6.4 Pain management

Non-pharmacological pain management strategies should always be included in pain management. Preoperative anxiety, catastrophising, depression and other mental health as well as neurodevelopmental issues can amplify or confuse a patient's expression of discomfort/pain. Addressing these aspects are important in adequately managing acute pain.

6.4.1 Pharmacological strategies

Multimodal analgesia refers to the use of a variety of treatment strategies, including both pharmacological and non-pharmacological. By employing these strategies, the complex pathophysiology of pain is addressed as multiple receptors are targeted, resulting in improved analgesia. Additionally, this allows for reduced doses of agents with unfavourable side effect profiles (e.g. opioids). These adjuvant agents include simple analgesics, opioids, α_2-receptor agonists (clonidine and dexmedetomidine), NMDA receptor antagonists (ketamine, tramadol, magnesium sulphate), inhalational agents, anxiolytics (Table III) and LAs (Table IV). Neuropathic pain is an important component of postoperative pain. Certain surgeries (e.g. amputations, thoracotomy, scoliosis, neurosurgical) have a higher component of neuropathic pain. This type of pain typically does not respond to simple analgesia or opioid therapy.

Table III: Pharmacological management of pain

	Mild	Moderate	Severe	Comments
Non-pharmacological strategies are beneficial for pain of any severity				
Simple analgesics	Paracetamol with or without NSAIDs			
Opiate analgesics	Not usually required	Tilidine SL **or** Morphine p.o. **or** Tramadol IV/p.o.	Morphine IV **or** Fentanyl IN	Titrate IV morphine for safety Consider PCA for ongoing moderate to severe pain > 24 hrs
Adjuvant agents	Ketamine, clonidine, dexmedetomidine, gabapentin			Useful for neuropathic elements of pain
Interventional modalities	Regional anaesthesia			

6.4.2 Local anaesthetics

LAs are sodium channel blockers. They are used for wound infiltration, nerve blocks and neuraxial blockade; all with or without catheters. Some of these techniques require specialist expertise. Additives are used to prolong the duration of analgesia (Table V).

Table IV: Guidelines for local anaesthetic doses in children

Lignocaine	Topical	• Spray (Xylocaine® spray 10 mg per spray) 5 mg/kg/dose • Gels: 2% • *Eutectic mixture of local anaesthetic cream:* 2.5% lignocaine + 2.5% prilocaine 1.5 g/10 cm^2 under occlusive dressing for 1–3 hours, effective after 45 mins
	Infiltration or nerve block	*With adrenaline:* 7 mg/kg/dose *Without adrenaline:* 3–4 mg/kg/dose
Bupivacaine		*Maximum dose:* 2–3 mg/kg/dose (with and without vasoconstrictor)
Ropivacaine		*Maximum dose:* 2–3 mg/kg/dose

Table V: Adjuvants for neuraxial anaesthesia

Additive	Dose	Effect	Comments
Clonidine	1–2 mcg/kg	Improved quality and duration of analgesia with approximately 4 hours	Systemic absorption causes some sedation Can cause apnoea in neonates
Dexmedetomidine	1 mcg/kg	Improved quality and duration of analgesia with approximately 4 hours	Marked sedation can occur
Ketamine*	1 mcg/kg	Improved quality and duration of analgesia for single-dose caudal injections only	Not for use if child is under 1 year

Morphine*	3 mcg/kg Maximum 150 mcg	Improved quality of epidural and intrathecal analgesia	Side effects include nausea, urinary retention, respiratory depression (may be delayed), pruritis
Dexamethasone	0.5 mg/kg IV	Prolongs duration of analgesia with approximately 1 hour, less additional analgesia needed for up to 48 hours	Dexamethasone given **IV** not as part of bupivacaine mixture

* Preservative free formulations only – not yet available in SA

6.4.3 Simple analgesics

Simple analgesics include paracetamol, NSAIDs and local anaesthetic agents. They are generally safe provided dosing instructions and other cautions are adhered to, and have favourable side effect profiles. These agents should be considered as part of any analgesic strategy and can reduce the amount of opioids needed to achieve equivalent levels of analgesia.

