Postoperative analgesia for cleft lip and palate repair in children

Reena, Kasturi Hussain Bandyopadhyay[1], Abhijit Paul[1]

Department of Anaesthesiology, Heritage Institute of Medical Sciences, Varanasi, Uttar Pradesh, [1]Department of Anaesthesiology, Perioperative Care and Pain Services, Medica Superspeciality Hospital, Mukundapur, Kolkata, West Bengal, India

Abstract

Acute pain such as postoperative pain during infancy was ignored approximately three decades ago due to biases and misconceptions regarding the maturity of the infant's developing nervous system, their inability to verbally report pain, and their perceived inability to remember pain. More recently, these misconceptions are rarely acknowledged due to enhanced understanding of the developmental neurobiology of infant pain pathways and supraspinal processing. Cleft lip and palate is one of the most common congenital abnormalities requiring surgical treatment in children and is associated with intense postoperative pain. The pain management gets further complicated due to association with postsurgical difficult airway and other congenital anomalies. Orofacial blocks like infraorbital, external nasal, greater/lesser palatine, and nasopalatine nerve blocks have been successively used either alone or in combinations to reduce the postoperative pain. Since in pediatric population, regional anesthesia is essentially performed under general anesthesia, association of these two techniques has dramatically cut down the risks of both procedures particularly those associated with the use of opioids and nonsteroidal anti-inflammatory drugs. Definitive guidelines for postoperative pain management in these patients have not yet been developed. Incorporation of multimodal approach as an institutional protocol can help minimize the confusion around this topic.

Key words: Analgesia, cleft lip, cleft palate, orofacial nerve blocks

Introduction

One of the fundamental emotions we experience throughout our life is "pain" which can be defined as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."[1] It is an offence to believe in the myth that "children cannot feel pain as much" in spite of the established fact that all the structures are in place for transmission of pain by the 30th week of gestation.[2] Postoperative pain belongs to the category of acute pain and can be felt by children as vividly as their grown up counterparts.

Address for correspondence: Dr. Reena,
Assistant Professor, Department of Anaesthesiology, Heritage Institute of Medical Sciences, Mohansarai-Ramnagar Bypass, Bhadwar, Varanasi - 221 311, Uttar Pradesh, India.
E-mail: reena216@gmail.com

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.175649

Cleft lip and palate (CLP) is one of the most common congenital abnormalities requiring surgical treatment in the early years of life.[3] Corrective surgical procedures subject these children to intense postoperative pain. This review article aims to elicit the fundamental knowledge and various approaches one can utilize to provide satisfactory, multimodal analgesia in this group of patients.

Embryology

The embryological mechanism that causes CLP in the premaxillary region occurs between the 5th and 8th week of embryologic development,[4] when fusion of the lateral and medial nasal processes with the anterior extension of maxillary processes on either side fails. On the other hand, development of a cleft in the secondary palate occurs

How to cite this article: Reena, Bandyopadhyay KH, Paul A. Postoperative analgesia for cleft lip and palate repair in children. J Anaesthesiol Clin Pharmacol 2016;32:5-11.

between the 7th and 12th weeks of intrauterine life and can result from:

1. Failure of palatal ridges to contact because of a growth deficiency or disturbance in the ridge elevation mechanism,
2. Failure of the ridges to merge after contact has been established because the epithelium lining does not reabsorb,
3. An unexpected rupture after the palatine ridges merge, or
4. Defective consolidation of mesenchymal palatine ridges.[4]

Cleft lip (CL) may be reliably diagnosed at the 18-20 weeks during anomaly scan; however, it is extremely difficult to visualize cleft palate (CP) prior to delivery.[5] Many classifications have been devised, but essentially the cleft can involve the lip, alveolus (gum), hard palate, and/or soft palate and can be complete or incomplete, unilateral or bilateral.

