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Research Article

Comparative Study of Neostigmine as an Adjuvent with Ropivacine during Postoperative Analgesia in Children

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Abstract: In order to evaluate the postoperative analgesic effect of caudal administration of neostigmine with or without ropivacine, 120 children of aged 2-10 years, who underwent elective infraumblical surgeries, were studied. The children were randomly divided into two groups: Group A (n -60) received 0.2% Ropivacaine 0.5 ml/kg, and Group B (n-60) received 0.2% Ropivacaine 0.5 ml/kg with 2µg/kg Neostigmine *via* the caudal route. Assessment of analgesia in post operative period done by Modified Children's Hospital of Eastern Ontario Pain Scale (MCHEOPS) for a period of 24 hrs the pain score was significantly lower in Group B as compared to Group A. The mean duration of analgesia in Group A patients was 440±25 minutes, and Group B patients were 690±31 minutes. There are no significant side effects seen in the patients. In the conclusion the caudal administration of Ropivacine with Neostigmine resulted in prolonged duration of analgesia as compared to Ropivacaine alone.
Keywords: Ropivacine, Neostigmine, MCHEOPS.

INTRODUCTION

Pain defines as unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. But infact pain experienced by children often goes unrecognized, and even neglected because of the operational definition of pain that requires self report [1]. Studies shows that pain treated less aggressively in children cause unnecessary suffering [2]. The use of regional anesthetic techniques in infant and children has become increasingly accepted as standard of care.

The regional anesthetic technique reduces the overall intraoperative anesthetic requirement and rapid return of the conscious preoperative state [3], however the mean duration of analgesia provided by single shot caudal analgesia is inadequate. Since then various additive are added to prolong the duration of analgesia like Epinephrine, Opiods, Ketamine, Clonidine and Neostigmine. [4,5].

Ropivacine is longer acting, with wide margin of safety, and lower potential for cardiovascular and central nervous system side effects. But because of less lipid solubility, the blockade of A and Aß fiber is slow, resulting in less motor blockade. Ropivacine produces more differential blockade allowing better separation between sensory and motor blockade resulting in early mobilization, hence a better choice for post operative pain relief.

Neostigmine, a cholinesterase inhibitor has been found to provide analgesia by both intrathecal as well as epidural routes. [6,7,8] It inhibits the breakdown of endogenous acetylcholine and thus indirectly stimulates both muscarinic and nicotinic receptors to produce analgesia [9,10] This effect is mediated via spinal M_1 muscarinic receptors and supraspinal M_1 and M_2 muscarinic and nicotinic cholinergic receptors [11].

In the present we study ropivacine alone and the increase in the duration of analgesia with the use of neostigmine as an additive is observed.

MATERIALS AND METHODS

The study was conducted at Rama Medical College, Ramacity, Kanpur. After obtaining Institutional Ethics Committee approval and written Informed consent from the parents. ASA I and II, 120 children, aged 2–10 yr, undergoing elective infraumblical surgery were included in study. The study is prospective randomized and double blinded. Patients were randomly allocated according to a Computer-generated randomization. Study solutions were prepared by an anesthesiologist not involved in the patients' care by using standardized written instructions for study

drug preparation. Group A (n -60) received 0.2% Ropivacaine 0.5 ml/kg, and Group B (n-60) received 0.2% Ropivacaine 0.5 ml/kg with 2µg/kg Neostigmine *via* the caudal route.

All the children were induced with inj propofol, oxygen and nitrous. Anesthesia was maintained with oxygen and nitrous. Intraoperative monitoring included electrocardiograme (ECG), oxygen saturation (SPO2), noninvasive blood pressure (NIBP), and Respiratory rate (RR). During surgery, adequate analgesia was also defined by hemodynamic stability, as indicated by the absence of an increase in MAP or heart rate (HR) of more than 15% compared with baseline values obtained just before the surgical incision. An increase in HR or mean arterial pressure (MAP) within 15 min of skin incision is indicated as failure of caudal anesthesia. If more than a 15% increase occurred, analgesia was considered inadequate and children received a rescue opioid during surgery. Fluid therapy was standardized during and after surgery. During surgery, children received lactated Ringer's solution 6 ml/ kg/ hr whereas 5% dextrose with electrolytes was given at a rate of 4 ml/ kg/ hr in the postoperative period. Intraoperative decreases in MAP and HR more than 30% from baseline values were defined as severe hypotension or bradycardia, respectively, and were treated by a rapid infusion of fluids or, if unsuccessful, the use of ephedrine, or atropine. , Assessment of analgesia in post operative period done by Modified Children's Hospital of Eastern Ontario Pain Scale (MCHEOPS) [12,13] for a period of 24 hours(hrs) at 1,2, 3, 4, 8 , 12, 24 hrs after caudal block, a pain score of <6 was considered as adequate analgesia. A pain score of 6 or greater resulted in the administration of 20 mg/kg rectal paracetamol. The duration of postoperative analgesia was defined as the time between caudal drug injection and the first rectal paracetamol administration. If no rectal paracetamol was necessary within 24 hrs, the duration of analgesia was counted as 24 hrs.

