6hrly (Max 40 mg/kg/day)
1 month to 6 months	IV/PO	10 mg/kg/dose Q6hrly (Max 40 mg/kg/day)
Above 6 months	IV/PO	15 mg/kg/dose Q6hrly (Max 1g/dose; 60 mg/kg/DAY; 4 g/DAY)
	PR	15 to 20 mg/kg/dose Q6hrly (Max 975 mg/dose; 75 mg/kg/DAY; 4g/DAY)

Caution in deranged liver function tests, particularly if prolonged use

Adverse effects: Paracetamol-related hepatotoxicity generally occurs in children who have received doses greater than 120 mg/kg as a single or repeated daily dosing, with contributions from rounding up or 10-fold dosing error and formulation substitution or confusion by prescribers and parents. Paracetamol has unclear vasoactive effects; in critically ill children, hypotension is reported with IV formulation.

NSAIDs

Nonselective NSAIDs (ibuprofen) are effective for moderately severe pain and decrease opioid requirements after major paediatric surgery and postoperative nausea and vomiting. Aspirin for acute pain indications, however, should be avoided in children. Parecoxib use in children reduces early postoperative pain scores, PONV (as compared to tramadol/fentanyl) and postoperative opioid consumption. Furthermore, Coxibs are a viable alternative in children with NSAID allergy to nonselective NSAIDs, this can be decided in consultation with an allergist.

Age	Drug	Dose
Above 6 months	Ibuprofen	PO 5 to 10 mg/kg/dose Q6 to 8hrly *(Max 400 mg/dose) IV 10 mg/kg/dose diluted in Normal Saline Q6 to 8hrly * minimum dilution concentration 3 mg/ml * (Max 400 mg/dose)
6 year old and above	Diclofenac	PR 0.5 to 1 mg/kg/dose Q8hrly *(Max 50 mg/dose)
2 years old and above	Celecoxib	PO 3 mg/kg/dose BD (Max 200mg/dose; 400mg/DAY)
16 years old and above, and 50 Kg and above	Etoricoxib	PO 60 to 90 mg OD limit prescription to less than 8 days.
	Parecoxib	IV 40 mg limit prescription to less than 8 days.

Cautions: May only be prescribed when ≥ 6 months

Asthmatic exacerbation in susceptible patients - Check for previous or recent use, as some patients with asthma are able to take NSAIDs safely. Potential for gastric irritation or ulcers - best taken with/after food. Beware: Platelet dysfunction/ active bleeding/ bleeding tendencies, renal impairment in dehydration, concomitant use of nephrotoxic drugs, and oncology patients.

Adverse effects: serious adverse effects after nonselective NSAIDs are rare in children over six months of age. NSAIDs do not increase the risk of either surgical or nonsurgical intervention for bleeding after paediatric tonsillectomy. However, there is some evidence that ibuprofen may increase the severity of haemorrhage post-tonsillectomy in patients returning to theatre and should be stopped in this context. On the other hand, Cox-2 inhibitors have a negligible effect on platelet function and less gastric effect than ketorolac or Ibuprofen.

Opioids

Initial doses of opioids should be based on the age, weight and clinical status of the child and then titrated against the individual's response. Postoperative intravenous opioid requirements vary with age in neonates, infants and children. Intermittent intramuscular injections are distressing for children and less effective for pain control than intravenous infusions. Patient controlled analgesia (PCA) can provide safe and effective analgesia for children as young as 5 years old. Intravenous opioids via continuous infusion, nurse-controlled analgesia and parental proxy use of caregiver-controlled analgesia devices can be used effectively and safely in children of all ages.

Age	Drug		Dose
Above 12 years	Tramadol		PO/IV 1 to 2 mg/kg/dose Q8hrly (Starting Max 50mg/dose; 400mg/DAY)
No age limit, however consider 50% dose reduction for below 6 months old.	Opioids	Morphine	PO 0.2 to 0.4mg/kg/dose Q6hrly (Starting Max 10mg/dose) IV morphine infusion 20 mCg/kg/hr
		Oxycodone	PO 0.1 to 0.2 mg/kg/dose Q8 to 6 hourly (Starting Max 10mg/dose)

IV Morphine infusion is commonly started for patients who have

- Constant severe pain; and
- Patients kept Nil-by-Mouth (NBM) due to primary pathology or surgery.
- It is not advisable in adults as the risk of respiratory dysfunction and sedation in this population outweigh the benefits. Listed below is the recommended IV Morphine infusion dilution and titration by weight.

