PAIN MANAGEMENT IN NEWBORN INFANTS IN THE GRACE CENTRE FOR NEWBORN INTENSIVE CARE - CHW

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Newborn infants routinely experience pain associated with procedures performed in intensive care.
- This document contains information on the assessment and management of newborn pain, including the use of the Modified Pain Assessment Tool (mPAT) and the Opioid Withdrawal Score (OWS).
- When pain medications are no longer deemed necessary, slow weaning of the infant from opioids over a prolonged period may be required. Planned and individualised management of an infant being weaned from a continuous infusion of opioid medication is desirable in order to prevent symptoms of neonatal withdrawal.
- A regular and consistent scoring method is required for making the diagnosis of opioid withdrawal.

CHANGE SUMMARY

New information:

- Removal of the PIPP-R pain assessment tool
- Addition of broader weaning guidelines and support

28/09/21: Minor review. Guidance for cessation of IV morphine infusion after first PO Morphine dose administration added.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st June 2021	**Review Period:** 3 years
Team Leader:	Nurse Practitioner	**Area/Dept:** GCNIC - CHW

READ ACKNOWLEDGEMENT

- To be read and acknowledged by all nursing and medical staff working in Grace Centre for Newborn Intensive Care (GCNIC).
- In-service sessions are held regularly.
- A hard copy available in the unit for all staff to sign to acknowledge they have read the changes.

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Pain

Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage"[1]. Neonates routinely experience pain associated with life sustaining and saving procedures performed in intensive care and have the right to receive effective and safe pain relief[2]. The sick or preterm infant may experience repetitive or prolonged pain resulting from many diagnostic, surgical or therapeutic procedures[3,4]. Neonates may suffer the consequences of pain both during the neonatal period and later in life[5,6]. Observation and measurement of the infant's response can guide the initiation of comfort measures or the administration of analgesia. However, this is impossible to report with the gold standard of self-reported pain assessment. Analgesics administered by infusions are preferred for infants recovering from surgery or requiring mechanical ventilation to avoid large variations in plasma concentration[4]. Opioids are used following careful consideration and the patient is assessed frequently for effectiveness and potential adverse effects on the respiratory and cardiovascular systems[4].

Consequences of Neonatal Pain

Neonatal pain has immediate, short and long term consequences, many of which remains widely unknown. Within the Neonatal Intensive Care Unit (NICU), pain is typically the result of life saving or sustaining interventions, yet it is not unknown to the extent that these consequences contribute to the neurodevelopmental outcomes of preterm and critically unwell neonates.

Short term consequences

*Table from Mathew and Mathew[7]

Physiological	Behavioural	Hormonal	Autonomic
Increased: -Heart rate -Blood pressure -Respiratory rate -Oxygen consumption -Mean airway pressure -Muscle tone -Intracranial pressure	-Grimacing -Screwing up eyes -Nasal flaring -Deep nasolabial groove -Curving of the tongue -Quivering of the chin	Increased release of: -Cortisol -Catecholamines -Glucagon -Growth hormone -Renin -Aldosterone Antidiuretic hormone Reduced secretion of: -Insulin	-Mydriasis -Sweating -Flushing -Pallor **Body Movements** -Finger clenching -Thrashing limbs -Writing -Back arching -Head hanging

Long Term Consequences

There are numerous long term consequences for neonates exposed to painful stimuli, particularly when repeated or poorly treated. These experiences can made life long modifications to the pain pathways of the body through the following mechanisms:

- Altered pain processing with increased pain sensitivity and hyperalgesia in term neonates[8]
- Developmental allodynia in preterm babies and reduced subsequent behavioural responses to pain[4,9]
- Reduced cognitive function[9]
- Motor development impairment[9]
- Reduced focused attention[9]
- Altered white matter microstructure[10], reduced cortical thickness[8]
- Reduced IQ[10]
- Altered temperament[8]
- Reduced early postnatal growth of body and head at 32 weeks in preterm babies[8]

Types of Pain

Procedural, physiological or transient pain (Nociception)

Acute or physiological pain is associated with tissue injury caused by diagnostic or therapeutic interventions that result in minimal or modest tissue injury[11,12] including; skin breaking procedures, catheter and cannula insertion and removal and physical examination.

Acute and inflammatory pain

Established pain is associated with surgery, birth trauma and localised inflammatory conditions where tissue injury and inflammation can be moderate or severe.

Chronic and complex pain

Prolonged or chronic pain associated with chronic inflammation, nerve damage or tumour.