Incidence

CL, with or without a CP, occurs in 1 in 600 live births. CP alone, is a separate entity and occurs in 1 in 2000 live births.[6]

Clefts (based on incidence) are divided into:[7]

1. Isolated CL — 26%.
2. CL + CP — 35% (unilateral 23%; bilateral 12%).
3. Isolated CP — 39%.

Associated Anomalies

Children with CL and CP may have multiple abnormalities even without a recognized syndrome. Venkatesh analyzed associated anomalies from a tertiary cleft center in India and found that associated anomalies were more frequent in patients with CLP (32%) than in patients with CL alone (11%) or patients with CP alone (22%).[8]

The list of associated problems can be summarized as:[6]

1. Associated congenital abnormalities — Pierre Robin syndrome, Goldenhar syndrome, Treacher Collins syndrome, Velocardiofacial syndrome
2. Congenital heart disease occurs in 5-10% of these patients
3. Chronic rhinorrhea
4. Chronic airway obstruction/sleep apnea
5. Right ventricular hypertrophy and cor pulmonale may result from recurrent hypoxia due to airway obstruction
6. Anticipated difficult intubation and extubation.[9]

Timing of Surgical Repair

Planning of postoperative pain relief following corrective surgery will essentially depend on the age of patient and associated co-morbidities if any.

CL is classically repaired between 3 and 6 months;[10] however recently, there is an increasing trend to operate in neonatal period.[6]

CP repair is done at a later age, between 9 and 18 months.[10] Timing and sequence of surgical repair (primary vs. staged repair) depend on surgeon preference in most cases. Timing of repair is aimed at preventing further speech abnormalities and at minimizing distortion in facial growth which can occur if repair is done too early. Surgery may be delayed to optimize the associated abnormalities as far as possible.

Anatomy and Physiology of Pain Following Cleft Lip and Palate repair

Pain experienced by patients after these surgeries is predominantly superficial suggesting a somatic rather than visceral origin, along the sensory nerve supply[11] of the respective regions [Figure 1].

CL: As it involves mainly the upper lip, the following nerves carry the pain sensation:

a. The infraorbital nerve: A branch of the maxillary division of the trigeminal nerve. It supplies not only the upper lip, but much of the skin of the face between the upper lip and the lower eyelid, except for the bridge of the nose.
b. The external nasal nerve: A branch of the ophthalmic nerve that supplies the integument of the ala and tip of the nose.

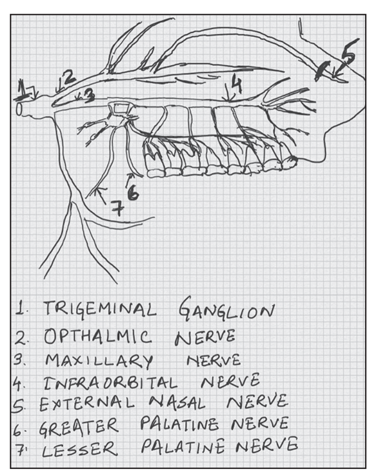

Figure 1: Sensory nerve supply of upper lip and palate

CP: The pain sensation from the palate is carried by the following nerves (all are branches of the maxillary division of trigeminal nerve):

a. The lesser palatine nerve: Supplies the soft palate, tonsil, and uvula.
b. The greater palatine nerve: A branch of the pterygopalatine ganglion, supplies the gums, the mucous membrane and glands of the hard palate, and communicates in front with the terminal filaments of the nasopalatine nerve.
c. Nasopalatine nerve: Supplies the palatal structures around the upper central and lateral incisors and the canines (the upper front six teeth).

Available Modalities of Postoperative Analgesia

1. Local anesthetic (LA) infiltration by surgeon.
2. Nerve blocks.
3. Opioid analgesics.
4. Nonopioid analgesics.

Infiltration of local anesthetic

Infiltration of the surgical field with LA solution has been used.[12-14] Local infiltration of the palate blocks the terminal branches of the nasopalatine and greater palatine nerves.

Preincisional infiltration tends to distort the margins of the cleft and makes esthetic repair difficult.[15] Therefore, postoperative analgesia cannot be satisfactorily performed under local infiltration.

Nerve blocks

For cleft lip surgery

Infraorbital nerve block

Anatomy: This nerve can be easily blocked as it emerges from the infraorbital foramen, just medial to the buttress of the zygoma.

