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SPECIAL ARTICLE

Management of acute postoperative pain in pediatric patients

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ABSTRACT

Pain is an unpleasant experience which can produce changes in all the systems of the body. Pain in children is not different from that in adults and can lead to similar detrimental effects on the body. The anticipation and effective treatment of pain in pediatric patients is thus, an essential component of care. A careful assessment of pediatric pain using age-specific pain scoring systems allows for exact quantification of pain. The use of various analgesics should be done early and in adequate doses for them to be effective. The use of multimodal approach with weaker analgesics along with regional blocks is an effective modality to control pain and prevent severe adverse effects associated with higher doses of potent analgesics. The advancement in the pharmacology of analgesics allows for their more widespread use with minimal side-effects. The use of patient or nurse controlled analgesia and continuous regional nerve blocks with the use of indwelling catheters can augment the pediatric pain management.

Keywords: Pediatrics; Postoperative pain management; Neuraxial

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INTRODUCTION

Pain, as defined by International Association for study of pain, is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. [1]The mechanism of pain perception in pediatric population is different and is complex and is often not adequately understood. Rather than emphasizing on clinical evaluation alone, biopsychosocial perspective needs to be looked deeply while managing pain in this special population. [2] The assessment of pain in small children is often difficult to interpret as the most common sign of pain is crying which is also seen in myriad of non-painful conditions. There have been recent developments in the pediatric postoperative pain management with emphasis on adequate treatment of pain early to prevent morbidity in this patient population. These developments are highly important for developing nations where progress of anaesthesia specialty has been non-uniform and at a varied pace. [3]

SEARCH STRATEGY

A systematic literature search was done using search engines like Pubmed and Google Scholar with the use of following single text words and combinations: pediatric pain management, neuraxial anaesthesia in children, pediatric pain score. The Pubmed search was made from the year 1990 till date. The references of the relevant articles were cross checked and the articles describing the pediatric postoperative pain management and pediatric neuraxial techniques of pain management were included

MYTHS ABOUT PAIN IN CHILDREN

Infants and Children do not feel pain:

It is now a well- established fact which is proved by various studies by neuroscientists and pain specialists that the components required for pain perception are fully developed at about 25 weeks of gestation while the endogenous descending inhibitory pathways remain underdeveloped till mid-infancy. [4, 5]All these can lead to a more enhanced inflammatory response to any noxious stimuli and can lead to perception of more pain as well as more pain-related physiological changes in children as compared to adults. The undertreatment of acute postoperative pain in children can lead to activation of physiological and biochemical stress response leading to impaired metabolic, endocrine, neurologic, pulmonary and immunologic functions. The end result can also be a significantly lowered pain threshold continuing for a long period after the painful stimulus.[6]

Lack of routine pain assessment in pediatrics:

It is always a challenging task to assess pain appropriately in pediatric population as they have limited experience and are unable to express their discomfort in words. The response to pain is different at different stages of development and depends upon cognitive, behavioural, emotional and psychosocial factors. The researchers have developed different pain assessment tools for different age groups for example for neonates and infants, an observational pain scale has been developed to assess pain as these are unable to vocalise and it is also incorporated with responses from distress other than pain like fear, hunger and anxiety. Simple self-assessment scales have been developed with different facial expressions to describe pain among pre-school and school age children.

Lack of knowledge of modalities and drugs for analgesia:

With the advancement in the regional anaesthesia and pharmacology, various newer drugs like levo-bupivacaine, articaine, ropivacaine [7, 8] and many other as well as newer modalities of pain management in children have emerged like spinal, epidural, caudal epidural and peripheral nerve blocks. [9-11] With continuing research in the field of regional anaesthesia in infants and children, the myth of danger of these techniques in this population has considerably decreased. The development of various newer drugs with shorter duration of action and more favourable safety profile in small children has increased their routine usage for pain alleviation.

Fear of respiratory depression and addiction of analgesic medications:

The use of strong opioid medications previously was associated with significant respiratory depression and potential for addiction in adult patients and was usually avoided in small children. But development of newer opioids like fentanyl, remifentanil with shorter duration of action and more favourable safety profile, has led to more common use of such drugs in pediatric patients. Moreover, use of multimodal analgesic technique with use of less potent analgesics in combination with more potent drugs can result in proper analgesia with reduced doses.

