Different modalities of Post-operative Pain Management in Infants and Children Undergoing Inguinal Hernia Repair

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Abstract

Adequate pain control is a prerequisite for the use of rehabilitation programs to accelerate recovery from surgery. Postoperative symptoms and complications can be prevented by a suitable choice of anesthetic and analgesic techniques for specific procedures. Thus, combining opioid and/or non-opioid analgesics with regional analgesic techniques not only improves analgesic efficacy but also reduces opioid demand and side-effects such as nausea and vomiting, sedation, and prolongation of postoperative ileus. On other hand, multiple pain assessment instruments or measures exist. However, choosing the correct age-appropriate and suitable instrument is difficult because many patients are non-verbal or are not cognitively aware. Knowledge of the properties and limitations of available assessment tools provides a means of choosing the correct one. Memories of previous pain experiences and socialization around painful events all influence subsequent reactions to pain. The increasing trend toward the use of multimodal and interdisciplinary approaches to pain management in children has provided more tools to effectively treat and possibly preempt pain. Therefore, this study aimed to review the different modalities in management of post-operative pain after inguinal hernia repair surgeries among infants and children.

Keywords: Inguinal Hernia Repair; Children ; Post-operative Pain Management

Introduction

Pain prevention is an important first step in controlling pain. Both non-pharmacologic and pharmacologic treatment have proven efficacy in children. The importance of the psychological state and complexity of a children's personality and their psychosocial background cannot be overlooked. It is known that the social and psychological composition of the children and their family dynamics influence pain sensitivity and therapeutic efficiency in multiple ways **(1).**

An example of these tools are the non-pharmacologic interventions like cognitive and behavioral techniques that include mind-body therapies such as play therapy, hypnosis, distraction. Other therapies such as acupuncture, acupressure, and massage are classified as manipulative therapies **(2)**.

It is important to ensure that any therapy is age appropriate and not contraindicated based on the child's medical condition, cultural, or religious beliefs.

Remember that these therapies are employed as adjuncts and may not relieve all pain by themselves **(3)**.

Prevention of pain whenever possible, using multi-modal analgesia, has been shown to work well for nearly all cases and can be adapted for day cases, major cases, the critically ill child, or the very young. Many acute pain services use techniques of concurrent or co-analgesia based on four classes of analgesics, namely local anesthetics, opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen (paracetamol) **(4)**.

In particular, a local/regional analgesic technique should be used in all cases unless there is a specific contra-indication. Also, the opioidsparing effects of local anesthetics, NSAIDs, and acetaminophen are useful **(5).**

- **Systemic analgesic:**

The importance of systemic analgesics in adults by efficacy when administered alone or in combination, probably applies also to infants and children. However, the pharmacokinetics and pharmacodynamics of these agents change during early life, and recent evidence has produced more logical dosing guidelines for opioids, NSAIDs, and (paracetamol) **(6)**.

Appropriate child-friendly formulations help child compliance and are now available as syrups, oral or sublingual wafers, soluble effervescent tablets, and eye drops (**7**).

Non-steroidal anti-inflammatory drugs (NSAIDs):

NSAIDs are important in the treatment and prevention of mild moderate pain in children. NSAIDs are highly effective with a local or regional nerve block, particularly in in day-case surgery **(5)**.

NSAIDs are often used in combination with opioids and the opioid Indeed, NSAIDs in combination with acetaminophen (paracetamol) produce better analgesia than either alone **(8)**.

NSAIDs should be avoided in infants less than 6 months of age, children with aspirin or NSAID allergy, those with dehydration or hypervolemia, children with renal or hepatic failure, or those with coagulation disorders, peptic ulcer or where there is a significant of hemorrhage risk **(6).**

Concurrent administration of NSAIDs with anticoagulants, steroids, and nephrotoxic agents is not recommended. The most commonly reported adverse effects of NSAIDs are bleeding, followed by gastrointestinal, skin, central nervous system, pulmonary, hepatic, and renal toxic effects **(9).**

Acetaminophen (paracetamol):

Acetaminophen inhibits prostaglandin synthesis in the hypothalamus probably via inhibition of cycloxygenase-3. This central action produces both antipyretic and analgesic effects **(10)**. Acetaminophen also reduces nitric oxide generation involved in spinal hyperalgesia induced by substance P or N-methyl D-aspartate (NMDA) **(11)**.

