Pain medication in children: a practical approach

Wels D
Correspondence to: David Wels, e-mail: dpwels@gmail.com

Ⓟ **Peer reviewed © Medpharm** **S Afr Fam Pract 2013;55(3)(Suppl 1):S23-S27**

Introduction

It was previously thought that infants and young children did not possess the neurological wiring to experience pain. We are now certain that the nervous systems of even the unborn foetus, as well as children, have developed enough in order for them to experience pain.[1] In fact, they may perceive pain greater than adults can, because of increased inflammatory responses and lack of inhibitory responses to pain. It is crucial to treat pain appropriately to prevent long-term lower pain thresholds later in life.[2]

In many ways, paediatrics can be likened to veterinary medicine. The patients cannot communicate verbally what they are feeling or complain about symptoms. Instead, signs need to be identified and body language read in order to assess whether or not a child is in pain. Unfortunately, even when it is obvious that children are experiencing pain, it is often not treated because of certain factors. These include the belief that children experience pain to a lesser degree than adults, lack of pain evaluation in children, the absence of knowledge of paediatric pain modalities and regimens, and fear of respiratory depression.[1]

Pain management in newborn and critically ill children seems to be neglected the most for fear of the side-effects. Often, pain prescriptions are written as *pro re nata* (as the circumstance arises) on an as-necessary basis. Since the ability to identify pain in children is already absent, pain medication is often not given at all!

There are three ways in which to assess pain in children: through verbal expression (saying that they have pain if they are old enough to do so), through behavioural observations, or physiological measurements, such as heart rate and blood pressure.[3]

Self-report techniques are considered to be the gold standard, but are really only useful in children who are older than three years of age. Cartoons that depict faces with varying expressions of pain are useful in measuring the severity of pain in this age group.[3] From 18 months of age, children have acquired words for pain. However, they cannot indicate severity or location.

Behavioural assessment is needed to assess pain in younger children. The face, legs, activity, cry and consolability (FLACC) scale has been validated for children aged two months to seven years.[4]

Pain initiates a stress response which can be observed through physiological parameters, such as cardio-respiratory changes and an increased heart rate, respiratory rate and blood pressure. Plasma cortisol and noradrenaline levels are also increased.[5]

Forty per cent of paediatric surgical patients have moderate to severe pain postoperatively and 75% receive inadequate treatment.[6] A multimodal approach to analgesia is always recommended.

The drugs used are classified according to five groups:

- Opioids.

Table I: The face, legs, activity, cry and consolability (FLACC) scale

	0	1	2
Face	No particular expression	Grimace or frown	Quivering chin and clenched jaw
Legs	Normal position	Restless	Kicking or drawn up
Activity	Quiet, moves easily	Squirming and restless	Arched, rigid or jerking
Cry	No crying (awake or asleep)	Moans or whimpers	Crying or sobs, and verbal complaints
Consolability	Content	Reassured by occasional hugging, touching or distraction	Difficult to console

- Nonsteroidal anti-inflammatory drugs (NSAIDs).
- Paracetamol.
- Ketamine.
- Other analgesics.
- Regional techniques with local anaesthetics.

Opioids

Opioids still remain the treatment of choice for moderate to severe pain. Their sedating properties make them very useful as premedication, or for painful procedures like dressing changes or lumbar punctures, in children. Neonates and infants up to one month of age have a reduced capacity to metabolise morphine. The half-life is up to 1.7 times longer in this age group. Morphine clearance is as per that in older children for those who are older than one month of age.[5] Morphine infusions are recommended for children with severe pain as the child cannot ask for analgesia. A background infusion of 10 µg/kg/hour with boluses of 20 µg/kg is very effective. Obviously, the child needs appropriate monitoring. Patient-controlled analgesia (PCA) devices can be used in any child who can play a video game (ages five and up). Often, these PCA devices are used with background infusions as described above. Nurse and parent-controlled analgesia is effective, but both need to be educated on the device, and care should be taken not to overdose patients.[7]

Opioids should never be administered intramuscularly to children because of the unpredictable absorption thereof. Popular routes include intranasal and transmucosal administration. When 2 µg/kg fentanyl is given intranasaslly, it produces analgesia similar to that of an intravenous dose.[8] Fentanyl lollipops are also effective as fentanyl is rapidly absorbed transmucosally (the dose of transmucosal fentanyl is 10-15 µg/kg). Another popular opioid that is used transmucosally is tilidine. However, the drug is often under-dosed. The dose is 1 mg/kg and each drop contains 2.5 mg. Therefore, the number of drops should be weight divided by 2.5, and not one drop per year of age.

Codeine is an ingredient in many paediatric analgesic medications. However, neonates, like 10% of the population, do not have cytochrome (CYP)2D6 enzymes to convert it to morphine. It is also one of the most emetogenic of the opioids.

Pethidine and tramadol are useful in children with obstructive apnoea, owing to their large tonsils. They increase the pharyngeal tone because of their serotonergic mechanism and have weak opioid receptor affinity.[9]

Slow-release formulations of oxycodone and morphine can be used in children with chronic pain, but care must be taken to never crush or break the tablets.