Table VI: Guideline for paracetamol doses in children

Route	Loading dose	Maintenance dose	Maximum daily dose
PO	20 mg/kg	20 mg/kg 6-hourly	90 mg/kg/day *Neonates:* 60 mg/kg/day in divided doses
PR	40 mg/kg	30 mg/kg/dose 6-hourly	5 g/day *Neonates:* 60 mg/kg/day in divided doses *Other infants and children:* 90 mg/kg/day
IV	20 mg/kg	*Neonates:* PMC 28–31 weeks 10 mg/kg 12-hourly; PMA 32–44 weeks 10 mg/kg 6-hourly *Other infants and children*: 15 mg/kg 6-hourly	30 mg/kg/day 60 mg/kg/day

PMC – post conceptual age, PR – per rectal, PMA – post menstrual age

6.4.4 Nonsteroidal anti-inflammatory drugs

- Owing to the risk of Reye's syndrome, aspirin should be avoided in febrile children, particularly those with concurrent viral infections.
- NSAIDs may cause pulmonary hypertension and alterations in cerebral, gastrointestinal (GI) and renal blood flow in infants under 3 months of age.
- Serious adverse events after administering NSAIDs are rare in children above 6 months of age.
- Ensure adequate hydration, avoid concomitant nephrotoxic drugs and exercise caution in children who are not fed orally.
- While it is acknowledged that certain NSAIDs have the potential to increase surgical bleeding, this blood loss remains clinically insignificant (i.e. it does not lead to increased reoperation rates, haemodynamic compromise or blood transfusions).

- The concern that NSAIDs cause delayed bone healing remains unproven in children and the use of NSAIDs is recommended as part of a multimodal approach in otherwise healthy children. Where the risk of nonunion is high, a risk/benefit approach must be followed.
- Paediatric trial data regarding the use of selective COX-2 inhibitors is limited. The understanding of the degree of COX-2 selectivity, the pharmacokinetic-pharmacodynamic (PK-PD) relationship and adverse effects of these agents in children remains poor and paediatric use is off-label.

Table VII: Guideline for NSAID doses in children

Ibuprofen	Under 3 months of age	*Oral:* 5–10 mg/kg/dose, 8-hourly, maximum 400–800 mg
Diclofenac	1–12 years of age	*Oral:* 1–2 mg/kg/dose, 8-hourly, maximum 50 mg *Rectal:* 1–2 mg/kg/dose, 12-hourly, maximum 50 mg
Ketorolac		*Oral:* 0.2 mg/kg/dose, 4–6-hourly, maximum 10 mg or 0.8 mg/kg/day *IV:* 0.2–0.6 mg/kg/dose, 6-hourly, maximum 30 mg or 120 mg/day; use for 5 days only, then de-escalate
Mefenamic acid		*Oral/rectal:* 10 mg/kg/dose, 8-hourly
Parecoxib*	Above 2 years of age	*IV:* 1 mg/kg (maximum 40 mg), 6–12-hourly, maximum 80 mg/day

* Not licensed for use in children younger than 18 years; this dosing is derived from study data

6.4.5 Opioids

- IV opioids can be used safely and effectively in children of all ages.
- The initial dose of opioids should be based on the age and weight of the child, and then titrated against response. There is no maximum or ceiling dose.
- Unwanted side effects should be anticipated and treated (e.g. prescribe antiemetics as needed in children at risk for nausea/vomiting).
- There is no lower age limit for PCA use in children. Children need to possess the physical dexterity to use the PCA, display a reasonable understanding of how it works and how to use the device. Effective PCA prescription in children incorporates a bolus and ***may*** include a low-dose background infusion to improve efficacy and sleep. The child needs to be cared for in a monitored environment with continuous oxygen saturation monitoring and appropriately trained nursing staff.

