Comparison of Bupivacaine Alone and in Combination with Fentanyl or Pethidine for Bilateral infraorbital Nerve Block for Postoperative Analgesia in Paediatric Patients for Cleft Lip Repair: A Prospective Randomized Double Blind Study

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ABSTRACT

Background: Cleft lip repair is one of the common surgeries performed in India and the usual method used for postoperative analgesia is perioperative opioids and NSAIDs. There has been an increase in use of regional techniques and Opioids are the common adjuvants but their efficacy and safety have not been studied extensively in children.

Patients & Methods: A prospective, randomized, double blind study was done to compare the efficacy, duration and safety of intraoral infraorbital nerve block on post operative pain relief using bupivacaine alone or in combination with fentanyl or pethidine in paediatric cleft lip repair.

45 children between the age group 5 - 60 months undergoing cleft lip surgery randomly allocated into 3 groups of 15 each received bilateral intraoral infraorbital nerve block with 0.75ml of solution. Group B received 0.25% bupivacaine; group P received 0.25% bupivacaine with 0.25mg kg\(^{-1}\) pethidine, group F received 0.25% bupivacaine with 0.25microgm kg\(^{-1}\) fentanyl. Sedation after recovery, post operative pain intensity and duration of post operative analgesia were assessed using Modified Hannallah Pain Score.

Results: The mean duration of analgesia was 17.8 hrs in Group B, 23.53 hrs in Group F and 35.13 hrs in Group P. There was statistically significant difference between the means of the three groups- ANOVA (p < 0.05).

Conclusion: Thus we conclude that addition of fentanyl or pethidine to bupivacaine for Bilateral Intraoral Infraorbital Nerve Block prolong the duration of analgesia with no complications and can be used safely in paediatric patients.

KEYWORDS: Paediatric infraorbital nerve block, Cleft lip, Post operative pain relief

Pain in children is usually an undertreated entity. Perioperative pain management is like a double edged sword for an anaesthesiologist, under treatment leads to various metabolic, physiologic and neurophysiological responses and the usual means of perioperative pain management i.e. the opioids is often underutilized as there is an increased incidence of respiratory depression in this age group. However, cleft lip surgery is associated with appreciable postoperative pain in children. Adequate postoperative analgesia in children is a vital part of perioperative care. Good pain relief minimizes the oxygen requirement, reduces cardio-respiratory demands, and promotes early ambulation and recovery. Regional block given preoperatively in combination with general anesthesia (GA) provides good preemptive analgesia. It is associated with perioperative hemodynamic stability, rapid and complete recovery and reduced analgesic requirement in the postoperative period.\(^1\)

Surgery for repair of cleft lip is a common procedure in infants and young children in India. Bilateral infra-oral nerve block provides sensory blockade of the upper lip, side of nose, mucous membrane lining the nasal vestibule and the skin of the lower eyelids.\(^1\)

Effectiveness of infraorbital nerve block for cleft lip surgeries has been long since established but there are very few studies of its use with opioids as an adjuvant for postoperative analgesia.

So this prospective, randomized, double blind study was performed to compare the efficacy of infraorbital nerve block using bupivacaine alone and in combination with fentanyl or pethidine for postoperative pain relief and also to study the safety of opioids as adjuvants in infraorbital nerve block in paediatric age group for cleft lip repair.

PATIENTS AND METHODS

After approval from the hospital ethics committee and written informed consent from parents, 45 children of either gender, aged between 5 months and 5 years and weighing between 5 and 15 kgs of ASA status I or I I were selected. Children with sensitivity to local anesthetics, bleeding disorders,
known major illnesses and prolonged duration of surgery (>90min) were excluded from the study. 45 patients were allocated by computer generated randomization into group B, F and P of 15 each. They were premedicated with inj. Glycopyrrolate 0.01 mg kg\(^{-1}\) IM + inj. Ketamine 5 mg kg\(^{-1}\) IM. Intravenous access was secured and intravenous fluid Ringer’s lactate was started. Monitors attached included NIBP, Pulse oximeter and ECG.