Patient Safety Considerations

- Painful or stressful procedures should be minimised and when appropriate, co-ordinated with other aspects of the infant's care.
- Consideration of the least painful method of undertaking specific procedures is important. The placement of invasive lines and catheters should be attended or supervised by a skilled practitioner.
- Gestational age and diagnosis can alter a neonate's response to pain.
- A lack of behavioural responses (including crying and movement) does not necessarily indicate a lack of pain.

- Comfort measures such as swaddling, non-nutritive sucking and positioning should be used for all procedures prior to any increases in analgesia[4].
- Validated assessment tools are used consistently[13] and the assessment continued as long as the infant requires treatment for pain[14].
- Pain is managed most effectively by preventing, limiting or avoiding noxious stimuli (acoustic, visual, tactile) and providing analgesia.

Neonatal Pain Assessment

Neonates are unable to verbalise pain. Therefore the development of specific pain assessment tools sensitive to the needs of neonates have been developed. Despite there being over 40 neonatal pain assessment tools, this has not been translated to uniform pain assessment and effective pain relief[15].

The Modified Pain Assessment Tool

Instructions for use

The Modified Pain Assessment Tool (mPAT)[13,16,17] is used to assess neonatal pain within GCNIC and is validated for use in preterm and term infants and for procedure and surgical pain.

- Staff should stand where they can clearly see the baby's face and entire body.
- The observation is completed over a full two minute period without interruptions.
- At conclusion of the 2 minutes, gently touch infant's limb to determine muscle tone/tension.
- Complete the parameter – 'nurse's perception of infant's pain' on a yes – no.
- Document the physiological and behavioural parameters on the mPAT.
- All parameters must be completed to give an accurate pain score.
- During the score please consider:
    - Physiological conditions that may influence the score, for example infants with cyanotic heart disease can be scored "0" for colour unless there is a change in the intensity of the cyanosis or duskiness.
    - Medications the infant is receiving or has recently received that may affect behaviour or physiological responses.
    - Other environmental issues that may contribute to an elicited response; sudden bright lights, noise and activity around the bedspace.
    - Document these potential distracters on the chart or in the notes at the time of the score.

When to complete a pain assessment

- On each neonate's admission to the NICU for a baseline score.
- On handover from one shift to the next the observation and scores are attended by both nurses to ensure consistency in interpretation. The observation of the infant's behaviour and sleep-awake state are taken for a period of 2 minutes prior to the score being documented.
- Clinical suspicion of pain.
- During prolonged illness or mechanical ventilation; every 4 hours.
- Following a painful procedure.
- Postoperatively:
    - On return to the ward following a surgical procedure
    - Every two hours in the immediate post-operative period for the first 24 hours
    - Then every four hours for the next 48 hours and continue as long as analgesia is being used for pain relief
    - Four hourly pain scores should continue until analgesia has been discontinued for 24 hours
- Within two hours following a change in dose of analgesia.

Action to be taken on the results of the pain assessment and score

- Scores <5 show no evidence of pain. If scores are consistently <5 and analgesia is maintained, consider reducing analgesia.
- Scores >5 require institution of comfort measures, with reassessment within two hours.
- Scores >10 require consideration to administer or increase the dose of analgesia, with reassessment within two hours.

The mPAT

	0	1	2
Posture / Tone	Normal Some flexion	Digits widespread Trunk rigid Limbs drawn out Shoulders raised off bed	Fists clenched Trunk guarded Limbs drawn to midline Head and shoulders resist posturing
Cry	No	Consolable Can be settled	When disturbed Doesn't settle after handling Loud Whimpering Whining
Sleep pattern	Relaxed	Easily woken	Agitated or withdrawn Wakes with startle Restless Squirming No clear sleep/wake pattern Eye aversion 'shut out'
Expression	Relaxed Normal	Frown Shallow furrows Eyes lightly closed	Grimace Deep furrows Eyes tightly closed Pupils dilated
Colour	Pink well perfused	Occasionally mottled or pale	Pale / dusky / flushed Palmar sweating
Respirations	Normal baseline rate	Tachypnoea - at rest	Apnoea - at rest or with handling
Heart rate	Normal baseline rate	Tachycardia - at rest	Fluctuating - spontaneous or at rest
Oxygen saturation	Normal	Fleeting desaturation	Desaturation with or without handling
Blood pressure	Normal		Hypo/hypertension at rest
Nurse's perception	No pain perceived	I think the baby is in pain only with handling	I think the baby is in pain

Comfort Measures

- Gently repositioning the neonate to make him/her more comfortable.
- Wrapping / containment of the infant to provide support for limbs.
- Decreasing environmental stressors; reducing noise, shading baby from light, reducing the activity around the baby.
- Tactile soothing; stroking the baby gently, supporting the limbs, and gently placing your hand on the neonate's head.
- Talking softly to the baby.
- Changing the baby's nappy.
- Using a pacifier/dummy to provide non-nutritive sucking.