Measurements were recorded by the same anesthesiologist who did not know which medication was administered. The same person performed measurements for all patients. The amount of supplementary analgesic required by each child in a 24 h period, total analgesic consumption during the study period, and any local or systemic complications were recorded.

OBSERVATION

Data from the 120 children included in the study were analyzed (60 children in each group). There were no differences between the group members in weight, Height, age, duration of surgery, duration of general anesthesia, or time to extubation ($P > 0.05$).

There were no significant differences between group members in systolic blood pressure and diastolic blood pressure and HR during the study (Fig 1- 3). Severe hypotension or bradycardia was not observed in any patient. SpO2 remain more than 99% throughout the study in both the groups.

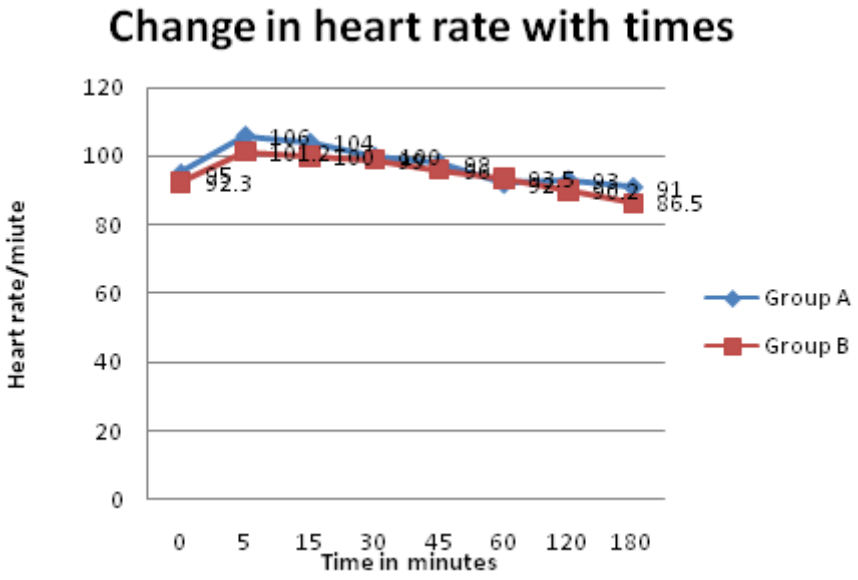

Fig-1: Shows change in heart rate with times

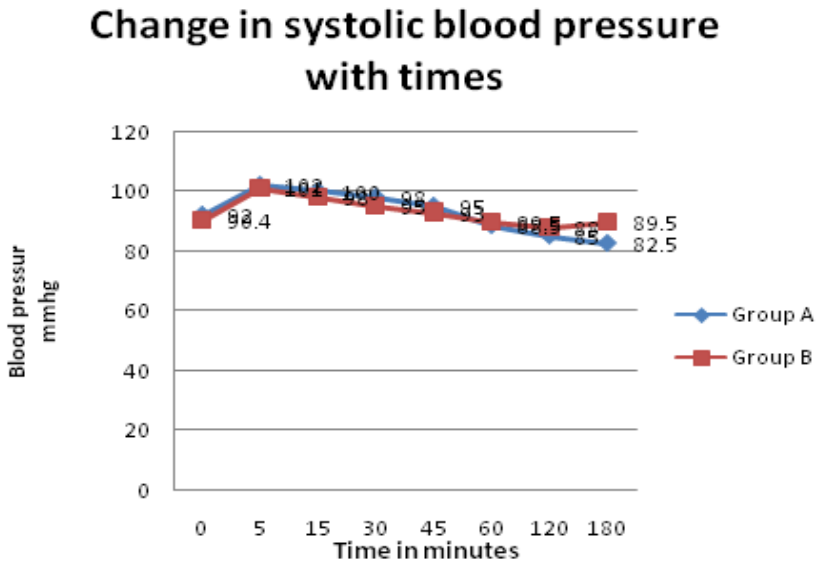

Fig-2: Shows change in systolic blood pressure with times

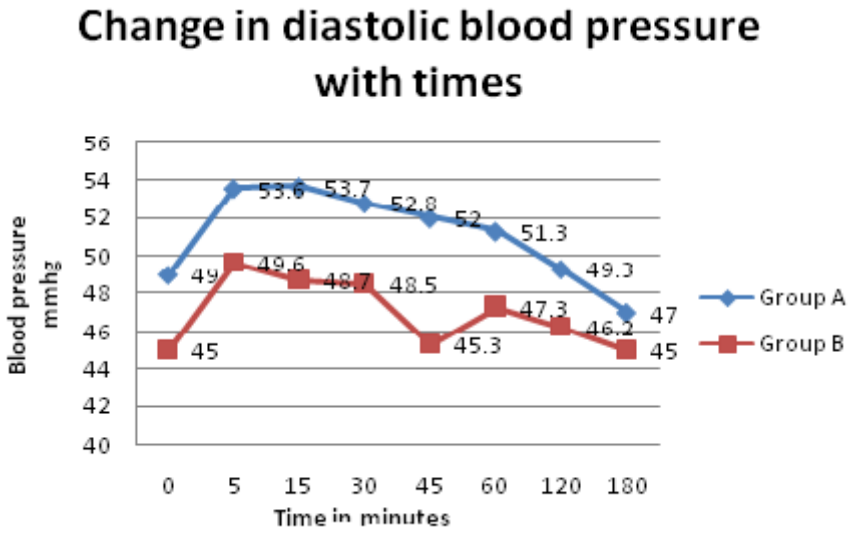

Fig-3: Shows change in diastolic blood pressure with times

All the patients do not require any analgesia at first and second and third hour and the Modified Children Hospital of Ontario Pain Score (MCHEOPS) was below 6 in both the groups. At the end of forth hour 8 patients have pain score more than 6, at the end of eight hour 27 patients had pain score more than 6, and at the end of 12 hour 34 patients had pain score more than 6, and at end of 24 hour 39 patients had pain score more than 6 in group A. In the group B At the end of forth hour 2 patients have pain score more than 6, at the end of eight hour 8 patients had pain score more than 6, and at the end of 12 hour 15 patients had pain score more than 6, and at end of 24 hour 19 patients had pain score more than 6 ($P<0.05$)(Fig- 4).

The mean duration of analgesia in group A patients was 440±25 minutes, and group B patients were 690±31 minutes ($P<0.05$)(Fig-5).

If the pain score was equal or more than 6 at 2 consecutive intervals of 10 minutes than supplementary analgesia with paracetamal 20mg/kg rectal was given. There are no significant side effects seen in the patients.