The analgesic potency of acetaminophen is relatively low and its actions are dose-related; a ceiling effect is seen with no further analgesia or anti-pyresis despite an increase in dose. On its own, it can be used to treat or prevent most mild and some moderate pain. In combination with either NSAIDs or weak opioids, such as codeine, it can be used to treat or prevent most moderate pain **(12).**

Acetaminophen is rapidly absorbed from the small bowel, and oral formulations in syrup, tablet or dispersible forms are widely available and used in pediatric practice. Suppository formulations vary somewhat in their composition and bioavailability, with lipophilic formulations having higher bioavailability. Absorption from the rectum is slow and incomplete, except in neonates **(13).**

Dosing guide for syrup and suppository paracetamol in pediatrics is illustrated in **(Table 1).** Also, mannitol solubilized paracetamol (Perfalgan^{TM}) has become available for intravenous infusion use. Interestingly, the higher effect site concentrations achieved in the brain after IV administration may result in higher analgesic potency. It is important to realize that the time to peak analgesia even after i.v. administration is between 1 and 2 hours. A dosing guide for i.v. paracetamol use in pediatrics is shown in **(Table 2) (5,14)**.

Table (1): Acetaminophen (paracetamol) dosing guide. (Arana et al., 2001)

	Oral			**Rectal**				
	Loading	**Maintenance**		**Loading**	**Maintenance**		**Maximum daily dose mg.kg^{-1}.d^{-1}**	**Duration at maximum dose (h)**
Age group	dose mg.kg^{-1}	dose mg.kg^{-1}	dosing interval (h)	dose mg.kg^{-1}	dose mg.kg^{-1}	dosing interval (h)		
Preterm 28-32 weeks	20	15	12	20	15	12	35	48
Preterm 28-32 weeks	20	20	8	30	20	8	60	48
0-3 months	20	20	8	30	20	8	60	48
>3 months	20	15	4-6	40	20	6	90	72

Table (2): Paracetamol intravenous dosing guide for children (14)

Age group	**Dose given every 4 hours**	**Dose given every 6 hours**	**Maximum single dose**	**Maximum total daily dose of acetaminophen (by all routes)**
Children 2 to 12 years of age	12.5 mg/kg	15 mg/kg	15 mg/kg (up to 750 mg)	75 mg/kg in 24 hours (up to 3750 mg)

Nalbuphine

Nalbuphine is a synthetic opioid agonist-antagonist analgesic derivative of the phenanthrene group, and its structure is similar to those of naloxone and oxymorphone. The drug is used for managing slight and moderate pain. It acts as an agonist of kappa opioid receptors (KORs) and mu opioid receptors (MORs) antagonist, thus providing analgesia as well as sedation, and it protects against mu opioid receptor blockade dependent respiratory failure **(15).**

Nalbuphine exhibits a ceiling effect; in other words, once its maximum plasma concentration has been reached, incremental doses do not potentiate its analgesic

effects or increase the risk of respiratory failure.Therefore, nalbuphine is considered a drug with a relatively slight risk of inducing respiratory failure. Because nalbuphine's specific mechanism of action provides potent analgesic effects, moderate sedation and relatively rare adverse side effects, and the drug is readily used for pain management in children **(16).**

Nalbuphine can be administered parenterally but is poorly absorbed from the gastrointestinal tract. Its thera- peutic plasma concentration to provide effective analgesia is 12 μg L-1. It is metabolised in the liver by cytochrome P-450, CYP 3A4 and 2C19 and broken down into N-hydroxy-ce- to-cyclo-butyl-methyl-nornalbuphine, and hydroxylated derivatives are excreted through the kidneys. The mechanism of hepatic clearance is strictly correlated with the extent of blood flow through the liver and is age dependent. Hepatic clearance is low during the neonatal period and increases with age, reaching its maximum at approximately 1 year of age and thereafter decreases gradually until adulthood **(17)**. Its elimination half-life ranges from 0.9 h in children aged 1.5−8.5 years **(15).**