Pain Management

Prevention

The most effective way to manage pain, is to prevent it from first occurring. Consideration should be made to the necessity of the intervention or procedure and if so, if it can be performed non-invasively (for example end tidal carbon dioxide measurement versus blood collection for pC02[18]) or by the least painful method (for example a venepuncture versus a heel lance for blood collection[19]). A non-emergency intervention or procedure should be delayed if there are not adequate caregivers to provide support to the neonate.

Procedural Pain

Skin to Skin Contact

Neonate's wearing only a nappy, held directly against their mother's bare chest is called skin to skin contact, and appears to reduce the neonate's pain response when performed during painful procedures[20].

Sucrose and Expressed Breast Milk

Sucrose is used for procedural pain in neonates and infants. See *Sucrose for Short Duration Procedural Pain in Infants*.

Note: Expressed breast milk with non-nutritive sucking (or a breast feed) is recommended for supporting infants through procedural pain where available[21].

Lignocaine 1%

There is limited available evidence for the use of lignocaine as a local anaesthetic in the neonatal population. However, it has been recommended for use during the insertion of some skin breaking procedures including intercostal catheter insertion and lumbar puncture[4,22].

Topical Anaesthetic Agents

Secondary to a paucity of safety and efficacy data for use in neonates, topical anaesthetics agents are not recommended for use in the GCNIC.

Acute and Inflammatory Pain Management

Postoperative pain management

Pain management in neonates in guided by the neonatal pain assessment scores and the clinician's perception of pain. A range of analgesic interventions are available for the management of post-operative pain and can often be used in combination.

1.1.1 Paracetamol

Paracetamol is effective for mild to moderate postoperative pain in neonates. Paracetamol is ineffective for pain associated with painful procedures[23].

<table>
<tr><th></th><th>Paracetamol[24]</th></tr>
<tr><td>Indication</td><td>Paracetamol as a sole agent should be considered following:
Herniotomy
Laparoscopic surgery
Laser eye therapy for retinopathy of prematurity
Following major surgery, paracetamol should be used in conjunction with other analgesic agents to reduce the overall dose and duration of opioid therapy[23]. All eligible neonates should receive paracetamol in the immediate postoperative period in conjunction with opioid therapy.</td></tr>
<tr><td>Action</td><td>Analgesic agent that inhibits the synthesis of prostaglandins.</td></tr>
<tr><td>Dosage and Interval</td><td><u>Oral and intravenous administration:</u>
<table><tr><th>Weight*</th><th>Loading</th><th>Maintenance</th></tr><tr><td><2.0kg</td><td>15 mg/kg</td><td>7.5 mg/kg every 6 hours</td></tr><tr><td>2.0 -3.0kg</td><td>15 mg/kg</td><td>10 mg/kg every 6 hours</td></tr><tr><td>>3.0kg</td><td>20 mg/kg</td><td>10 mg/kg every 6 hours</td></tr></table>*Current/ best weight</td></tr>
<tr><td>Administration</td><td>Oral.
Intravenous infusion over 15 minutes.</td></tr>
<tr><td>Patient Safety</td><td>Monitor liver function. Liver toxicity has been suggested with the use of paracetamol in neonates[25]
Hepatotoxcity is unlikely, however paracetamol should be used with caution in neonates with hepatocellular disease[26,27]
Interdiciplinary review is required after 48 hours of regular administration.</td></tr>
</table>

1.1.2 Regional Anaesthesia

Regional anaesthesia is increasingly used in neonatal surgical patient and is supported by published literature[28,29]. Regional anaesthesia provides direct anaesthesia to the surgical wound. This reduces the need for systemic sedation and analgesia and may reduce intubation time[28,30], decrease length of stay and improve developmental outcomes[13].