After pre-oxygenation for 3 minutes, the children were induced with inj. Midazolam 0.05 mg kg\(^{-1}\), inj. Fentanyl 1 microgm kg\(^{-1}\), inj. Ketamine 1 mg kg\(^{-1}\) and inj. Scoline 1.5 mg kg\(^{-1}\) IV and intubated with an oral RAE South polar ET tube of appropriate size. Patients were maintained on N2O:O2 (50:50), inj. Vecuronium 0.1 mg kg\(^{-1}\) IV and 0.02 mg kg\(^{-1}\) IV boluses later on.

In Group B 0.75ml of 0.5% Bupivacaine was taken in a 2ml syringe and diluted to 1.5 ml with saline. In Group F, 0.75ml of 0.5% Bupivacaine was taken and 0.25microgm kg\(^{-1}\) Fentanyl (drawn using tuberculin syringe) was added to it and diluted to 1.5ml with saline. In Group P, 0.75ml of 0.5% Bupivacaine was taken and 0.25mg kg\(^{-1}\) Pethidine (drawn using tuberculin syringe) was added to it and diluted to 1.5ml with saline.

The drug was prepared by anaesthesia resident and both the person administering the block and the person observing and recording the parameters were blinded to the study.

Infraorbital foramen was located and a finger was placed over it. Lip was everted and a 24G needle was introduced towards the foramen. Bilateral intraoral infraorbital nerve block was given to all patients with 0.75ml solution on each side.

Hemodynamic parameters and EtCO2 were monitored. At the end of the surgery, patients were reversed with inj. Glycopyrrolate 0.02 mg kg\(^{-1}\) and inj. Neostigmine 0.05 mg kg\(^{-1}\) and extubated.

The success of the block was assessed by the lack of sympathetic response to surgical stimulation. Patients with failure of block or requiring additional analgesia during intraoperative period were excluded from the study.

Pain was assessed in PACU for the initial four hours and later in the ward by trained nursing personnel blinded to the study. Modified Hannallah Pain Score was used for monitoring the postoperative pain. Any complications were noted.

Pain score was assessed hourly and when it exceeded 3, inj. Fentanyl 1 microgm kg\(^{-1}\) in PACU and syrup Paracetamol 15mg kg\(^{-1}\) in the ward were administered as rescue analgesics. Study terminated at the first demand of rescue analgesic or 36 hours postoperatively.

**STATISTICAL ANALYSIS**

Using the results obtained from previous studies and assuming an alpha error of 0.05 and power of the study >90%, a sample size of 45 was calculated. Randomization was done using computer generated randomization table. The gender, age, weight and duration of surgery were compared using the Chi Square test. Pain scores were compared using the Kruskal-Wallis test. The duration of analgesia was analyzed in the three groups using ANOVA and Tukey’s Test for multiple comparisons.

**RESULTS**

All 45 patients were included and there were no drop outs due to failure of block. The patient characteristics were comparable between the three groups. There was no statistically significant difference on comparison of highest pain scores between the three groups.

The mean duration of analgesia observed was 17.8 (±3.52) hrs in Group B, 23.53 (±3.52) hrs in Group F and 35.13 (±3.52) hrs in Group P respectively. There was statistically significant difference between the means of the three groups- ANOVA (p < 0.05). Differences in the Mean and 95% Confidence Interval (CI) was calculated using Tukey’s Test and was statistically significant (p < 0.05).

**Comparison of patient characteristics between the three groups**

|                     | Age (MTHS) | (MTHS) | Gender (KGS) |
|---------------------|------------|--------|--------------|
| Group B             | 14         | 10:5   | 7.353        |
| Group F             | 16.4       | 6:9    | 8.153        |
| Group P             | 14.93      | 6:9    | 7.553        |

**Comparison of the Mean duration of Analgesia Between the Three Groups**

|                      | Differences of Mean (Hrs) | Confidence Interval (Hrs) |
|----------------------|---------------------------|---------------------------|
| Group F – Group B    | 5.73                      | 3.25 – 8.21               |
| Group P – Group F    | 11.6                      | 9.12 – 14.8               |
| Group P – Group B    | 17.33                     | 14.85 – 19.81             |