ASSESSMENT OF PAIN

The assessment is done by various pain screening tools depending on the age of child as children of different age groups perceive pain differently and thus react differently. The various pain assessment tools are:

Neonates and infants

These are mainly assessed by observational or behavioural pain scales. These combine physiological parameters with facial expressions to assess the degree of discomfort. The commonly used pain scales in neonates and infants are Premature Infant Pain Profile (PIPP), CRIES postoperative pain scale, FLACC scale etc. The CRIES pain scale is a good tool which involves behavioural and physiologic parameters and is depicted in Table 1:[12]

Table 1: The CRIES pain scale

Indicator	Score		
	0	1	2
Crying	No	High pitched but consolable	Inconsolable
Requires oxygen for Saturation > 95%	No	FiO2 < 30%	FiO2> 30%
Increased Vital Signs	No	HR or BP increased < 20%	HR or BP increased > 20%
Expression	No	Grimace	Grimace and Grunt
Sleepless	No	Wakes often	Constantly awake

Score < 4: Initiate non-pharmacological methods
Score > 4: Initiate pharmacological and non-pharmacological methods

Toddlers

One of the important pain scale used in this age group is FLACC scale which is a behavioural scale and is validated by studies to be effective among the age group of 2 months to 7 years. [13]It includes five behaviour descriptions with a score given to each such behaviour and is shown in Table 2:

Table 2: FLACC behavioural Pain Score

Categories	Score		
	0	1	2
Face	No particular expression Or smile	Occasional grimace or frown, Withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless or tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers: occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Total score between 0-10

Children between 3-8 years

This age group of children are able to self-report pain with its location and some may also describe its characteristics. Self-reporting of pain is the gold standard for pain assessment and the tools developed for this are Poker Chip scale, Wong- Baker faces scale, Faces Pain scale- Revised and Oucher scale. [14-17]The Poker Chip scale allows children to quantify pain by 'pieces of hurt' such that more poker chips indicate severe pain. The Oucher scale allows the children to match their pain intensity to the photographs of other children's faces thus depicting increasing levels of pain.

Children more than 8 years

This age group of children are able to understand the proportionality of numbers and colours so these children can easily describe their pain on a Visual Analogue Scale (VAS) or Numerical Rating Scale like that of adults. The older children may rate a pain less severe which has been rated as severe by a younger child due to exposure of older child to wide array of painful states. [18, 19]

MANAGEMENT OF POSTOPERATIVE PAIN

Acute pain is far more common than chronic pain in pediatric population and which is mainly postoperative. As such post-op anaesthetic rounds by the anaesthesiologists assume a significant role in relief of pediatric pain. [20] However, as pointed out earlier, this acute pain is associated with considerable distress leading to long term physiological and behavioural changes besides numerous clinical side effects during post-op period such as nausea and vomiting. However, nausea and vomiting can be managed with use of newer anti-emetic drugs. [21] It is essential to provide safe and effective analgesic modalities to prevent and treat pain in small children. The various modalities are:

Non-pharmacological pain management:

Assessment and relief of pain in pediatric patients require a huge amount of patience and motivation besides clinical knowledge and skills. [22] This includes psychological methods, parental support and education. It has been established that cognitive behavioural psychotherapy can relive the distress and anxiety associated with repeated painful procedures. [23]These therapies are aimed at preparing the child to cope up with a distressing situation. Some of the techniques which may be used preoperatively are distraction techniques to divert the child's attention away from the painful stimulus or may be positive incentive technique where a small reward is offered to cope up the painful stimulus. All these techniques are not effective on their own but have to be used along with the pharmacological methods to reduce the intensity of postoperative pain. These techniques and modalities have to be individualized based on the clinical evidence and experience of the pediatric anaesthesiologist. [24]

Pharmacological pain management:

The pharmacological therapy in small children is mainly based on difference in physiological systems when compared to adults. Most of the organs have delayed functional maturity in neonates till about three months of age after which they attain maturity rapidly. The various differences in organ systems in neonates with their implications on drug therapy are depicted in Table 3.