	Bupivacaine & Ropivacaine regional infusions
Indication	Regional anaesthesia may be used following surgical procedures (at the discretion of the surgeon and anaesthetist) and may include the following: • Rectus sheath and TAP catheters for laparotomy: Intestinal atresia, duodenoduodenostomy, intestinal malrotation and diaphragmatic hernia repairs. • Intercostal and extrapleural catheters for thoracotomy: There is growing support for use following patent ductus arteriosus ligation. • Epidural
Caution	Continuous infusions of local anaesthetics have been associated with complications. Whilst these risks are uncommon careful nursing and medical assessment is required. The known complications include: • Toxicity for systemic drug absorption with or without drug accumulation. Both CNS and Cardiovascular toxicity can be severe • Bleeding • Infection • Dislodgement
Action	Bupivacaine and ropivacaine are amide type local anaesthetics providing a reversible block of nerve conduction. Both are long-acting drugs. Ropivacaine is slightly less potent and may be slightly less cardiotoxic.
Dosage	For specific dosing requirements please refer to the consulting Anaesthetist and Pain Team.
Administration	Local anaesthetic drugs (either bupivacaine or ropivacaine) are infused continuously via a multi-hole wound catheter. **Never** infuse local anaesthetic drugs intravenously.
Patient Safety	Ropivacaine half-life is approximately 5-6 hours in patients aged newborn to 1 month, compared to 3 hours in older children[21].
Note	*Pain Management Practice Guideline - CHW* *Please insert a link to the SCHN Epidural Infusion guideline*

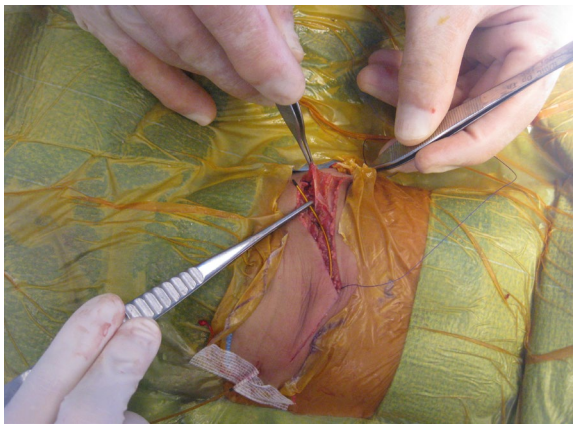


Figure 1- Regional catheter insertion

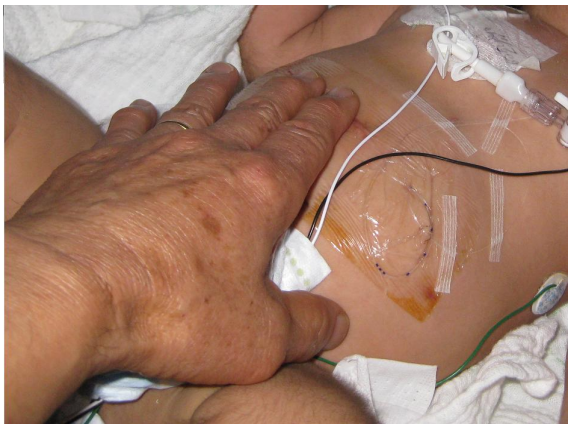


Figure 2- Regional catheter in use

Nursing Management of Regional Anaesthesia

Appropriate nursing management of regional anaesthesia can provide the patient with good pain management. The following details the basic nursing management required.

Syringe and label checks

During handover, the syringe and label should be checked by both the incoming and the outgoing nurses. The label should be checked against the order from the Pain Team. The syringe does not need to be changed unless the infusion syringe runs out. The reason for this is to decrease the risk of infection to the patient. Not changing the syringe does not increase the risk of infection to the patient as the infusion was inserted and commenced in a sterile field.

If the syringe runs out, a new syringe can be prepared within GCNC. Bupivacaine is kept in the medication room in a 100 mL bag and is already prepared so it can be drawn up directly from the bag.

SAFETY NOTE: Regional local anaesthetic infusions are NEVER connected to a venous cannula. Local anaesthetic lines should be placed separate to other venous infusions when in use. Extreme care must be taken to ensure correct labelling of pumps and infusion lines.