Procedure: The site of the infraorbital foramen varies with age and concerns about the close proximity of the eye in the neonate led Bösenberg and Kimble[15] to perform an anatomical study on neonates that showed that the infraorbital nerve lies halfway between the midpoint of the palpebral fissure and the angle of the mouth, approximately 7.5 mm from the side of the nose. The nerve is blocked by inserting a needle perpendicularly to the skin and advancing it until bony resistance is felt.

In children, since the oral commissure and the infraorbital foramen is placed more medially as compared with adults, direction of the injection is angled slightly more laterally[16] [Figure 2].[17] The needle is then withdrawn slightly and 1-2 ml of 0.5% bupivacaine with 1:200,000 adrenaline is injected after performing a negative aspiration test. Salloum *et al*. suggested that in patients older than 12 years, a mixture of equal volumes of 1% lidocaine with epinephrine 1:100,000 and 0.5% bupivacaine with epinephrine 1:100,000 can be used. A volume of 0.25 cc of this mixture was injected into each side.[17] For children younger than 12 years, the authors used a mixture of equal volumes of 0.5% lidocaine with epinephrine 1:200,000 and 0.25% bupivacaine with epinephrine 1:200,000, and injected 0.25 cc into each side. To avoid direct contact with the nerve and injury to the globe, injections were performed while palpating the infraorbital rim, avoiding penetration of the foramen.

Another more classical "dental approach" described by Tremlett consists of inserting the needle into the sulcus between the lip and gum, with a finger placed anteriorly to confirm the extent of needle advancement as LA is administered.[7]

External nasal nerve block

Anatomy: This is a branch of the ophthalmic division of the trigeminal nerve and is not affected by infraorbital nerve block. Patients will feel discomfort in the nasal region if this branch is not blocked.

Procedure: The aforementioned mixture of LA was injected (0.25 cc into each side) at the nerve's exit from the distal nasal bone, superior to the upper lateral cartilage, approximately 7 mm lateral to the midline of the nasal dorsum [Figure 2].[17,18]

For cleft palate surgery

Greater palatine nerve block

The greater palatine nerve block [Figures 3 and 4][19] is useful for anesthetizing the palatal tissues distal to the canine. It is less traumatic than the nasopalatine nerve block because the palatal tissue in the area of the injection site is not as anchored to the underlying bone.

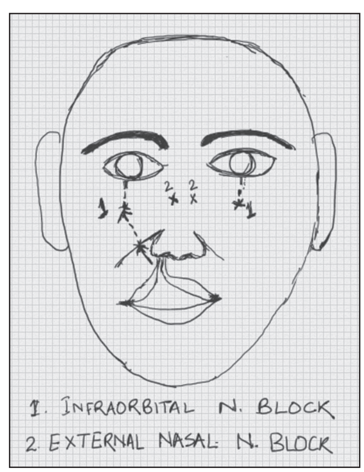

Figure 2: Nerve blocks for cleft lip surgery: (1) Infraorbital, (2) external nasal

Procedure: The greater palatine foramen is localized by placing the needle on the palatal tissue approximately 1 cm medial to the junction of the second and third molar. While this is the usual position for the foramen, it may be located slightly anterior or posterior to this location. Also, it's been seen that a wide variation exists in the location of greater palatine foramen. The relative location of the greater palatine foramen in infants' and children's craniums was found to be distal to the posterior molar. As the next posterior tooth erupted, the relative position of the foramen moved posteriorly.[20] Also, the optimum age for eruption of upper first molar tooth is 11-18 months of age. So the block can be performed in this age group, and the site of injection will be behind the posterior molar. The syringe is directed into the mouth from the opposite side at a right angle to the target area with orientation of the needle bevel toward the palatal soft tissue to deposit a small volume of LA solution.

This technique provides anesthesia to the palatal mucosa and hard palate from the first premolar anteriorly to the posterior aspect of the hard palate and to the midline medially.

Lesser palatine nerve block

It is quite similar to the greater palatine block and provides analgesia in the soft palate region postoperatively [Figure 3].