Nalbuphine-induced analgesia and sedation as well as the ability to cause dysphoria result from the activation of KORs, whereas its antagonistic effects against MORs reduce the risk of respiratory depression caused by the agonist opioids that are used during surgical procedures. Moreover, because of its ceiling effect, nalbuphine protects against respiratory depression during treatment. The dose of maximum analgesic action is 0.3–0.4 mg per kg. Higher doses neither increase the analgesic effects nor substantially increase the risk of respiratory failure. A neonate mistakenly administered a dose ten-fold higher than required has been described and resulted in only a prolonged sedation without respiratory failure **(16).**

The drug used in recommended doses is believed not to induce respiratory depression in children. Nevertheless, caution should be exercised in patients with an increased risk of respiratory failure, including children with neuromuscular diseases or impaired regulation of the respiratory center, following cerebrocranial injuries, or in patients who are con-currently receiving other drugs that are likely to induce respiratory depression. In such patients, dosing of nalbuphine should be cautious and meticulously titrated; moreover, basic vital functions should be continuously monitored **(15).**

The other adverse effects of nalbuphine, although relatively rare, include drowsiness, vomiting, dysphoria and skin redness. According to Bressole et al., drowsiness is observed in 32% of patients, whereas 13.6% experience vomiting or urine retention after receiving nalbuphine following laparoscopic fundoplication for gastroesophageal reflux **(17)**.

Nalbuphine for postoperative pain management can be used in boluses at a dose of 0.2 mg per kg, repeated every 3-6 h as needed. If the repeated boluses are insouciant or a child requires too frequent a supply of further doses, a continuous intravenous infusion at a dose of 0.1 mg per kg per hour should be contemplated, which provides stable and effective postoperative analgesia **(Table 3)**. In patients undergoing procedures with more extensive tissue damage, patients requiring forced immobilization after surgery, and patients in whom moderate sedation can be

beneficial for the postoperative period, nalbuphine should be administered in a continuous intravenous infusion in a dose of 0.1 mg kg per hour immediately after surgery. In cases of insufficient analgesia, the rate of infusion can be increased up 0.2 mg kg per hour **(16)**.

Moreover, nalbuphine can be administered by patient-controlled analgesia (PCA). This method ensures stable analgesia, and the potential applications of the drug in cases of increased pain are well understood and accepted in older children. The basic PCA dosing includes a basal infusion in a dose of 0.02 mg per kg per hour and a bolus dose of 0.02 mg kg the interval between successive boluses is 5 min. The max dose during a 2-hour period should not exceed 0.4 mg per kg **(18).**

Table (3): The nalbuphine dosage for postoperative pain management in children (16)

Bolus dose	0.2 $mg.kg^{-1}$	Repeated every 30-6 h
Continous infusion	0.1-0.2 $mg.kg^{-1}.h^{-1}$	Continuous intravenous infusion
PCA	Basal infusion 0.02 $mg.kg^{-1}.h^{-1}$ Bolus 0.02 $mg.kg^{-1}$ Intervals between boluses 5 min Max. dose within 2 h 0.04 $mg.kg^{-1}$	

- **Local and Regional anesthesia:**

With the introduction of ultrasound, real-time visualization of anatomical structures become possible, thus guiding the blocking procedure itself, and showing the spread of the local anesthetic solution injected **(19).**

Mechanism of action of local anesthetics:

Local anesthetics induce reversible block of voltage sensitive sodium channels on the neuronal cell membrane by binding to the intracellular portion of the channels preventing sodium influx into nerve cells, which prevents depolarization. In general, the progression of anesthesia is related to the diameter, myelination and conduction velocity of the affected nerve fibers **(20).**

All local anesthetics contain three structural components: an aromatic ring, a connecting group which is either an ester (procaine) or an amide (bupivacaine), and an ionizable amine group. In addition, all LAs have two chemical properties that determine their activity **(19)**. Lipid solubility determines potency, duration of action, and plasma-protein binding of local anesthetics. Local anesthetics enter nerve fibers as a neutral-free base. Ionized forms and the cationic form blocks conduction by their interaction on the inner surface of the Na^+ channel. Moreover, LAs with lower pKa has a more rapid onset of action, meaning more of it exists in an uncharged form, which renders faster diffusion to the cytoplasmic side of the Na^+ channel **(21)**.