Dosing

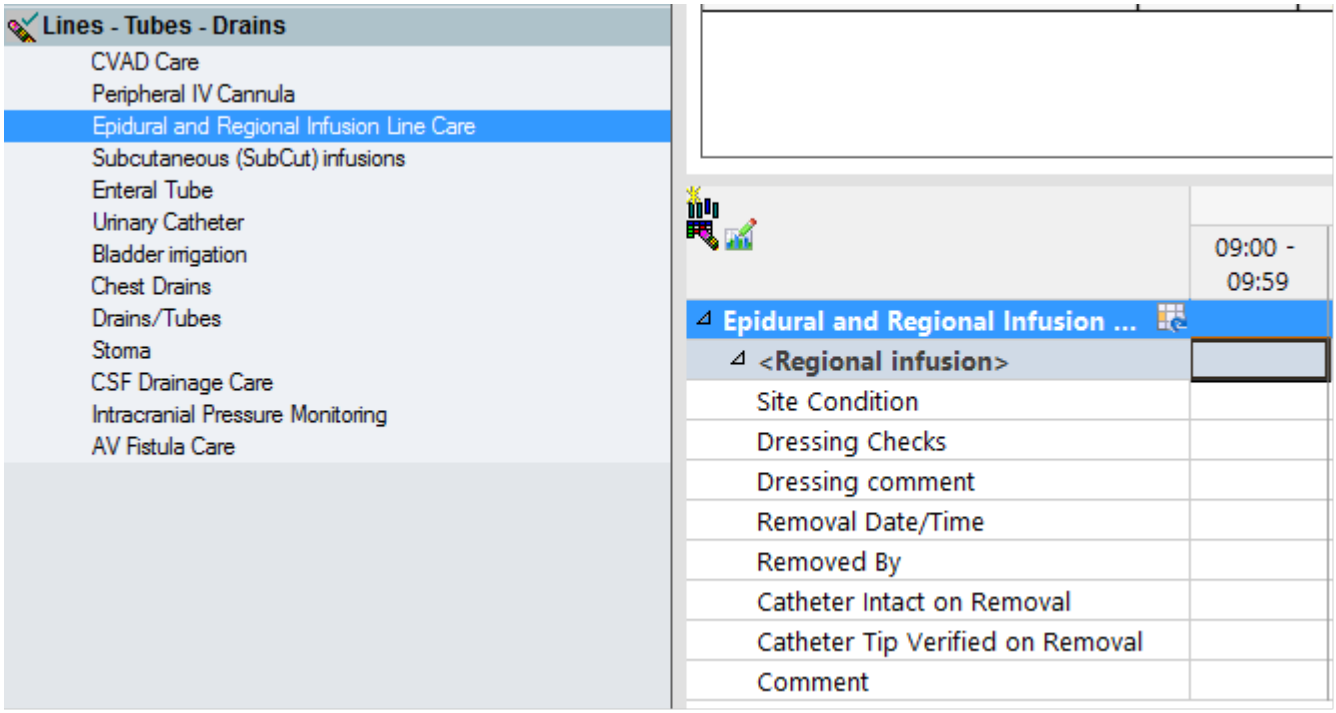
Refer to the Pain Management – CHW guideline for dosing ranges for patients <3 months. Typical dosing for bupivacaine is 0.25 mg/kg/hr, and ropivacaine is 0.375 mg/kg/hr however is subject to review by the Pain Team.

Pain scoring

Pain scoring using the modified Pain Assessment Tool (mPAT)[17] should be attended two hourly for the duration of the infusion – this is often up to 72 hours[17]. The infusion rate of the regional anaesthesia should only be altered by the Pain Team.

Hourly infusion documentation

The Pain Team provides a local anaesthetic regional anaesthesia chart which needs to be completed hourly by the bedside registered nurse (Chart number M34B). Every hour, the syringe volume and amount administered to the patient should be documented. There is additional documentation in the patient electronic medical record (eMR) which should be completed hourly for site and dressing assessments. See below:



Opioid infusions

It is appropriate for neonates with regional anaesthesia to also require an opioid infusion, such as morphine. Recent, best evidence suggests to commence a morphine infusion at 10 microgram/kg/hour and titrate according to pain scores[28,29,31]. Regular paracetamol should also be administered post-operatively to assist in minimising opioid dosage.

Site management

The fenestrated catheter has been inserted intra-operatively, therefore cannot be visualised, however the insertion site should be visible. The remaining length of the catheter is often coiled in a circle on the neonate's abdomen and secured with a clear waterproof dressing. It is common to have leaking from under the dressing[28,29,31-35], however this does not decrease the effectiveness of the infusion.

Troubleshooting can include cleansing the surrounding skin with saline and reinforcing with additional clear waterproof dressing. The original dressing should not be removed without prior discussion with the Pain Team as there is a risk of the catheter dislodgement.

Catheters for regional anaesthesia may be associated with complications including CNS and cardiac toxicity, bleeding, infection and dislodgement. Careful nursing assessment and medical/ surgical review where required is necessary to reduce and manage these risk factors.

Patient Positioning

To optimise the benefits of the infusion, repositioning the patient with cares every four to six hours can assist in providing the patient with the best pain relief [36, 37,38]).

Cuddles are important and should not be withheld despite the patient receiving regional anaesthesia. Parents should be educated in the importance of ensuring the infusion syringe does not become entangled and to note if there is any additional leaking.