Table VIII: Guideline for opioid doses in children

Opioid doses in children		**Additional comments**
Morphine (intermediate-acting)		
IV	0.1–0.2 mg/kg/dose 4–6-hourly	

Oral	Neonates: 0.05 mg/kg 1 month–1 year of age: 0.05–0.2 mg/kg Above 1 year of age: 0.1–0.4 mg/kg/dose, 4–6-hourly	Peak analgesic effect at 1.5 hours
Infusion	5–40 mcg/kg/hour	0.5 mg/kg of morphine sulphate in 50 ml normal saline Run at 5–40 mcg/kg/hour (0.5–4 ml/hr) (1 ml = 10 mcg/kg morphine)
PCA	20 mcg/kg bolus with 5–15 minute lockout time If a background infusion is used, dose at 4 mcg/kg/hour	Weight in kg = mg of morphine, dilute up to 50 ml volume This will give 20 mcg/kg/ml
Tilidine hydrochloride (Valoron®) (intermediate-acting)		
Sublingual	1 mg/kg/dose 6-hourly	1 drop = 2.5 mg Weight (kg) divided by 2.5 = number of drops
Pethidine (intermediate-acting)		
IV	0.5–1 mg/kg/dose stat	Avoid repeat dosing Metabolites can cause seizures
Tramadol (intermediate-acting)		
PO/IV	Above 1 year of age and less than 50 kg: 0.5–1 mg/kg/dose 4–6-hourly More than 50 kg: 50–100 mg	Max daily dose 6 mg/kg Lowers the seizure threshold; avoid repeat dosing in seizure prone patients
Fentanyl (short-acting)		
IV	0.5–3.0 mcg/kg/dose Titrate at 5–10 minute intervals to desired effect	Clearance in preterm neonates is slow Can cause prolonged respiratory depression
IV infusion	1.0–5.0 mcg/kg/hour	Only in theatre or ICU environment (careful, unfavourable context sensitive t1/2)
Intranasal	1.5–2.0 mcg/kg/dose stat	Use neat fentanyl with or without atomiser Peak analgesia within 5 minutes
PCA	0.3 mcg/kg bolus with lockout time If a background infusion is used, dose at 0.3 mcg/kg/hr	15 mcg/kg fentanyl diluted to 50 ml with 0.9% saline For children more than 50 kg: maximum 750 mcg fentanyl in 50 ml 0.9% saline bolus = 15 mcg Background 15mcg/hr Alternative to morphine in patients with renal or hepatic impairment Caution: unfavourable context sensitive t1/2
Alfentanil HCl (short-acting)		
IV	10 mcg/kg/dose titrate at 10–15 minute intervals	Shorter t1/2 in children
Sufentanil		
Remifentanil (ultra-short-acting)		
IV	*Infusion:* 0.05–1 mcg/kg/minute	Only in theatre or ICU

* The use of slow/modified/controlled-release opioids is not recommended in children with acute pain

Monitoring in patients receiving opioids

- All patients receiving opioids MUST have the following ***monitored*** and ***documented***:
  - Heart rate
  - Oxygen saturation via continuous saturation monitoring for the first 15 minutes
  - Respiratory rate
  - Level of consciousness
  - Pain score
- Frequency of monitoring
  - Observe closely for 15 minutes after administering opioid dose
  - Then do observations every 30 minutes for the first hour
  - Thereafter, observations must be documented 2-hourly
- A suitably trained nurse must be available to monitor, initiate management and escalate care, or call the doctor when necessary
- Resuscitation equipment must be readily available, checked and in working order
- Naloxone must be immediately available: the dose is 10 mcg/kg slowly IV or IM or subcutaneously; can also be given intranasally 1 mg; repeat if necessary

6.4.6 Alpha-2 agonists: clonidine and dexmedetomidine

Clonidine has excellent analgesia and opioid-sparing properties. In addition, it has anxiolytic effects, which are beneficial in the paediatric population. The associated bradycardia is usually not clinically significant, and rarely requires any intervention, unless when associated with hypovolaemia and bleeding. It is a cost-effective drug that is well tolerated and has been extensively studied for a wide variety of indications in paediatric practice. Clonidine is available as a 25 mcg tablet. In order to make administration easier, consider prescribing the following convenient doses: 25 mcg, 50 mcg, 75 mcg and 100 mcg.

