To Compare the Quality and Duration of Analgesia by Caudal Bupivicaine and Clonidine Combination with Caudal Bupivicaine and i.v Clonidine Combination

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ABSTRACT

Introduction: Regional anesthesia undertaken when the child is under general anesthesia (GA) can give prolonged analgesia in the post operative period. Caudal block since its first description in 1933 for paediatric urological interventions has evolved to become the most popular regional anaesthetics technique for use in children. Our study was designed to compare the analgesic efficacy of caudal bupivacaine and caudal clonidine with caudal bupivacaine and intravenous clonidine for postoperative analgesia in children undergoing subumblical surgeries.

Method and Materials: A prospective randomized double blind study was conducted in the department of anaesthesiology and critical care medicine sheri-kashmir institute of medical sciences soura, Srinagar, from 2009 to 2011. After taking the institutes ethics committee approval 60 healthy children ASA-1, of either sex in age group of 2-8 years undergoing elective below umbilical surgery were taken up for the study. For the purpose of study patients were randomly allocated to one of the following groups of 30 patients each. GROUP A. received 1ml/kg of 0.25 percent bupivicaine hydrochloride in addition to 2mcg/kg of clonidine caudally and similar volume of normal saline intravenously. GROUP B. received 1ml/kg of 0.25 percent bupivicaine hydrochloride and 2mcg/kg clonidine intravenously and simultaneously same volume of saline caudally.

Results: 14 patients in group A required rescue analgesia at least once as compared to group B where 16 patients needed rescue analgesia once during the 12 hours study period. Similarly 12 patients in group A and 10 patients in group B required rescue analgesia twice during 12 hour study period. It was observed from the study that comparable number of patients in the two groups required rescue analgesia and the difference was found to be statistically non significant. (P >0.05)

Conclusion: The duration of analgesia in group B was 404 ± 196 minutes while in group A the duration was 428 ± 197 minutes. Maximum observational pain score (OPS) scores were comparable between the two groups. The number of rescue analgesia dose requirement was comparable between the two groups. The difference was statistically insignificant (P>0.05).

Keywords: Pain, Clonidine, Bupivicaine, Analgesia, Regional Anesthesia

INTRODUCTION

Pain is derived from the Latin word "poena", which means penalty or punishment[1]. Pain is no longer considered a penalty or punishment. It is a protective mechanism designed to alert the body to potentially injurious stimuli. The International Association for study of pain has defined pain as "an unpleasant sensory and emotional experience, associated with actual or potential tissue damage"[1]. Pain after surgery is inevitable. Relieving pain has been the focus of continuing human effort. However, it has been recognized for some time that the management of acute pain, especially post operative pain, has been consistently and systematically inadequate. If anything, the situation in children has been even worse, who have long been under medicated for acute pain[2]. The provision of adequate analgesia is necessary after any surgery and it is all the more important in children. Under treatment of post-operative pain even in the children and newborns may trigger biochemical and physiologic stress response and cause impairments in pulmonary, cardiovascular, neuro-endocrine, gastrointestinal, immunological, and metabolic functions. Painful surgical incisions involving the upper abdomen result in reflex mediated increase in tone in abdominal muscles during expiration and decrease in diaphragmatic functions[3]. The result is reduced pulmonary compliance, muscle splitting and inability to breathe deeply or cough forcefully and in some cases hypoxia, hypercarbia, retention of secretions, atelactasis and pneumonia[4]. Suprasegmental reflex responses to pain results in increased sympathetic tone, hypothalamic stimulation, increased catecholamine and catabolic hormone secretion and decreased secretion of anabolic hormones. All these are responsible for sodium and water retention, hyperglycemia, free fatty acids, ketone bodies and lactate[5]. Assessment presents a major challenge in pain management of children. Generally two types of techniques are useful for pain assessment i.e., self report and observation of behaviour. The simplest and reliable method of self report of pain intensity is a visual analog scale (VAS), which is 10 cm long graded scale "No pain" at one end "worst possible pain, on other. Patient is instructed to make a mark on this scale and

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the position of the mark will indicate intensity of pain. This method of self report in children rely on cooperation of child which may be lacking in strange setting of hospital after a painful operation has been performed on a child[6]. Various methods of post operative pain relief in children include:

1. General measures which include presence of parent with child, preparatory information, nursing in comfortable position, reassurance and distraction[7].
2. Non-Opioid analgesic drugs which include Acetaminophen (paracetamol) and NSAIDS.
3. Opioids
4. Ketamine.
5. Local and Regional Anesthesia.