1.1.3 Opioid infusions

Opioid infusions are the predominant analgesic used following neonatal surgery, with the two most commonly used medications being morphine and fentanyl. The trend of the pain scores and nurses' observation will guide the regulation of the opioid infusions[38]. Opioids are not effective in relieving procedural pain[39, 40].

	Morphine[35]	**Fentanyl[41]**
Action	Opioid analgesic drugs that stimulate and bind to specific G protein-coupled opioid receptors in the brain and spine.	
Dosage	Starting: 10 microgram/kg/hour Maintenance: Up to 40 microgram/kg/hour Bolus: 50-100 microgram/kg/dose	Starting: 0.5 -2 microgram/kg/hour Maintenance: Up to 5 microgram/kg/hour Bolus: 0.5- 4 microgram/kg/dose
Administration	Continuous intravenous infusion Intravenous bolus	Continuous intravenous infusion Intravenous bolus
Patient safety	May cause respiratory depression, hypotension, bradycardia and urinary retention. Fentanyl may cause glottic and chest wall rigidity, particularly when used as a bolus. The half-life of morphine is far greater in term and pre-term neonate	
Note	• Consider a bolus dose prior to increasing the continuous infusion rate when treating pain. • Infants requiring doses greater than 20 microgram/kg/hour may require alternative (fentanyl) and/or adjunct therapy (midazolam). • Infants older than seven days may require higher doses of morphine[38].	• Preferred opioid for neonates with pulmonary hypertension. • Potency (theoretical) up to 100 times that of morphine.

1.1.4 Sedative and Adjunct Therapy

To facilitate optimum comfort for neonates following major surgery, sedative adjunct therapy may be required.

Midazolam

	Midazolam[42]
Indication	Stand-alone sedative or adjunct therapy to reduce total opioid dose.
Action	Benzodiazepine sedative and anticonvulsant agent with a short half-life.
Dosage (for sedation only)	Starting: 0.2-1 microgram/kg/min Maintenance: Up to 5 microgram/kg/min (in term infants) Bolus: 50-150 microgram/kg/dose every 2 hours when required
Administration	Continuous infusion Intravenous bolus
Patient safety	• The half-life increases from term infants at 4-6 hours to up to 22 hours in preterm infants. • Liver dysfunction increases half-life. • May cause drowsiness, hypotension, reduced cardiac output and respiratory depression, particularly when used with opioids.
Note	• A continuous infusion for sedation is preferred. • Higher rates of poor neurodevelopmental outcome are noted with use at 28 days postnatal age[43].

Chloral Hydrate

	Chloral Hydrate[44]
Indication	Sedation for a diagnostic/non-painful procedure (neuroimaging) Sedative/ hypnotic for short term use not currently supported in the literature for ongoing sedation requirements. Consider other agent.
Action	Sedation-hypnotic agent. The exact mechanism is not known. The CNS depressant effects are due to its active metabolite trichloroethanol. Nil analgesic properties.

Dosage	• Sedation for painless procedures (hypnotic dose)
	  ○ Term infants: 50 mg/kg/dose
	  ○ Preterm infants: 25 mg/kg/dose
	• Short term sedation: 8 mg/kg/dose 6-8 hourly
	Maximum daily dose: 100mg/kg/day

Administration	Oral- should be diluted with sterile water 1:3 to reduce gastric irritation
Patient safety	• May cause respiratory depression, gastric irritation and bradycardia in former preterm infants. • Associated with neurologic injury. • Do not use in patients with renal and hepatic injury.
Note	• Chloral hydrate for sedation and sleeping support should only be considered when other comfort measures including swaddling, skin to skin care and non-nutritive sucking have been exhausted. • Rectal administration is not recommended due to erratic absorption. • Patients should receive cardiorespiratory monitoring during sedation. • Sedation should be short term only with a gradual reduction in dose.

Clonidine

	Clonidine[45]
Indication	Sedation Adjunct to managing iatrogenic opioid withdrawal Hypertension Neonatal abstinence syndrome
Action	Alpha-2 agonist used to produce reduction in blood pressure and sedation
Dosage	IV infusion: loading dose of 0.5 to 1 microgram/kg over 15 minutes followed by a continuous infusion of 0.2 microgram/kg/hour and titrate up to a maximum of 1 microgram/kg/hour pending haemodynamic stability Oral: 1 microgram/kg/dose 8 hourly and titrate up to a maximum 2 microgram/kg/dose 6 hourly Doses provided are for sedation purposes only. See ANMF for guidance regarding hypertension or neonatal abstinence syndrome.
Administration	• Continuous infusion • Oral
Patient safety	• Use a dedicated infusion line to avoid boluses • Hypotension • Consider dose reduction in renal impairment • Contraindicated in infants with heart block or severe ventricular dysfunction
Efficacy	Evidence is insufficient to show the efficacy and safety of clonidine for sedation and analgesia in term and preterm neonates receiving mechanical ventilation.