Nasopalatine nerve block

The nasopalatine nerve block, also known as the incisive nerve block, anesthetizes the nasopalatine nerves bilaterally. In this technique, anesthetic solution is deposited in the area of the incisive foramen [Figures 3 and 5].[19]

Procedure: There are two techniques; single penetration and multiple penetrations.[19] The former technique consists of a single penetration of the mucosa directly into the incisive foramen relying on pressure anesthesia and slow deposition of anesthetic solution for pain management. Some clinicians feel this technique is traumatic, especially for the pediatric patient and suggest a multiple penetration technique to minimize pain.[19] The suggested technique is after buccal anesthesia is achieved with local infiltration, anesthetic solution is injected into the interdental papilla penetrating from the labial side and diffusing the solution palatally. The palatal tissue is sufficiently anesthetized to proceed with an atraumatic nasopalatine block.

Practical difficulties with palatal blocks: The nasopalatine block can be performed in incomplete CP; in complete clefts where premaxilla is malformed, this block cannot be performed.

Opioid analgesics

Patients undergoing CLP correction benefit from careful use of intraoperative opioids.

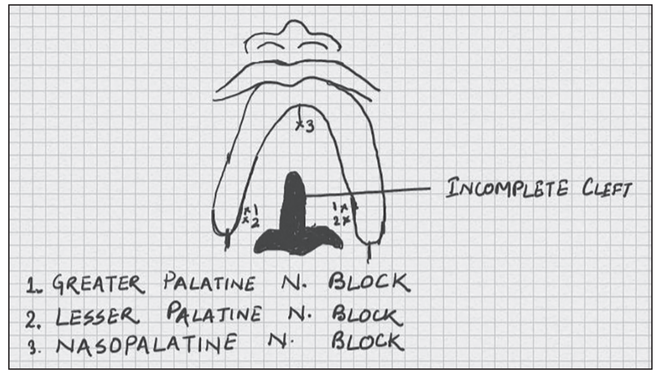

Figure 3: Nerve blocks for cleft palate surgery: (1). Greater palatine, (2). lesser palatine, (3). nasopalatine

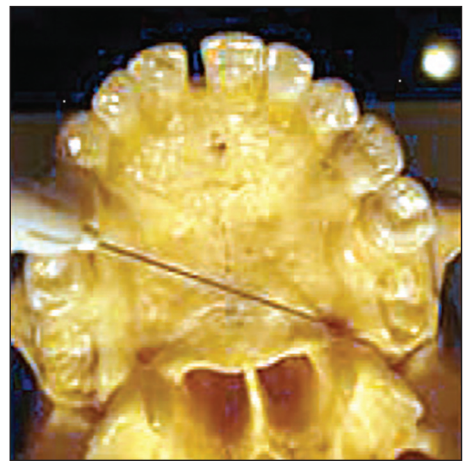

Figure 4: Greater palatine nerve block

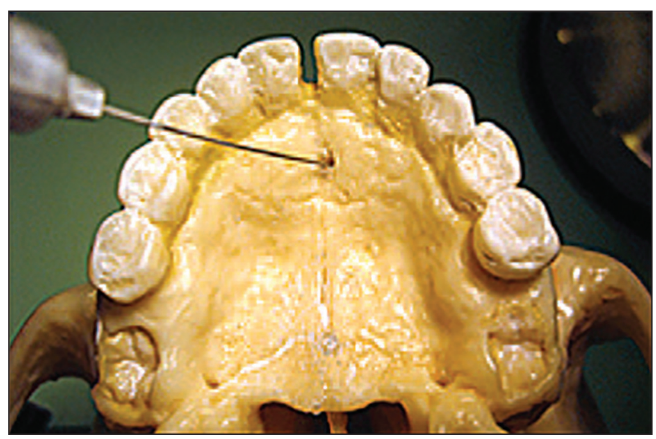

Figure 5: Nasopalatine nerve block

Advantages

The use of opioids results in a smoother emergence and less crying on extubation that in turn reduces trauma to the airway and decreases the risk of postoperative bleeding.