The side-effects of opioids include pruritis, nausea and vomiting, sedation, urinary retention and respiratory depression. However, this should not prevent doctors from prescribing them. An effective way to limit side-effects is a concomitant infusion of an ultra-low dose of nalaxone (0.25 µg/kg/hour).[10]

Nonsteriodal anti-inflammatory drugs

NSAIDs produce their analgesic and antipyretic effects by decreasing prostaglandin synthesis via cyclo-oxygenase (COX) inhibition. They are most effective when tissue damage has occurred. Unfortunately, they have a ceiling effect and have significant side-effects which limit their use. Side-effects include bleeding and renal toxicity. Interestingly, these side-effects are encountered much less in children, than in adults. Asthma is not a contraindication to NSAIDs unless the child specifically has aspirin-induced asthma.[11] In fact, an improvement in lung function may occur after the administration of NSAIDs because of their anti-inflammatory effects. NSAIDs are not indicated for postoperative or routine analgesia in neonates and small infants, but are used to close the ductus arteriosus in preterm babies. They may also prevent intraventricular haemorrhages by an unknown mechanism.[12]

The most commonly used NSAIDs in children are ibuprofen and ketorolac. Parenteral ketorolac (0.8 mg/kg) decreases opioid consumption significantly for 12 hours after a single dose.[13]

Aspirin is not used for pain management in children because of the association with Reye's syndrome.

COX-2 inhibitors have less unwanted side-effects and do not prolong the bleeding time. The dose of celecoxib is 6 mg/kg twice daily, and it is particularly useful in conditions like juvenile arthritis.[14]

Paracetamol

Paracetamol is the most commonly used analgesic and antipyretic in children. It has virtually no side-effects, except for hepatotoxicity in doses exceeding 100 mg/kg/day. Young infants and children have higher levels of glutathione than adults. Glutathione binds to the toxic metabolite of paracetamol. This offers children protection from hepatotoxicity. The mechanism of action is at multiple sites and includes inhibition of central COX enzymes, augmentation of descending serotonergic pathways, activation of cannabinoid receptors and inhibition of nitric oxide pathways.[15] Interestingly, 5-hydroxytryptamine (5-HT3) antagonists, like granisetron, appear to abolish the analgesic effect of paracetamol.[16] Paracetamol can be given orally (10-15 mg/kg), rectally (a 30-40 mg/kg loading dose, followed by 20 mg/kg six-hourly), and intravenously (10-15 mg/kg).

Ketamine

Ketamine has long been a favourite drug in paediatric anaesthesia because of its efficacy, safety profile and various routes of administration. Ketamine is very useful in paediatric burn units. Burn patients are notorious for being opioid-resistant and ketamine infusions have been used to effectively treat these patients. Dressing changes can also be performed under ketamine cover.

In a meta-analysis of 35 randomised, blinded, control studies, ketamine was associated with a decreased recovery pain intensity and need for non-opioid analgesia. However, ketamine did not show an opioid-sparing effect postoperatively.[17]

When given together with local anaesthetics in caudal anaesthesia, ketamine prolonged the sensory block of the caudal block, but did not have any effect on pain intensity after the block had worn off.[17]

Other analgesics

A mixture of nitrous oxide and oxygen (Entonox®) is effective for procedural pain relief. It is easy to administer and is very safe. It is more suited to older children who are cooperative and it is necessary for the child to be starved. This technique is particularly useful for dressing changes and the administration of local anaesthesia and the removal of drains.[18] Clonidine, and the more selective, dexmedetomidine, have opioid-sparing, sedative and analgesic properties.

Unfortunately, the analgesic doses of these drugs cause significant side-effects in the form of sedation, hypotension and bradycardia. They are also very long acting and can cause delayed awakening after general anaesthesia.[19] Oral clonidine (1 µg/kg) and intramuscular dexmeditomidine (1-1.5 µg/kg) provide excellent premedication and cause minimal haemodynamic changes. Peak plasma levels are reached 1.5 hours after administration and analgesic effects persist beyond six hours.[20]

Regional techniques and local anaesthetics

Topical local anaesthetic mixtures [lignocaine and prilocaine (EMLA®)] are very effective during trans-cutaneous procedures, such as venous cannulation, lumbar puncture, immunisation and circumcision. The problem with these formulations is that they require at least 60 minutes contact time with the skin before they are fully effective. Newer formulations, such as liposomal lignocaine, have a faster onset of action (approximately 30 minutes).[1]

Regional techniques in children are very popular as they are very effective, provide excellent analgesia, can be used postoperatively if catheters are left in, and prevent the unwanted side-effects of parenteral analgesics. Epidural catheters can be placed at any age. Feeding the catheter through the sacral hiatus is safe and the tip of the catheter can be checked via fluoroscopy or ultrasound. Placement of epidural catheters needs to be performed under general anaesthesia in order to achieve optimal conditions.

Ultrasound-guided regional techniques are easier to perform in children as tissue depth is considerably less than that in adults. Clear visualisation of structures and fascial plains allows for accurate needle placement and local anaesthetic administration.