Chronic and Complex Pain

1.1.5 Mechanical Ventilation

Mechanical ventilation is recognised as a painful procedure for infants[46]. However, there is lacking evidence to support the use of routine administration of opioid therapy during this time. Opioid therapy, preferably morphine, should be administered based upon a clinical judgement and pain assessment using the aforementioned score.

1.1.6 Inflammatory pain

Medical conditions including necrotising enterocolitis and scalded skin syndrome are associated with neonatal pain. Infants with inflammatory or medical conditions should be assessed for pain using the aforementioned method and given appropriate analgesia as required. Due to its anti-inflammatory properties, paracetamol is the first line treatment options for infants with inflammatory pain[24].

1.1.7 Palliative Care

The adequate, proficient and timely management of discomfort during palliative care is of upmost importance. Pain assessment and pharmacological therapy should be considered and reviewed regularly to offer holistic care to newborns and their families.

Pain management in the GCNC during palliative care is ideally provided via the oral route following the de-intensification of medical support (removal of intravenous access). Alternatively, small subcutaneous catheters (Insuflon®) may be used to administer morphine

to facilitate the removal of venous access cannula. However, intravenous opioids may be continued for ongoing support if this is required.

Oral and subcutaneous morphine are the standard opioid for pain relief. However, more novel measures including intranasal fentanyl and buccal midazolam should be considered. If intravenous devices remain in situ, they should be used over the aforementioned methods.

Extended Management of Pain

When opioid or other sedating medications are administered for a prolonged period, physical dependence and tolerance may develop. Opioid or sedative requirements may increase. Opioids and sedatives should not be ceased abruptly.

Weaning

When pain medications are no longer deemed necessary, slow weaning of the infant from the therapy over a prolonged period may be required. Planned management of an infant being weaned from a continuous infusion of opioid or benzodiazepine therapy is desirable in order to prevent symptoms of neonatal withdrawal[47]. The Opioid Withdrawal Scoring tool (outlined below) should be used.

Tolerance and Withdrawal

Tolerance results in declining responsiveness to analgesia and/or an increased opioid requirement. This results from changes to the opioid receptor system within the central nervous system. Opioid tolerance can develop gradually over time or rapidly within only a few hours of use[47]. Opioid dependence refers to a physiological state in which abrupt opioid withdrawal results in adverse symptoms and signs[47,48]. A regular and consistent scoring method is required for making the diagnosis of opioid withdrawal[47-49].

Neonatal Opioid Withdrawal Syndrome

Neonatal opioid withdrawal syndrome can occur if opioid therapy is weaned or ceased abruptly[47-49]. Characteristics of neonatal opioid withdrawal can be clustered into three groups; neurological excitability, gastrointestinal dysfunction and autonomic dysfunction. The most commonly seen indicators of neonatal opioid withdrawal include central nervous system hyperirritability and autonomic nervous system dysregulation (sneezing, yawning, sweating, tachycardia, mydriasis), gastrointestinal dysfunction (diarrhoea, nausea, vomiting), respiratory distress (tachypnoea), and abnormal motor movements (tremors, hypertonia, hyper-reflexivity, repetitive movements)[48].

Neonates who receive opioid therapy for more than four days are at an increased risk of developing opioid withdrawal and tolerance[48-50]. Regular and thorough assessment of physiological and behavioural parameters during the weaning process is essential in the identification of neonatal opioid withdrawal syndrome[49].

Clinically diagnosed opioid withdrawal is managed through thorough and regular assessment using the Opioid Weaning Score (OWS) to guide planned and individualised weaning of opioid therapy.

Patient Safety Considerations:

- All infants who have received a continuous infusion of opioid for more than four days are to be commenced on a weaning program once their pain assessment scores indicate no or decreasing pain.
- Weaning is a gradual reduction in the daily drug dosage with frequent reassessment to ensure the infant is free of withdrawal symptoms.
- Opioid antagonists must be used with caution in neonates who have received opioid for greater than 4 days as the antagonist may precipitate acute opioid withdrawal[3].