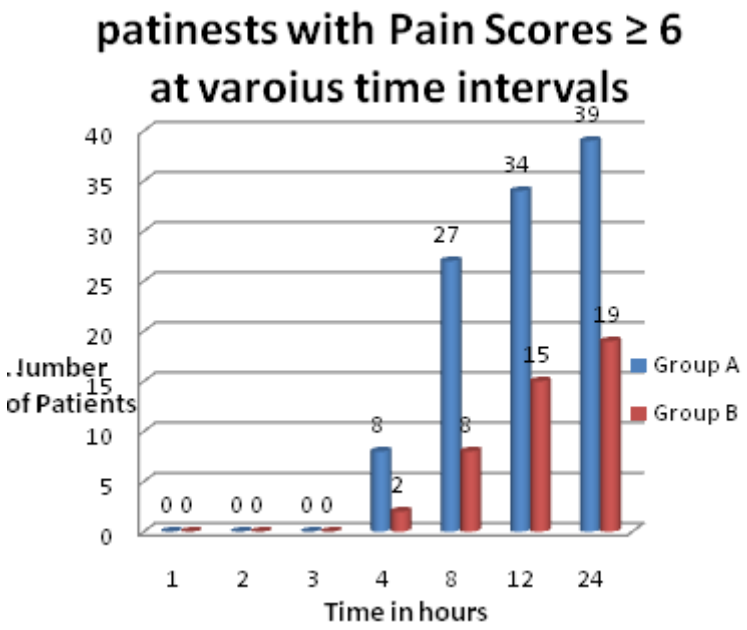

Fig- 4: Shows patients with pain scores>6 at various time intervals

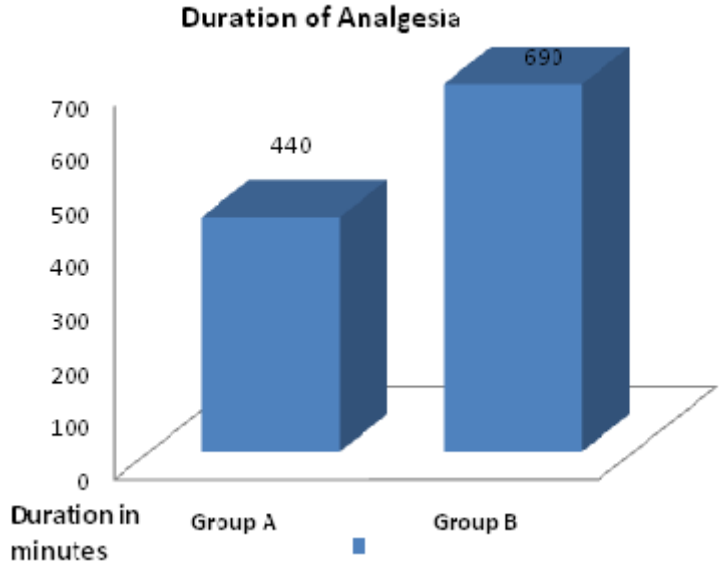

Fig-5: Shows duration of analgesics

DISCUSSION

There are number of incorrect myth and assumption for under treatment of pain in children. Major one is that the nervous system of children is immature and are unable to perceive pain as adult do, but the studies shows that structural component necessary to perceive pain are already present by 25 week of gestation [14]. Similarly immature myelination was previously equated with reduced pain perception; however the slower conduction in peripheral nerves is offset by shorter axonal length to be traveled by nerve impulse in the body, also nerve tract in spinal cord myelinated by 30 week, in brain stem and thalamus by 37 week [15]. Other myth is children metabolize analgesic differently than adults [16] Also some says that children have no memory of pain however pain memory is illustrated by exaggerated pain response to vaccination as long as 6 months fallowing circumcision.

The basic mechanism of pain perception in infant and children are similar to adults that include transduction, perception and modulation [17]. Also pain evokes negative physiological, metabolic and behavioral response including increase in heart rate, respiratory rate, and blood pressure, release of catecholamine, glucagon and corticosteroids. The catabolic state induced by pain in infant and children is more damaging because of higher metabolic rate and less nutritional reserves, that lead to anorexia, delayed wound healing, sleep disturbances, irritability and developmental regression [18].

It was suggested that duration of analgesia by local anesthetics alone was of short duration and prolongation of the effect can be achieved by use of additive like opiods, clonidine, and ketamine. This causes synergistic effect and also causes dilution effect thereby decreasing the toxicity of local anesthetics [19]. Studies suggested that Ropivacaine is more advantageous for children when compared with other local anesthetics, because of its specificity to sensory C fibers, producing less motor block [20].