Na^+ channels are membrane proteins that propagate action potentials in axons, dendrites, and muscle tissue. They initiate and maintain membrane potential in

specialized heart and brain cells. Depending on the tissue Na^+, channels contain one larger alpha subunit and one or two smaller beta subunits **(20)**.

The alpha subunit, the site of ion conduction, and local anesthetic binding have four similar domains, each with six alpha-helical membrane-spanning segments. The external surface of the alpha-subunit is heavily glycosylated, which allows the channel to orient properly within the cytoplasmic membrane. In contrast to local anesthetics, scorpion toxins and tetrodotoxin have binding sites on the extracellular surface of the Na^+ channel **(21)**.

Neuronal tissues have different susceptibility to local anesthetics. Depolarizing currents in nerves move along nodes of Ranvier, and 2 to 3 nodes must be blocked to impair neuronal conduction completely. Smaller fibers have smaller internodal distances and, therefore, get blocked by local anesthetics more quickly **(19).**

Choice of local anesthetic solution:

A large safety study has established safe-dosing guidelines for the widely used local anesthetic bupivacaine in children and this has greatly reduced the incidence of systemic toxicity **(22)**.

Bupivacaine is a potent local anesthetic with unique characteristics from the amide group of local anesthetics. Local anesthetics are used in regional anesthesia, epidural anesthesia, spinal anesthesia, and local infiltration. Local anesthetics generally block the generation of the action potential in nerve cells by increasing the threshold for electrical excitation **(23)**.

The progression of anesthesia is dependent on factors such as the diameter, degree of myelination, and conduction velocity of nerve fibers. In clinical practice, the order of a loss of nerve function is as follows: pain, temperature, touch, proprioception, and skeletal muscle tone **(22).**

Bupivacaine is offered in three different concentrations: 0.25%, 0.5%, and 0.75% **(23)**. Administration is by local infiltration (post-surgical analgesia), peripheral nerve blocks (dental or other minor surgical procedures, orthopedic surgery), spinal anesthesia (injected into the CSF to produce anesthesia for orthopedic surgery, abdominal surgery, or cesarean delivery), epidural anesthesia/analgesia for labor pain, and a caudal block (anesthesia and analgesia below the umbilicus, usually for pediatric surgery) **(24)**.

Bupivacaine may interact with ergot medications used for migraine headaches, blood thinners, antidepressants, or monoamine oxidase inhibitors. Immunologic reactions to local anesthetics are rare. Allergic reactions to preservative-free amide-type local anesthetics are rare and usually not reported. A true anaphylactic response appears more common with ester local anesthetics or preservatives; epinephrine-containing local anesthetics reactions are often misdiagnosed as allergic reactions. Patients may also react to preservatives such as methylparaben, which are included with local anesthetics **(25)**. Some more common adverse effects include nausea, vomiting, chills or shivering, headache, back pain, dizziness, sexual dysfunction, restlessness, anxiety, vertigo, tinnitus, blurry vision, tremors which may precede more

severe adverse effects such as convulsions, myoclonic jerks, coma, and cardiovascular collapse **(26)**.

For a patient of less than 70 kg, bolus 1.5 mL/kg lipid emulsion 20% rapidly over 2 to 3 minutes, followed by an infusion of 0.25 mL/kg/min for ideal body weight to an upper limit of 12 mL/kg **(Table 4)**. A cardiopulmonary bypass should also still be considered early in case other treatments are ineffective **(27)**.

Table (4): Suggested maximum dosages of bupivacaine, levobupivacaine, and ropivacaine in neonates and children (27).