Regional anesthesia undertaken when the child is under general anesthesia (GA) can give prolonged analgesia in the post operative period. Caudal block since its first description in 1933 for pediatric urological interventions has evolved to become the most popular regional anesthetic technique for use in children[8]. It provides excellent analgesia during surgery as well as during postoperative period in subumblical surgeries in children, the anesthetic use of an alpha-2 adrenergic receptor agonist has been of considerable and prolonged interest over the last 20 years. It is a partial α2-adrenergic agonist that has a variety of different actions including antihypertensive effects as well as the ability to potentiate the effects of local anesthetics. It can provide pain relief by an opioid-independent mechanism[9].

Opioids like morphine, fentanyl, and sufentanyl have been traditionally used as adjuncts but they are associated with objectionable side effects such as nausea, respiratory depression, pruritis etc[10]. The analgesic action of epidurally administered clonidine is due to stimulation of descending noradrenergic medullo-spinal pathways inhibiting the release of nociceptive neurotransmitters in the dorsal horn of spinal cord[11].

Our study was designed to compare the analgesic efficacy of caudal bupivacaine and caudal clonidine with caudal bupivacaine and intravenous clonidine for postoperative analgesia in children undergoing subumblical surgeries.

METHOD AND MATERIALS

A prospective randomized double blind study was conducted in the department of anaesthesiology and critical care medicine sheri-kashmir institute of medical sciences soura, Srinagar, from 2009 to 2011. After taking the institutes ethics committee approval 60 healthy children ASA-1, of either sex in age group of 2-8 years undergoing elective below umbilical surgery were taken up for the study. Patients with history of allergic reactions to local anaesthetic or bleeding diasthesis or pre-existing neurological or spinal disease were excluded from the study. Preoperatively all the patients were clinically evaluated and investigated. Informed written consent to participate in the study was taken from the parents. On arrival in anaesthesia room, an intravenous line was established. Monitoring of ECG, SPO2 and non-invasive blood pressure was done as for routine purposes. For the purpose of study patients were randomly allocated to one of the following groups of 30 patients each.

GROUP A. received 1ml/kg of 0.25percent bupivicaine hydrochloride in addition to 2mcg/kg of clonidine caudally and similar volume of normal saline intravenously.

GROUP B. received 1ml/kg of 0.25 percent bupivicaine hydrochloride and 2mcg/kg clonidine intravenously and simultaneously same volume of saline caudally.

All children had emla (prilocaine 2.5% and lidocaine 2.5%) applied to dorsum of both hands 1hr before surgery. All operations were carried out under general anaesthesia and the technique was common to all. General anaesthesia was induced with Thiopentone [5-6mg/kg] and 0.5mg/kg Atracurium to facilitate intubation. Anaesthesia was maintained with oxygen 40 percent in nitrous oxide and halothane 0.5-1 percent. A nurse not involved in study prepared the study medication .1ml of clonidine [150mcg/dl] was diluted with 9ml of normal saline in 10 ml syringe. For each child two syringes were prepared .One syringe contained the diluted clonidine [15mcg/ml] to give a dose of 2mcg/kg [a total volume of 0.13ml/kg] and the other contained same volume of normal saline. The caudal block was performed with the child positioned in left lateral position using an aseptic technique and a 22 gauge needle. After negative aspiration of blood and cerebrospinal fluid, bupivicaine 0.25 percent, 1ml/kg was injected.

Simultaneously, the content of second syringe, containing, the same volume of either study medication or saline was administered i.v. The anaesthetist and all nursing staff involved in the care of child during the study period were blinded to the contents of the two syringes with the study medication. Heart rate, non-invasive blood pressure and peripheral oxygen saturation [SPO_2] were recorded after induction of anaesthesia and every 10 minutes there after intra-operatively. An intra operative decrease in baseline arterial pressure or heart rate of greater than 15 percent from preoperative values were defined as hypotension or bradycardia respectively and were treated with rapid infusion of normal saline 10-20ml/kg or i/v atropine 10mcg/kg. An intra-operative increase in baseline arterial blood pressure or heart rate of greater than 10 percent were defined as insufficient analgesia and were treated with additional doses of intravenous morphine 1micro gm/kg as needed. After surgery the children were transferred to the recovery room when they were sufficiently awake and capable of maintaining airway. In the recovery room the patients were given nurse controlled analgesia [NCA] which means children were given intravenous paracetamol [10-15ml/kg] by nurses for analgesia.

At the time of inclusion all children and their parents were told the principles of nurse controlled analgesia. In recovery heart rate, SPO_2 and blood pressure were monitored every 30 minutes until the child was awake and cooperative. During the study period pain was recorded by experienced nurses blinded to the treatment groups, every 1 hour after surgery using a scale of observational pain score. The indication for administering first paracetamol dose [intravenous] and subsequent doses was at a pain score greater than 4. In post-

operative ward the children were under constant supervision by experienced nurses, and hence any pain experienced by children were treated if and when it occurs.