**Modified Hannallah Pain Score**

| No. | Observation | Criteria       | Points |
|-----|-------------|----------------|--------|
| 1   | Crying      | No crying      | 0      |
|     |             | Crying responding to TLC | 1      |
|     |             | Crying not responding to TLC | 2      |
| 2   | Movement    | None           | 0      |
|     |             | Restless       | 1      |
|     |             | Thrashing       | 2      |
| 3   | Agitation   | Asleep/calm    | 0      |
|     |             | Mild           | 1      |
|     |             | Hysterical     | 2      |
DISCUSSION

Pain is perhaps the most feared symptom of any disease, which man is always trying to alleviate and conquer since ages\(^2\). There is no longer any debate whether infants and children have the capacity to feel pain or that the experience of pain by a child can have negative short and long term consequences\(^3\).

The unpredictable response to intravenous opioids in pediatrics is due to their altered pharmacokinetic response and increased sensitivity\(^4\). Opioids have lead to profound respiratory depression in paediatric patients for cleft lip repair\(^5\). This has lead to reluctance in use of adequate doses of opioids leading to inadequate postoperative analgesia and its complications.

Regional anesthesia can reduce the intraoperative requirement of both inhaled and intravenous anesthetics and allows a more rapid return to the preoperative state while providing effective postoperative pain relief with minimal sedation\(^6\).

During the development of the lip, the infraorbital nerve of the opposite side innervates part of the skin in the midline. In addition, surgical correction usually involves dissection and mobilization of tissue supplied by the infraorbital nerve of the opposite side. Hence bilateral infraorbital nerve block is usually given to provide postoperative analgesia for the correction of unilateral cleft lip repair\(^1\).

Modified Hannallah pain scale was used for measurement of pain intensity \(^6\,7\,8\).

We used a pain score of more than 3 as the criteria for supplementing rescue analgesia. The duration from the time of administration of the block to the first supplementation of rescue analgesic was used as the postoperative duration of analgesia.

In our study the mean duration of analgesia was 17.8hrs in patients who received 0.25% plain bupivacaine. It was approximately 1.5 times for F group (23.53hrs) and 2.0 times for P group (35.13hrs) as compared to B group. There was statistically significant difference between the means of the three groups, ANOVA (\(p < 0.05\)).

Opioids as adjuvants have been shown to prolong the duration of postoperative analgesia in peripheral nerve blocks\(^6\,10\) and the synthetic opioids of phenyppiperidine series viz pethidine and fentanyl also have a local anaesthetic action\(^9\).

The observed period of analgesia outlasts an additive or even synergistic effect of the drugs used and, instead, infers preemptive analgesia\(^11\). In our study, there were no systemic side effects with this dose of opioids suggesting mainly a peripheral action.

These results were in accordance with the studies conducted by other authors. Nicodemus HF et al used inj. bupivacaine 0.5% (1 to 1.5 ml on each side) with inj. Adrenaline (1:200,000) for infraorbital nerve block and the mean duration of postoperative analgesia observed was 19.4 ± 5.06 hours\(^12\).

Gaonkar. V et al compared the efficacy and duration of postoperative analgesia of preoperative infraorbital nerve block and peri-incisional infiltration with inj. bupivacaine 0.25% with inj. adrenaline (1 in 200,000) in patients undergoing cleft lip surgeries or corrective surgery like cleft rhinoplasty. Patients in Infraorbital nerve block group had a postoperative analgesia of 29.00 ± 2.08 hours and 24.08 ± 1.82 hours in perincisional group\(^1\).

Armstrong et al showed that, in IVRA, the addition of pethidine to prilocaine 0.25% substantially increases the onset of sensory and motor block probably due to a local anaesthetic than an opioid effect\(^6\).

Gobeaux and Landais found that the addition of 100 µg fentanyl to 30ml lignocaine 1.5% with adrenaline 1:200 000 for axillary brachial plexus block improved intra-operative analgesia, while the addition of pethidine 100 mg reduced postoperative analgesic requirements\(^13\).