Single bolus injection	**Maximum dosage**
Neonates	2 mg/kg
Children	2.5 mg/kg
Continuous postoperative infusion	**Maximum infusion rate**
Neonates	0.2 mg/kg/h
Children	0.4 mg/kg/h

- **Caudal epidural block**

Most of anesthesiologists would prefer caudal block because all surgeries below the umbilicus can be covered by it (one technique fits all) which is relevant, as not all are familiar with the necessary spectrum of peripheral nerve blocks in children **(28).**

Single-shot caudal anesthesia is remarkably proved to be safe; as in a retrospective audit report, on more than 158 000 patients, showed that there was no report of permanent damage (**29**), meanwhile other two prospective studies examining 12111 and 8493 caudals showed the same beneficial results**(30,31)**.

In general, neuro-axial blocks have a higher number of side effects and complications compared with peripheral nerve blocks, but, remarkably, there was not a single case of epidural abscess, epidural hematoma, or paraplegia after a single-shot caudal block in world's literature, in contrast to other neuro-axial techniques in children (e.g. thoracic epidural anesthesia) where three cases with severe neurologic damage has been reported despite the fact that this technique is rarely used in children **(28)**.

The landmark technique for caudal block: (29)

- **Positioning:** A left lateral position is obtained with the upper hip flexed 90º and the lower one only 45º. Alternatively, the prone position can be used.
- **Disinfection:** Before palpating the landmarks, the region is swabbed in a cranio-caudal direction with 70% alcohol solution to reduce the amount of bacteria. Intensive disinfection with an alcoholic solution, sterile drapes, and the use of sterile gloves should be standard for every neuro-axial blockade.
- **Landmarks:** The both posterior superior iliac spines and the sacral hiatus form an equilateral triangle, the apex of which is the hiatus. Epidural puncture is achieved in the most proximal region of the sacral hiatus with the needle inclined 45º-60º to the skin. The palpating index finger of the left hand lies on the spinous process S4.

The needle should be inserted just below the spinous process of S4. The distance between the dural sac and the puncture site can be remarkably short and accidental intra-thecal injections with total spinal anesthesia can occur. With flexion of the spine, the end of the dural sack moves cranially to increase the margin of safety.

- **Equipment:** different types of needles and cannulae have been used; the size of the used needle should not be bigger than 25G, as a fine needle causes less trauma.

Ultrasound guided caudal block technique:

The ultrasound can be used to confirm correct placement of the needle and/or catheter in the sacral canal, detection of local anesthetic spread in the canal and is useful when the anatomy is difficult or the landmark technique failed **(32)**.

With the monitor on the opposite side to the operator and under complete aseptic conditions **(Fig. 1 & 2)**, the linear high frequency transducer is applied in midline sagittal plane over the lumbosacral region, then it is moved caudally and the level of the dural sac can be visualized according to the degree of ossification, thereafter, the sacral hiatus and the saco-coccygeal membrane can be imaged **(29)**. The probe is then turned 90º at the level of the sacral hiatus with direct visualization of the sacral cornua, to confirm visualization of the hiatus and the sacro coccygeal membrane (SCM) **(30)**.

Finally, the probe is turned back to the midline and the needle is inserted in-plane with its advancement through tissues as a hyperechoic line, thereafter the needle is left for 10 seconds open to air to allow detection of blood or CSF followed by negative aspiration and injection of the local anesthetic with displacement of the posterior dura anteriorly**(32)**.

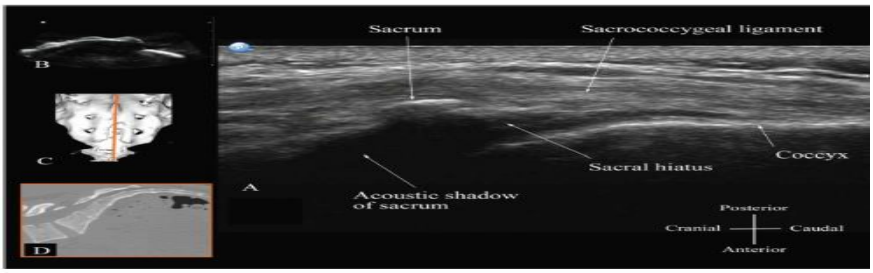

Figure (1): Longitudinal midline plane US of caudal space (32).