Table 3: Age-Related Physiological Changes As Relevant to the Drug Therapy

Physiological System	Age-Related Changes	Clinical Importance
Body Compartment	Higher percentage of body weight as water and less as fat, increased volume of distribution of water soluble drugs	Increased duration of action of water-soluble drugs so less frequent dosing
Plasma protein binding	Decreased levels of alpha1 acid glycoprotein and albumin	Increase in unbound fraction of protein bound drug with potential for toxicity
Hepatic enzyme systems	Immature microsomal enzymes and conjugation till 6 months of age	Decreased clearance of drugs so increased dosing intervals and decreased infusion rates
Renal filtration & excretion	Decreased glomerular filtration rates	Accumulation of renally excreted drugs so decreased infusion rates and increasing dosing intervals
Metabolic rate and oxygen consumption	Increased metabolic rate and oxygen consumption	Increased rate of onset and offset of inhalational anaesthetics, rapid desaturation with respiratory pauses or apnea
Respiratory system	Decreased airway calibre, increased resistive work of breathing, decreased pharyngeal muscle tone, decreased ventilator responses to oxygen and carbon dioxide, functional residual capacity near alveolar closing volume	Increased risk of atelectasis or respiratory failure, increased risk of hypoventilation in response to opioids or sedatives

The various classes of drugs used are:

Non-narcotic analgesics:

This class of drugs have become very popular in postoperative pain management in pediatric patients as these have fewer side-effects with good analgesic properties and when used in conjunction with opioids can result in effective analgesia with reduction in side-effects of opioids. These act peripherally by reducing the synthesis of prostaglandins at the site of tissue injury thus reducing the inflammatory mediators responsible for pain.

a) *Acetaminophen (Paracetamol):*

This is most common analgesic used among neonates and infants owing to its favourable safety profile and is used in mild to moderate postoperative pain. It is often combined with opioids for more severe postoperative pain. The usual dose is 15-20 mg/kg orally every 4 hourly. The daily maximum dose is 75 mg/kg in children, 60 mg/kg in term neonates and 45 mg/kg in premature infants. [25]The rectal route can be utilised in neonates not willing to take oral medication with a single dose of 30 to 45 mg/kg. The intravenous formulations are available and are very useful in postoperative period when the oral medications are not recommended. [26] The main toxicity is hepatic due to an oxidised metabolite of acetaminophen which is usually bound to glutathione but in excess can lead to hepatotoxicity. The term neonates and children produce large quantities of glutathione and thus are protected against its toxicity. [27, 28]

b) *Non-steroidal Anti-inflammatory Drugs (NSAID's):*

The pharmacokinetics of this class of drugs has been found to be similar to that in adults except in neonates where their safety has not been established. The usual toxicities of NSAID's seen in adults are less commonly seen in infants and children due absence of other comorbid conditions. [29]Ibuprofen is most commonly used drug by oral route as it is easily available in a syrup form for mild to moderate postoperative pain and is comparable to paracetamol in analgesic effect. [30] Ketorolac is another potent NSAID commonly used for postoperative pain and have been found to reduce the requirements of opioids. The recommended dose is 0.25-0.5 mg/kg intravenously every 6 hours. Diclofenac is more potent anti-inflammatory drug than ibuprofen or paracetamol but the incidence of nephrotoxicity and gastrointestinal side-effects are more. The usual dose is 1-1.5 mg/kg per oral 12 hourly. The common side-effects of NSAID's are nephrotoxicity, thrombocytopenia, precipitation of asthma, gastrointestinal ulceration and hepatotoxicity. The emergence of cyclooxygenase 2 inhibitor drugs has led to their more common use for postoperative pain as these have fewer incidences of serious gastrointestinal ulcerations or bleeding tendencies. [31]

Narcotic analgesics:

This group of drugs provide excellent analgesia for more severe form of postoperative pain. The various differences in the pharmacokinetics between neonates and adults should be kept in mind while dosing such drugs to avoid toxicity. Due to immature renal system, the elimination of active metabolites of morphine is slowed and results in accumulation. [32] There is high risk of development of apnea and periodic breathing among neonates and infants in the first 3 to 6 months of life after receiving even small doses of opioids. So the administration of opioids in infants of 2-3 months of age should be done with strict monitoring of cardiorespiratory functions. However, premature infants and former premature infants may exhibit respiratory depression upto 5-6 months of age after opioid administration. Newer opioids like fentanyl and sufentanyl also show reduced hepatic metabolism in premature and term neonates. The opioid administration is deemed to be safe in children over 1 year of age and is suitable for severe postoperative pain. The intravenous route is usually preferred as it provides immediate and reliable pain relief. The various routes of opioid administration are:

- *Oral Route:*

Codeine is the most commonly used drug by this route for moderate pain relief as it is considered to be a weak analgesic and it is considered to be safe among children above 3 years of age. It is usually combined with acetaminophen in a ratio of 20:1 i.e. acetaminophen in a dose of 10-15 mg/kg with codeine 0.5 mg/kg. It is metabolised to morphine which causes analgesia.

- *Intravenous Route:*

It is preferred route of analgesia in postoperative period as it provides immediate pain relief and since oral route is not available in immediate postoperative period. Many opioids can be given through this route like morphine, fentanyl, sufentanyl etc. The intermittent bolus route is usually used, however, the continuous infusions and patient or nurse controlled analgesia regimen is better for attaining a sustained analgesic effect and to avoid fluctuations in the plasma concentrations of the analgesic. This patient controlled analgesia (PCA) technique is very effective and can be utilised in children of 6-7 years after proper teaching. For younger children, nurse controlled analgesia technique has gained popularity in which the nurse caring for the child ascertain the need for analgesia and gives the bolus accordingly. [33]Typical parameters to be used for PCA using most commonly used drugs are shown in Table 4:

Table 4: Typical parameters for Patient Controlled Analgesia (PCA) Regimen

Drug	Bolus Dose (μg/kg)	Continuous Rate (μg/kg/hr)	Lock out Interval (min)	4 hour limit (μg/kg)
Morphine	20	4-15	5	300
Fentanyl	0.25	0.15	5	4

The basal/continuous infusions are thought to improve the sleep quality but have been shown to result in episodes of hypoventilation and hypoxia and can be replaced by a combination of PCA bolus only with regular administration of NSAID's or paracetamol.

- *Adverse effects of PCA in pediatric patients:*

The incidence of adverse effects of PCA in children is high and may be due to the need to calculate the exact individual doses based on weight or body surface area and changing pharmacokinetics of drugs at various ages. The most common complication is respiratory depression with an incidence of 0-1.1%. [34] The strategies to reduce such complications are to periodically review the usage of PCA by the child so that proper adjustments can be made and addition of adjuvants to reduce the dose of the opioids like ketorolac, ketamine etc.

Regional techniques:

The regional anaesthesia techniques have become popular in pediatric postoperative pain management as these provide excellent analgesia, reduce intraoperative anaesthetic drug requirements, ensures pain free recovery from anaesthesia, decrease stress response and avoids deleterious adverse effects of narcotic drugs. The various regional techniques are usually used along with general anaesthesia as these children are unable to cooperate. The various regional techniques used are topical anaesthesia, infiltration, regional nerve blocks and neuraxial analgesia.

- **Topical Anaesthesia**

A number of new local anaesthetic drugs and techniques have been developed which eliminates the need for injection into the skin for their anaesthetic effects. Eutectic Mixture of Local Anaesthetics (EMLA) is an example of mixture of lignocaine and prilocaine which effectively reduces the pain of venepuncture as well as other needle stick procedures in young children. [35, 36]

Iontophoresis is another technique which uses an electrical field to drive local anaesthetic drugs in their charged ionic form across the stratum corneum. This technique can provide analgesia to the deeper levels with shorter onset time and is usually well tolerated.

Local anaesthetics dispersed in liposomes have been used for transcutaneous anaesthesia providing effective analgesia with shorter application times. [37]

- **Infiltration Anaesthesia**

Injection of local anaesthetics into the skin is utilised when topical anaesthesia is not feasible. It can be used for providing good analgesia for superficial procedures like venepuncture, arterial cannulations and also can be used for postoperative analgesia after infiltration into the incision site.