If the patient has received clonidine for more than 7 days, it is necessary to wean to avoid withdrawal symptoms. Withdrawal is characterised by peripheral hyperactivity of the sympathetic nervous system, including anxiety, sweating, insomnia, nausea and vomiting, severe hypertension, and palpitations. If the dose was administered three times per day, reduce the dosage interval to twice daily (bd) for two days, followed by once daily for two days and then stop.

Dexmedetomidine is more α_2-selective with similar pharmacodynamics. It is available as an intravenous injection (IVI) only and administered as an infusion. It can also cause withdrawal syndrome when stopped abruptly.

Table IX: Guideline for the use of alpha-2 agonists

Clonidine		
PO	1–5 mcg/kg/dose 6–8-hourly	Start at 1–3 mcg/kg nocte, increase to 12-hourly, then 8-hourly over 3 days If pain is moderate to severe, initiate treatment with a full dose 6–8-hourly
IV	*Bolus*: 1–2 mcg/kg	Slow bolus
IV	*Infusion*: Loading dose 1–3 mcg/kg, followed by 0.7–1 mcg/kg/hr	Infusion Limited to theatre and ICU
IN	4 mcg/kg stat	
Dexmedetomidine		
IV	*Infusion*: Loading dose 0.5–1 mcg/kg over 10–20 minutes, followed by 0.5–1 mcg/kg/hr	Bolus can cause bradycardia and hypertension
IN	1–4 mcg/kg	Higher doses will cause sedation
Buccal	3–4 mcg/kg	

6.4.7 Gabapentin

Gabapentin has been shown to decrease the incidence of chronic pain after scoliosis surgery, reduce morphine consumption after multilevel scoliosis repair, and decrease phantom limb pain after amputation. Gabapentin has also been successfully used to treat visceral hyperalgesia and neuropathic pain in children with cerebral palsy. The dose range is 3–10 mg/kg/dose 8-hourly. The starting dose is 3–5 mg/kg and the maximum dose is 10 mg/kg.

- Gabapentin is available as a 100 mg capsule. When dissolved in 10 ml of water, it produces a solution of 10 mg/ml. To facilitate administration, consider prescribing the following convenient doses: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg and 200 mg.
- *Initiating* gabapentin
  - Day 1 – start with a dose at night
  - Day 2 – increase to a dose twice per day
  - Day 3 – increase to three times per day, then titrate upward as required
- *Stopping (weaning)* gabapentin
  - If gabapentin has been used for more than seven days, titrate the dose down to avoid withdrawal symptoms
  - If receiving a dose tree times per day, reduce the frequency to bd for two days, then once daily for two days and then stop administration
  - Alternatively, retain the frequency and halve the dose every two days

6.4.8 Ketamine

Ketamine is an NMDA receptor antagonist which is known for its haemodynamic and respiratory stability. It is effective in the management of acute, chronic and neuropathic pain, as well as allodynia and hyperalgesia. It displays synergism with opioids, resulting in reduced opioid requirements with a better side effect profile. This agent should be considered for patients with high opioid requirements or opioid tolerance, or where there is a significant component of neuropathic pain (e.g., scoliosis, amputation, neurosurgical procedures, burns, mucositis of chemotherapy) or severe surgical pain. When used with morphine in PCA, ketamine has been found to result in improved sleep and pain control with no increase in side effects (nausea, hallucinations). The IV infusion dose is 5 mg/kg diluted to 50 ml 0.9% saline (0.1 mg/kg/ml) and administered at 0.2–0.5 mg/kg/hr IV (2–5 ml/hr).