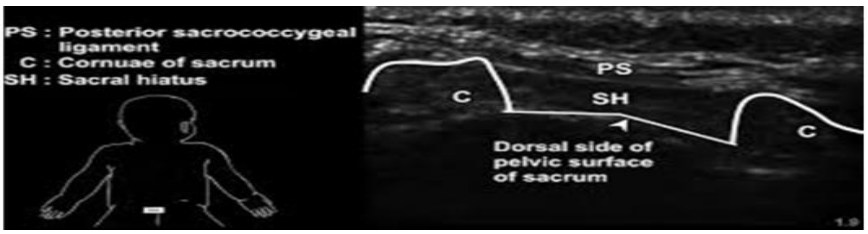

Figure (1): Transverse plane US of caudal space (32).

Complications of caudal block:

Complications are rare, and are more likely due to inadequate equipment used. However, some of these complications are serious and potentially fatal, which include dural tap, epidural hematoma, vascular puncture, sacral perforation, delayed respiratory depression, urinary retention and infection as epidural abscess or sacral osteomyelitis **(32).**

- **ESP block technique for lower abdominal surgery in pediatrics:**

ESP blocks are performed using a high resolution US machine probe with a sterile cover. A 22 G, 50 mm, insulated facet type needle is used. Patients are positioned to lateral position for block performance. Following antiseptic preparation of block site, US probe is placed 1–2 cm lateral to spine at L1 level with counting upwards from the sacrum. After identifying the erector spinae muscle and transverse process, needle is inserted with in-plane technique in cranio-caudal direction **(Fig. 3)**. Following confirmation of the correct position of the needle tip with administration of 0.5–1ml of local anesthetic (LA), 0.5 ml/kg 0,25% bupivacaine (maximum dose limited to 20 ml is injected deep to the erector spinae muscle for the block **(33).**

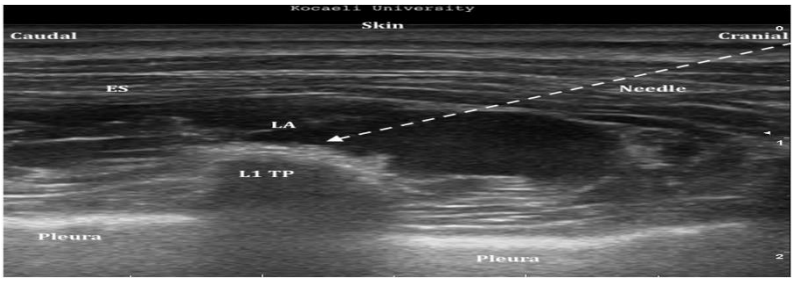

Figure (3): Ultrasound image of the block (ES: erector spinae, TP: transverse process, LA: local anesthetic)

ESP block technique is simple, safe, and easy visualization of the sonoanatomy. There are no structures in the immediate vicinity at risk of needle injury. A catheter can be inserted to extend the duration of analgesia **(34).**

Till date only 2 complications have been reported: pneumothorax and motor weakness. There is a paucity of data for erector spinae plane block being a relatively new block and more studies are required to determine the extent of the block, inter individual variations and complications **(35).**

CONCLUSION:

Good pain control after surgery is important to prevent negative outcomes such as tachycardia, hypertension, myocardial ischemia, decrease in alveolar ventilation, and poor wound healing.

The aim of analgesic protocols is not only to reduce pain intensity and decrease the incidence of side-effects from analgesic agents, but also to improve patient comfort.

Exacerbations of acute pain can lead to neural sensitization and release of mediators both peripherally and centrally. Advances in the knowledge of molecular

mechanisms have led to the development of multimodal analgesia and new pharmaceutical products to treat postoperative pain.

Indeed, regional versus systemic analgesia decreases postoperative pulmonary complications, and this impact is greater following abdominal surgery.

Regional anesthesia produces excellent postoperative analgesia and attenuation of the stress response in infants and children. Peripheral nerve blocks provide prolonged analgesia restricted to the site of surgery and should be preferred.

No Conflict of interest.

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