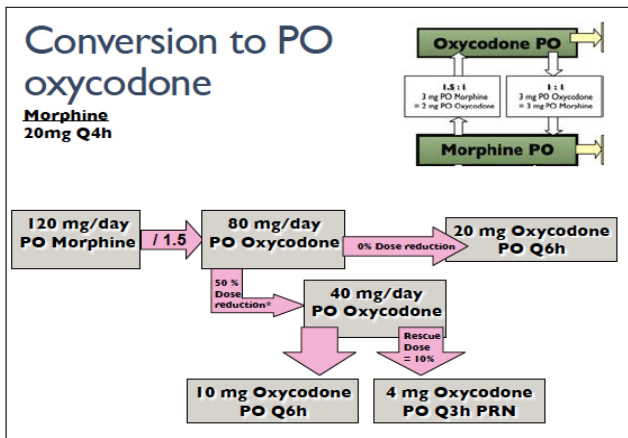
IV Morphine Infusion	< 50 Kg	>=50 Kg
Dilution	(BW)mg in 50 ml N/S 1ml/h=20 mcg/kg/h	50 mg in 50 ml N/S 1ml/h=1mg/h
Starting rate	Start at 1 ml/h (20 mcg/kg/h) UNLESS there are concerns regarding airway, over sedation or respiratory complications, decrease by 50%.	
Step-wise escalation	By 0.5ml/h Q4H; alert registrar if escalation is required	
Maximum dose	1.5ml/h = 30 mcg/kg/h	
Co-Analgesics	Ensure multimodal analgesics are ordered and served regularly	

High-risk patients are those with :

- altered mental status,
- respiratory compromise,
- risk factors for obstructive sleep apnoea,
- limited respiratory reserve,
- hemodynamically unstable

Pharmacologic treatment for opioid-induced side effects:

- For nausea or vomiting then, options for antiemetics are the following:
 - o Ondansetron 0.1-0.2 mg/kg/dose Q8H, maximum of 8 mg/dose
 - o Dexamethasone 0.1-0.2 mg/kg/dose, Q8H, maximum of 8 mg/dose (if no contraindication)
 - o Single or double antiemetics can be prescribed depending on the patient's requirement.
 - o If Ondansetron and Dexamethasone are not adequate, please refer to your consultant—possible options to add: scopolamine patch and antihistamines.
- For constipation / Ileus for more than 24 hours, add laxatives (e.g. lactulose, senna)
- Urinary retention - consider catheterisation
- Pruritus - add antihistamine / calamine/ Suubalm®
 - o PO options:
 - PO Cetirizine 5 mg/ml (less sedating)
 - 6 - <24 months: 2.5 ml ON
 - 2 - <6 years: 5ml ON
 - ≥ 6 years: 10 ml ON
 - PO Diphenhydramine 1 mg/kg/dose maximum of 50 mg Q8H to Q6H (more sedating)
 - o IV options:
 - IV Diphenhydramine 1 mg/kg/dose maximum of 50 mg Q8H to Q6H (more sedating)
 - If neither PO Cetirizine nor PO/IV Diphenhydramine relieves pruritic symptoms, please escalate to Naloxone (refer to the dosing below).
- Sedation - monitor sedation score
- Respiratory Depression - monitor SpO2 and respiratory rate
- Tolerance - consider opioid rotation (refer Children's Pain Service)



- Steps for Conversion of IV to Oral Opioid

STEP 1: Determine the total 24-hour dose of current IV opioid.

Example: Total 24 hr usage = 16 mg (IV Morphine)

STEP 2: Calculate the 24-hour OME (Oral Morphine Equivalents).

24-hour OME = 24-hour dose of current IV opioid x number of equianalgesic units in current opioid

Example: IV Morphine \rightarrow PO Morphine (24-hour OME) :
16x3 = 48mg

STEP 3: Convert to new opioid using the RATIO of the new opioid to PO Morphine.