The ropivacine alone for caudal blockade in concentration of 0.5% lead to 362±42 min. and in 0.25% lead to 248±30 min of motor blockade [21]. The total and free plasma concentration of ropivacine was measured by high performance liquid chromatography shows adequate and safe plasma concentration of ropivacine and adequate analgesia after caudal analgesia [22].

Neostigmine, like all cholinesterase inhibitors, causes analgesia by preventing the breakdown of acetylcholine in the spinal cord thus associated with the deceleration of pain transmission. Its advantages include the analgesic effect itself through the above mentioned mechanism, the prolonged analgesic effect of the local anaesthetic and the reduced dose, as well as sympathetic block side-effect compensation, a higher respiratory rate [23]. Its use in post-operational analgesia was described as early as the 1990s, both in adults and in children [24].

Neostigmine 10 ug/kg with bupivacaine given through epidural route produced longer duration of post hysterectomy analgesia as compared to bupivacine alone in one study by Nakayama *et al.* [25].

Lauretti et *al.* Found that epidural neostigmine 1, 2, 4 ug/kg with lidocaine produced a dose-dependent analgesic effect and a reduction of postoperative analgesic consumption without increasing adverse event [26]. In peadiatric anesthesia study done by Turan *et al*.[27] similar to our study. They used neostigmine 2 ug/kg and 0.2% ropivacine 0.5ml/kg. the results shows increase in duration of analgesia from 7.1±5.5 hr to 19.2±5.5 hrs in neostigmine group.

In the present study we try to establish the role of neostigmine as an adjuvant to ropivacine. We use the dose of neostigmine as 2µg/kg because higher dose lead to post operative complication like nausea, vomiting, arrhythmia, bradycardia . Our study show that with the ropivacine alone duration of analgesia is 7.3±2.5 hr that is almost same as Turan et al study, and with neostigmine as an adjuvant the duration of analgesia was increased to 11.5 ±3.1 without any increase in side effects. The duration of analgesia was shorter in our study than Turan et al study [27],that may be due to the difference in the way of evaluating pain and how the child could express feeling pain.

CONCLUSION

The casual administration of Ropivacine 0.2 %(2mg/kg) with Neostigmine (2µg/kg) resulted in prolonged duration of analgesia as compared to Ropivacaine alone without any increase in the side effects.

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