Disadvantage

The use of opioids in neonates and infants raises justifiable concerns regarding postoperative sedation, respiratory depression, and consequent airway compromise. A review of anesthesia for CL repair reported profound respiratory depression after opioid administration.[12] With regard to unpredictable sensitivity and pharmacokinetic responses to opioids in the pediatric population,[21,22] nerve-blocking techniques have gained interest for postoperative analgesia as it provides good pain relief and avoids the complications of opioid analgesics. It is vital that the child leaves the theater fully awake and in control of his airway.

However, under proper supervision in a high dependency unit, the following opioids can be used for postoperative pain relief [Table 1].[23]

Nonopioid analgesics

Paracetamol given 20 mg/kg orally as premedication or rectal paracetamol postinduction (40 mg/kg) can achieve adequate analgesia by the end of surgery.[6] Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective analgesics. However, they may increase the risk of postoperative bleeding, thus some advocate delaying administration until 12 h postoperatively.[6] The nonopioid analgesics and their advocated doses are mentioned in Table 2.[23]

Role of Multimodal Approach

Recently there is an increasing awareness regarding the need for complete wellbeing of the child in the postoperative period and not just a pain-free state. Adverse events produced by opioids do not help in achieving such a goal. As initial CL repair is increasingly performed in early infancy, most infants are sensitive to opioid-induced respiratory depression due to both immaturity of the central nervous system and the unpredictable clearance of opioids by the immature hepatic enzymes.[24] The airway is further compromised by the presence of other craniofacial anomalies, as seen in up to 43% of cleft patients.[25,26] LA with nerve blocks appears to be the answer in such circumstances.

Table 1: Opioid analgesics for pediatric patients

Drugs	Dosages	Forms
Fentanyl	1 mcg/kg	IV
Morphine	0.05-0.1 mg/kg	IV
Meperidine	1 mg/kg	IV
Codeine	1.5 mg/kg q4h	PO: 15 mg, 30 mg, 60 mg tablets; syrup 15 mg/ml
Oxycodone	0.15 mg/kg	PO: 5 mg tablets, syrup 5 mg/ml

IV = Intravenous

Rajamani *et al.*[27] showed that infraorbital block alone can bring down the requirement of fentanyl and provide effective analgesia in postoperative period. There are 2 well-known approaches to the infraorbital nerve: Intra- or extra-oral. After intraoral approach, ocular penetration has been reported in a patient with absent right upper palate.[28] Since many patients have combined clefts of the lip and palate, extraoral approach may be considered safer.

Infraorbital nerve block complications are rare but may be associated with swelling and ecchymosis of the lower eyelid, injury to the nerve or accompanying artery, puncturing the floor of the orbit and orbital injection of anesthetic solution resulting in diplopia, exophthalmos, and blindness.[29] Takmaz *et al.*[30] performed the block with Bösenberg and Kimble's[15] technique, and found no major complications except erythema and hematoma on the cheek near the injection site.

Salloum *et al.* proposed that by combining infraorbital and external nasal nerve blocks, optimal and extended analgesia can be achieved in CL surgery, further reducing the need for postoperative opioids.[17]

Since there is no single effective block for CP surgeries, it should always be supplemented with the other modalities of pain management, particularly opioid analgesia along with close monitoring. Nevertheless, the blocks can bring down the required dose of opioids effectively in the perioperative period. Kamath *et al.* compared the efficacy, safety, and ease of the greater palatine nerve block for CP surgeries in children with intravenous pethidine for postoperative pain management and found that those who received pethidine were often deeply sedated or agitated at various points of time in the observation period whereas those who had greater palatine nerve block were mostly awake and calm.[31] NSAIDs are highly effective

Table 2: Nonopioid analgesics for pediatric patients

Drugs	Dosages	Forms
Acetaminophen	10-15 mg/kg PO maximum 2600 mg/day	Tablets: 80 mg Syrup: 325 mg/5 ml Suppositories: 120, 325, 650 mg
Ibuprofen	10-20 mg/kg PO q6h	Tablets: 300 mg, 400 mg Syrup: 100 mg/5 ml
Ketorolac	0.5 mg/kg IV to load (maximum dose 30 mg) 0.5 mg/kg q8h IM or IV (limit use to 48 hrs.) Parenteral form used IM or IV	