Example: PO Morphine \rightarrow PO Oxycodone: 48/1.5 = 32mg

STEP 4: Adjust for incomplete cross-tolerance by decreasing the new drug dosage by 50% for opioid naïve acute pain patients, and 25% for chronic pain patients.

Example: 50% reduction in dose to account for incomplete cross-tolerance = $0.5 \times 32 = 16 \text{ mg}$ Oxycodone

- Note that generally **do not need** to adjust for incomplete cross-tolerance when **converting from different routes for the same drug**, such as from IV to PO morphine.

STEP 5: Divide the new 24-hour opioid dose by the number of times the drug is to be given per day. This is determined by the duration of action and formulation.

Example: Regular doses $16 \text{ mg}/4 = 4 \text{ mg Q6h}$

- Important Considerations:

- o If the calculated conversion dose is less than the recommended dose for the opioids, please prescribe according to the opioid recommended starting dose:
- o Oxycodone 0.1-0.2 mg/kg Q6H Maximum 10 mg **
- o Morphine 0.2-0.3 mg/kg Q4-6H Maximum 10 mg **
- o **Adjust for current level of pain:**
- o Moderate pain (4-6/ 10) increase the calculated dose by 25-50%
- o Severe/uncontrolled pain (7-10/ 10) increase calculated dose by 50-100%
- o Please do not exceed the maximum allowable dose**
- o Consider **breakthrough doses** for uncontrolled or episodic pain.
- o 10% of the 24H computed dose Q3H
- o Example: $10\% \text{ of } 16 \text{ mg} = 1.6 \text{ mg} \approx 1.5 \text{ mg q3H PRN}$
- o Account for renal and liver dysfunction and drug interactions.

Special Precautions:

Do NOT use codeine* due to inter-individual variation in metabolism to morphine. Risk of overdose.

* Codeine and Tramadol have FDA contraindication. The latter to be used with caution and only on advice of a pain physician.

Adverse effects:

Young and obese children with a history of obstructive sleep apnea are at higher risk of developing serious opioid-induced ventilatory impairment and death. Safety of oral codeine in children is unpredictable due to genetic differences in the metabolism and should not be used in children, particularly after tonsillectomy and adenoidectomy due to an increased risk of opioid-induced ventilatory impairment and death. Postoperative opioid therapy in children and adolescents may lead to long term opioid use and misuse in later life. Risk factors include type of surgery, psychological and social factors and other substance abuse. Adverse drug events in children and adolescents sent home with prescription opioids are common. A sensible approach should be used in prescribing discharge opioids, with consideration for child's anticipated opioid requirements. The tablet number/volume of opioid solution should be judicious and individualised. Carer/parental/patient education is necessary about risks of opioids and how to safely dispose of unused medications and should ideally be both verbal and written.

Opioid overdose

In Event of Opioid Overdose

Observe the following symptoms or signs:

- Oversedation
- Miosis
- Hypoventilation

DO NOT LEAVE THE PATIENT ALONE

- Conduct airway, breathing, and circulation check.
- Call for help as soon as possible.
- Administer NALOXONE in the following cases:

Respiratory Arrest

- the resuscitation guidelines are :
- **0.1mg/kg or 100 mcg/kg in neonates & those <5yrs or <20kg**, to be given over 2 minutes, maximum of 2 doses (2minutes interval).

Respiratory Depression

- in the presence of likely pain (post-op):
- **0.5-2 mcg/kg in titrated or repeated boluses**, to be given over 2 minutes, maximum of 2-3 doses (2 minutes interval).

Reversal of Side Effects Without Reversal of Analgesia

- **0.10 - 0.25 mcg/kg/h**
- Doses above 3 mcg/kg/h result in loss of analgesia.

Dilution of naloxone:

1. Comes in 0.4 mg/ml vial
2. Dilute into 10 ml with normal saline
3. Give 0.04 mg/ml aliquots or less, titrated to effect

*Caution : Boluses may result in pulmonary oedema (mostly in postop cases or in cases of pre-existing cardiorespiratory disease)

Reassessment will be required within 30-45 min after iv bolus to ascertain if a continuous infusion required to prevent re-narcotization