The Opioid Weaning Score (OWS)

	1	2	3
Crying/ agitated		25-50%	>50% of interval
Sleeps	>75% of interval	26-75% of interval	<25% of interval
Moro		Hyperactive	Markedly hyperactive
When disturbed	Mild tremors	Moderate/ severe tremors	
Temperature	37.2-38.4°C	>38.4°C	
Extubated		RR>60	
Intubated		Suction twice per interval	
Behaviour	Sweating Frequent yawning Sneezing Nasal stuffiness		
Vomiting		Emesis	Projectile
Stool		Loose	Watery

Instructions for use:

- The assessment should be completed when the baby is at rest.
- The time period from the last assessment to the current assessment must be considered.
- Adjustments to narcotic dose based upon OWS score should be carefully considered and done so only after adequate clinical assessment.

When scoring please consider:

- Physiological conditions which may affect score, for example a baby with a gastrointestinal condition may have vomiting as a result of their physiological state rather than opioid withdrawal.
- Medications the baby is receiving that may affect their behaviour and physiological state.
- Environmental issues that may illicit a response, for example sudden bright lights and loud noises, and babies that are nil by mouth.

Weaning opioid infusions in use greater than 4 days:

- When to do the assessment and score:
  - Every 4 hours for all babies who have been receiving opioids for more than 4 days.
  - Every 4 hours when opioids are being weaned
  - Scoring should continue every 4 hours for 48 hours after cessation of opioid therapy
  - 2 hours after making an adjustment to the dose of narcotic
  - Dose reductions are rarely made more frequently than every 24 hours
- Actions to be taken on the results of the opioid assessment and scores:
  - If the OWS is greater than 8 for 3 consecutive scores, or greater than 12 for 2 consecutive scores consider increasing the opioid dose by 10% of the original dose.
  - If the OWS is less than 8 for 24 hours the opioid is weaned by 10-25% of the original dose.
  - The weaning of opioid therapy should be a planned and individualised process.
  - Doses or oral morphine need not to be weaned to 100 micrograms once or twice daily prior to cessation.

Weaning opioid infusions in use less than 4 days:

- The OWS is not required to assess neonates for opioid withdrawal if opioid therapy has been in use for less than four days.
- Weaning opioid therapy that has been in use for less than four days should be guided by the mPAT score. The recommended rate is 10% of the original dose every 4-6 hours. This may also be at the discretion of the Neonatologist. The planned reducing rate is documented in the patient's medical notes.

Opioid and Benzodiazepine Conversion and Weaning

As previously identified, prolonged administration of opioids greater than four days requires a slow tapered wean. This process is often supported by transition to an oral opioid preparation. Weaning treatments should always be guided by the OWS. IV opioid infusion should be ceased 1 hour after the first enteral dose of PO morphine is administered.

	Intravenous fentanyl to intravenous morphine	Intravenous morphine to oral morphine	Intravenous midazolam to oral diazepam	Intravenous clonidine to oral clonidine
Ratio	• 1:10 • 1 microgram of intravenous fentanyl is equivalent to 10 microgram of intravenous morphine.	• 1:2 • The estimated bioavailability of oral morphine in neonates is 48.5%[51].	Diazepam oral/ NG dose in mg three times daily = Midazolam infusion rate microg/kg/min x weight in Kg x 0.16	• 1:1
Weaning	• The dose should be weaned by 10% of the original dose per day. • Dose reduction should be no more than daily then therapy has been in used for > 4 days.	• The dose should be weaned by 10% of the original dose every 48 hours • The suggested weaning frequency is; 4 hourly, 6 hourly, 8 hourly and finally 12 hourly prior to cessation. • A total single dose of less than 100 micrograms should not be prescribed.	• The dose should note be weaned by more than 10% of the original dosing daily	• The dose can be weaned by up to 50% daily when therapy has been used for >4 days • Slower weaning in vulnerable and ill neonates may be required – 20% of the original dose alternate daily
Practice note	It is recommended that intravenous fentanyl infusions are converted to the equivalent daily dose of intravenous morphine (for calculation purpose) prior to any oral opioid administration.	During concurrent administration of opioid and benzodiazepine therapy it is suggested that: • When opioid is at 50% of original dose, begin weaning benzodiazepine. • Weaning should occur on alternate days – I.e. opioid and benzodiazepines should not be weaned on the same day. • Enteral formulation during weaning is preferred unless otherwise clinically contraindicated.		In concurrent administration of opioid or benzodiazepine therapy, the dose of clonidine should not be changed until other therapies have been completely discontinued. This is because clonidine will facilitate weaning of the other therapies.

Narcotic abstinence syndrome

Information pertaining to narcotic abstinence syndrome secondary to maternal opioid dependency can be found in the local guideline - Neonatal Abstinence Syndrome - Care & Management - GCNC - CHW

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