IM = Intramuscular, IV = Intravenous

in combination with a regional nerve block.[32] NSAIDs are often used in combination with opioids and their "opioid sparing" effect in adults is 30-40%.[33] One study found that the co-administration of NSAIDs and opioids decreased both postoperative opioid requirement and side effects and increased pain relief in children.[34] NSAIDs in combination with acetaminophen produce better analgesia than either alone.[32,33] However, NSAIDs should be avoided in infants <6 months of age due to risk of inhibition of prostaglandin synthesis applicable to neonates include disruption of the sleep cycle, increased risk of pulmonary hypertension, alterations in cerebral blood flow, decreased renal function, disrupted thermoregulation, and alterations in hemostasis balance.[32,35]

Acetaminophen inhibits prostaglandin synthesis in the hypothalamus probably via inhibition of cycloxygenase-3.[36] When compared to NSAIDs, acetaminophen exerts minimal anti-inflammatory effects and is associated with significantly less gastropathy and platelet dysfunction. Acetaminophen is predominantly metabolized by phase 2 hepatic conjugation pathways (>95%) through both glucuronidation and sulfation. Neonates rely more on sulfate pathways.[37] Hepatotoxicity is the major concern and is related to the production of the toxic metabolite N-acetyl-p-benzoquinone-imine (via phase 1 oxidative metabolism). It is generally a problem of overdose, in which the usual phase 2 clearance pathway becomes saturated or when the metabolite "mop," glutathione, is depleted.[37] Neonates may be somewhat protected because of immaturity of oxidative clearance pathways.[38]

The approach of multimodal analgesia was first suggested by Kehlet in 1997.[39] In theory, the use of multiple analgesics that are effective on different mechanisms of nociception will increase efficacy while minimizing the dose, and therefore potential for adverse effects, of each drug. As already mentioned, a recent meta-analysis of studies involving the use of NSAIDs as part of a multimodal technique, reduced opioid consumption and the incidence of postoperative nausea and vomiting.[34] Tang *et al*. investigated the effects of multimodal analgesia on analgesia and sedation during emergence from general anesthesia for CL and/or palate surgery in pediatric patients. They concluded that multimodal analgesic regimen of infiltration of LA at surgical site and rectal paracetamol and intravenous fentanyl provides sufficient analgesia and minimizes the incidence of agitation after general anesthesia.[40] With LA blocks, analgesia extends into the early postoperative phase following a single injection, thereby reducing the need for other analgesics. Moreover, regional and general anesthesia techniques are no longer considered as alternative but instead, as complementary. This is especially true in pediatrics where regional anesthesia is essentially performed under general anesthesia.

Challenges of performing nerve blocks under general anesthesia in pediatric patients:

- Difficulty in identifying intravascular injection of LA.
- Difficulty in identifying intraneural placement of needle or LA.

Despite the issues of the safety of regional anesthesia in children, studies have shown that the risks and complications of regional anesthesia in children are quite low and often preventable.[41-44] The largest of these studies was published by the French-Language Society of Pediatric Anesthesiologists (ADARPEF).[43] This prospective report included 24,409 regional blocks performed over 1-year in children. Only 25 complications occurred in the study, and all the complications occurred in children who received central blocks. Thus, the overall complication rate of regional anesthesia was 0.9 per 1000. In a retrospective review of 24,005 regional anesthetics administered over a 10-year period, Flandin-Bléty and Barrier reported 108 events without sequelae (0.45%).[45]

As the field of pediatric regional anesthesia grows, it may become the primary method of providing both intraoperative and postoperative analgesia if strategies continue to diminish the risks, and if studies are carried out to promote the benefits.

Conclusion

It is evident that the pediatric population needs better understanding, care, and vision for postoperative pain management following CLP surgeries. It needs to be customized according to the age, extent of surgery, chances of postoperative airway compromise and the availability of resources for proper monitoring. The different modalities described should be seamlessly blended together according to the above-mentioned requirements. Multimodal analgesia is always preferred as it reduces complications of sole individual modalities. Institutional protocols can be depicted describing different scenarios and age groups so that confusion around this topic gets minimized, and the patients can get freedom from pain as much as possible.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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