However, in an earlier study, Gobeaux and colleagues found a faster onset of both sensory and motor blockade on addition of fentanyl 100 µg to 30ml lignocaine 1.5% with adrenaline 1:200 000 for brachial plexus block\(^14\).

Gissen et al in their study on the peripheral mammalian nerve found that the conduction block produced by fentanyl and sufentanil on isolated rabbit vagus nerve was not reversed by naloxone, indicating that the block was independent of the drug’s opioid activity\(^15\).

Oldroyd et al demonstrated using an IVRA technique that, that pethidine in low concentrations does have a local anaesthetic action on peripheral nerves\(^16\).

In our study, the duration of analgesia was significantly prolonged with addition of opioids.
Conclude intraoral infraorbital nerve block when given before incision has approximately 100% success rate with minimal complications. Addition of fentanyl or pethidine prolong the duration of block with pethidine providing the maximum duration of analgesia. Thus, the use of opioids as adjuvant to the infraorbital nerve block is not only safe but also provides excellent postoperative analgesia in pediatric age group.

REFERENCES
1. Gaonkar V, Daftary SR. Comparison of infraorbital block with peri-incisional infiltration for post operative pain relief in cleft lip surgeries. Indian J Plastic Surg 2004; 37(2): 105-9.
2. Gehdoo RP. Postoperative pain management in paediatric patients. Indian J Anaesth 2004; 48(5): 406-14
3. Brislin RP, Rose JB. Pediatric acute pain management. Anesthesiol Clin N Am 2005; 23(4): 789-814
4. Purcell-Jones G, Dorman F, Summer E. The use of opioids in neonates. A retrospective study of 933 cases. Anaesthesia 1987; 42: 1316-20
5. Doyle EH. Anaesthesia for primary repair of cleft lip and cleft palate. A review of 244 procedures. Pediatr Anesth 1992; 2: 139-45
6. Markakis DA. Regional anaesthesia in pediatrics. Anesthesiol Clin N Am 2000; 18(2): 355-81.
7. Hannallah RS, Broadman LM, Belman AB. Comparison of caudal and ilioinguinal / iliohypogastric nerve blocks for control of post orchiopexy pain in pediatric ambulatory surgery. Anesthesiology1987; 66: 832-4.
8. Viitanen H, Annila P. Analgesic efficacy of tramadol 2 mg/kg for paediatric day case adenoidectomy. Br J Anaesth 2001; 86: 572-5.
9. Armstrong PJ, Morton CP, Nimmo AF. Pethidine has a local anaesthetic action on peripheral nerves in vivo. Addition to prilocaine 0.25% for intravenous regional anaesthesia in volunteers. Anaesthesia 1993; 48: 382-6.
10. Bazin JE, Masoni C, Bruelle P, Fenies V. Groslier D, Schoeffler P. The addition of opioids to local anaesthetics in brachial plexus block: the comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia 1997; 52: 858-62.
11. Zouheir Naja, Mohammad Fouad Ziade, Per-Arne Lonnqvist. Nerve stimulator guided pudendal nerve block decreases posthemorrhoidectomy pain. Can J Anaesth 2005; 52 (1): 62 – 8
12. Honorato F. Nicodemus, Maria Josephine R Ferrer, Victoria Cases Cristobal, Luisita de Castro. Bilateral Infraorbital Block with 0.5% Bupivacaine as Post-Operative Analgesia Following Cheiloplasty in Children. J of Plast Surg and Hand Surg 1991, Vol. 25, No. 3: Pages 253-257
13. Gobeaux D, Landais A. Use of two opioids in blocks of the brachial plexus. Cah Anesthesiol 1988; 36:437–40.
14. Gobeaux D, Landais A, Bexon G, et al. Addition of fentanyl to adrenaline lidocaine for the brachial plexus block. Anesthesiology 1987; 35: 195–9.
15. Gissen AJ, Gugino LD, Datta S, et al. Effects of fentanyl and sufentanil on peripheral mammalian nerves. Anesth Analg 1987; 66: 1272–6.
16. Oldroyd GJ, Tham EJ, Power I. An investigation of the local anaesthetic effects of pethidine in volunteers. Anaesthesia 1994; 49: 503–6.