- **Neuraxial Analgesia**

It includes caudal, epidural and spinal blocks. These are often used in conjunction with general anaesthesia to provide excellent intraoperative and postoperative analgesia thus reducing the need for more potent analgesics and reducing the stress response. There are some anatomic differences between infants and adults with regard to termination of spinal cord (L3) and the dural sac (S2-S4) which are more caudal. The various techniques are:

Caudal Epidural

It is a relatively safe and simple technique to provide intraoperative and postoperative analgesia for upper abdomen and perineal surgeries in which the local anaesthestic drug is injected into the caudal epidural space. The volume of local anaesthetic can be calculated from Armitage's formula which depends upon the site of surgery i.e. 0.5 ml/kg for sacrolumbar dermatomes, 1 ml/kg for lumbar and lower thoracic dermatomes and 1.25 ml/kg for mid thoracic dermatomes. The various local anaesthetics commonly used are 0.25% bupivacaine, 0.2% ropivacaine etc. and the addition of additives can prolong the analgesic effects like clonidine, dexmedetomidine, tramadol, butorphanol etc. [10, 11, 38, 39] The side-effects are rare and may include systemic local anaesthetic toxicity, bloody tap, urinary retention, nerve injury, motor blockade and neurological deficit.

Epidural Analgesia

The epidural catheters should be placed by an experienced anaesthesiologist to avoid any complications. Continuous infusions of local anaesthetics in dilute concentrations can be continued in postoperative period for analgesia. Nurse or parent controlled analgesia technique can also be utilized after proper education and training.

Spinal Analgesia

Spinal subarachnoid space is usually used for providing anaesthesia in premature neonates or in infants at high risk. Combined spinal epidural technique can be used to provide postoperative analgesia in infants.

The use of ultrasonography in regional blocks allows real time visualisation of anatomic structures and visualisation

of injected local anaesthetic solution and thus can help to establish analgesia with the use of low volume of drugs. It has been found to be useful in guiding caudal and epidural blocks as the ossification of sacrum and vertebrae are not complete in infants. [40, 41]

Neuraxial Opioids

Opioids like morphine, fentanyl and sufentanyl can be given through the epidural route for providing postoperative analgesia without motor or sensory blockade. However, these should be avoided in premature infants and whenever used, a strict monitoring of respiratory rate and pulse oximetry is essential. [42]Recently, the use of neuraxial opioids has been questioned due to the associated complications but less severe complications like itching, nausea, urinary retention and decreased motility have been found to be more troublesome. [43, 44] The neuraxial opioids are still beneficial in extensive surgeries with significant postoperative pain where the spread of local anaesthetic blockade cannot be achieved with permitted doses. [45, 46]

- **Peripheral Nerve Blocks**

The peripheral nerve blocks play an important role in management of postoperative pain in neonates and infants. The use of continuous catheter techniques helps in extending the analgesia in postoperative period. [47-49] The use of ultrasonography helps in locating various peripheral nerves and thus these nerves can be blocked with minimal local anaesthetic volume. The peribulbar block for pediatric cataract surgery after induction with general anaesthesia can provide prolong post-op analgesia. [50] The common peripheral nerve blocks used for postoperative analgesia in children are brachial plexus block, lumbar plexus block, femoral nerve block, sciatic nerve block, fascia illiaca block etc. Penile block can work excellently in providing adequate post-op pain relief after penile surgeries. [51] The use of various additives already described in neuraxial blocks can also be used in these blocks to prolong the duration of postoperative analgesia.

CONCLUSION

In conclusion, the acute postoperative pain among neonates and children deserves a compassionate and effective treatment which is essential to prevent long term psychological changes. Effective pain control should be provided to all children even for minor painful procedures to prevent development of fear and anxiety. A careful assessment of severity of pain using various age-specific pain scoring systems is essential for providing effective analgesia. The development of newer more potent analgesic medications with minimal side-effects allows for better control of postoperative pain. The use of multimodal approach to pain management involving cognitive, behavioural, physical and pharmacological interventions is required for effective management of pediatric pain.

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