Adjuvants to local anaesthetics prolong the duration and increase the efficacy of regional procedures. The addition of clonidine or ketamine to caudal epidurals has been shown to significantly prolong the duration of action of the epidural.[21]

Nonpharmacological techniques

These techniques include counter-irritation (heat, cold and massage) or psychological means (distraction and relaxation). Distracting children with toys often provides an opportunity for quick unpleasant procedures to be carried out.

Oral dextrose or sucrose solutions are analgesic in infants up to the age of three months. The mechanism is probably via the release of central endorphins and also distracts the child from the procedure.[22]

Chronic pain in children

Chronic medical diseases, such as juvenile arthritis, cancer, cystic fibrosis and sickle cell anaemia, are associated with severe pain and the procedures involved to treat them are often very painful. Aggressive analgesia should be employed in these children. Memory of pain exacerbates both current and future experiences of pain.

Chronic pain conditions that occur in children include headaches, complex regional pain syndrome type 1, and abdominal, chest and pelvic pain, as well as cancer-related pain. These conditions require multidisciplinary treatment and will not be discussed in this article.

Conclusion

Paediatric pain control is poorly administered because of lack of knowledge of paediatric drug regimens and fear of side-effects. Pain control in children is not only an ethical obligation, but essential, as memory of pain exacerbates future pain experiences.

References

1. Russell. Pediatric pain management. American Medical Association. CME. 2013; Module 6.
2. Taddio A, Katz J, Ilersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine vaccination. Lancet. 1997;349(9052):599-603.
3. Reaney R. Assessing pain in children. Anaesth Intensive Care Med. 2007;8(5):180-183.
4. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. Pediatr Nurs. 1997;23(3):293-297.
5. Henneberg S. Acute paediatric pain. Curr Anaesth Crit Care. 2007(18):126-134.
6. Mather L, Mackie J. The incidence of postoperative pain in children. Pain. 1983;15(3):271-282.
7. Monitto CL, Greenberg RS, Kost-Byerly S, et al. The safety and efficacy of parent-/nurse-controlled analgesia in patients less than six years of age. Anesth Analg. 2000;91(3):573-579.
8. Galinkin JL, Fazi LM, Cuy RM, et al. Use of intranasal fentanyl in children undergoing myringotomy and tube placement during halothane and sevoflurane anesthesia. Anesthesiol. 2000;93(6):1378-1383.
9. Rosen GM, Muckle RP, Mahowald MW, et al. Postoperative respiratory compromise in children with obstructive sleep apnea syndrome: can it be anticipated? Pediatrics. 1994;93(5):784-788.
10. Maxwell LG, Kaufmann SC, Bitzer S, et al. The effects of a small-dose naloxone infusion on opioid-induced side effects and analgesia in children and adolescents treated with intravenous patient-controlled analgesia: a double-blind, prospective, randomized, controlled study. Anesth Analg. 2005;100(4):953-958.
11. Short JA, Barr CA, Palmer CD, et al. Use of diclofenac in children with asthma. Anaesthesia. 2000;55(4):334-337.
12. Gournay V, Roze JC, Kuster A, et al. Prophylactic ibuprofen versus placebo in very premature infants: a randomised, double-blind, placebo-controlled trial. Lancet. 2004;364(9449):1939-1944.
13. Vetter TR, Heiner EJ. Intravenous ketorolac as an adjuvant to pediatric patient-controlled analgesia with morphine. J Clin Anesth. 1994;6(2):110-113.
14. Foeldvari I, Szer IS, Zemel LS, et al. A prospective study comparing celecoxib with naproxen in children with juvenile rheumatoid arthritis. J Rheumatol. 2009;36(1):174-182.
15. Boutaud O, Aronoff DM, Richardson JH, et al. Determinants of the cellular specificity of acetaminophen as an inhibitor of prostaglandin H(2) synthases. Proc Natl Acad Sci USA. 2002;99(10):7130-7135.
16. Pickering G, Loriot MA, Libert F, et al. Analgesic effect of acetaminophen in humans: first evidence of a central serotonergic mechanism. Clin Pharmacol Ther. 2006;79(4):371-378.
17. Dahmani S, Michelet D, Abback PS, et al. Ketamine for perioperative pain management in children: a meta-analysis of published studies. Paediatr Anaesth. 2011;21(6):636-652.
18. Gall O, Annequin D, Benoit G, et al. Adverse events of premixed nitrous oxide and oxygen for procedural sedation in children. Lancet. 2001;358(9292):1514-1515.
19. Smith I. Alpha-2-agonists in day case anaesthesia. Curr Opin Anaesthesiol. 2011;24(6):644-648.
20. Scheinin H, Karhuvaara S, Olkkola KT, et al. Pharmacodynamics and pharmacokinetics of intramuscular dexmedetomidine. Clin Pharmacol Ther. 1992;52(5):537-546.
21. De Negri P, Ivani G, Visconti C, De Vivo P. How to prolong postoperative analgesia after caudal anaesthesia with ropivacaine in children: S-ketamine versus clonidine. Paediatr Anaesth. 2001;11(6):679-683.
22. Twycross A. The management of acute pain in children. Prof Nurse. 1998;14(2):95-98.