The duration of post operative analgesia was defined as the time between administering the study drug [caudally or i/v] and the first activation of NCA with intravenous paracetamol.

STATISTICAL ANALYSIS

The statistical analysis of the data was done by using test statistic student's 't'-test for difference of means and chi-square test for nominal data. These tests were two sided and were referred for p-values for their significance. Any p-value less than 0.05 i.e. ($p < 0.05$) was considered statistically significant otherwise non-significant. The analysis of the data was performed by using comprehensive statistical package, Statistical Package for Social Sciences (SPSS, Version 14.0), Chicago, U.S.A. For Windows.

RESULTS

This prospective randomized double blind study was conducted to evaluate the efficacy of caudal bupivaciane supplemented with caudal clonidine or i/v clonidine for caudal block in children for post operative analgesia undergoing sub umbilical surgeries. Sixty patients selected for this study were randomly divided into two groups of 30 patients each:

GROUP A. received 1ml/kg of 0.25percent bupivicaine hydrochloride in addition to 2mcg/kg of clonidine caudally and similar volume of normal saline intravenously.

Group B received 1ml/kg of 0.25 percent bupivicaine hydrochloride and 2mcg/kg clonidine intravenously and simultaneously same volume of saline caudally.

The mean age in group A was 4.48 ± 2.27 and in group B was 3.87 ± 1.75. The difference in age (years) in two groups was non-significant. 96.67% males were present in group A, while as 93.33% males were present in group B. Also 3.39% females were present in group A and 6.67% females were present in group B. From chi-square value the difference was found out to be statistically non-significant.

In group A an analgesic time was 428 ± 197, while in group B it was 404 ± 196. The difference was statistically non-significant. The patients in the two groups did not differ significantly with respect to duration of surgery. ($p > 0.05$).

At 30 min 93.33% cases were having pain score of 3 in group A and 96.67% were having pain score of 3 in group B. In group A 6.67% and in group B 3.33% were having pain score of 4. At 12 hours a pain score of 3 was observed in 46.67% children in group A and 33.33% in group B. Pain score of 4 was observed in 33.33% children in group A and 46.67% in group B. Pain score of 5 was observed in 20.00% patients in both groups. The difference in pain score between two groups was found to be statistically nonsignificant. The mean pain scores were comparable between two groups at all stages post operatively till 12 hours. 14 patients in group A required rescue analgesia at least once as compared to group B where 16 patients needed rescue analgesia once during the 12 hours study period. Similarly 12 patients in group A and 10 patients in group B required rescue analgesia twice during 12 hour study period. It was observed from the study that comparable number of patients in the two groups required rescue analgesia and the difference was found to be statistically non significant. ($P > 0.05$)

Vomiting was observed in 3 patients in group A and 2 patients in group B. Nausea was observed in only 1 patient in group B, whereas urinary retention in 2 and 3 patients respectively in groups A and B. 1 patient in each group had pruritis. 24children in group A and 23 children in group B had no complications. The difference in incidence of complications in both the groups was statistically insignificant. ($P > 0.05$).

DISCUSSION

Caudal epidural block is one of the most common regional anaesthetic techniques used in children. It is generally considered a simple and safe procedure but its main disadvantage is its relatively short duration of action, even with the use of long-acting local anaesthetic agents such as bupivacaine[12]. In order to improve the duration of action and quality of analgesia of a caudal block with bupivacaine, various drugs have been used, e.g. opioids, epinephrine, midazolam, neostigmine, ketamine and clonidine[11]. All these agents have potential side-effects. Since the discovery that epidural clonidine, an alpha 2 receptor agonist, produces analgesia[13], the drug has been used increasingly in anaesthetic practice[14]. During the last decade the use of clonidine has become increasingly popular in paediatric anesthesia, particularly when administered caudally with a local anaesthetic agent[15]. Clonidine has been shown to produce analgesia without causing significant respiratory depression after systemic, epidural or spinal administration. Serious adverse effects are uncommon in the dose range (1-2 µg/kg body weight) normally used in children[16]. The addition of clonidine as an adjuvant has allowed the use of lower concentration of the local anaesthetics for achieving the same level of anesthesia but with a prolonged duration of analgesia which increases the margin of safety and reduces the incidence of unwanted motor blockade[17]. The present study was carried out to evaluate the analgesic efficacy of caudal or i/v clonidine as an adjunct to caudal bupivacaine for post operative pain relief in children. Two groups of 30 patients each were randomly selected for the study: GROUP A. received 1ml/kg of 0.25percent bupivicaine hydrochloride in addition to 2µg/kg of clonidine caudally and similar volume of normal saline intravenously. GROUP B. received 1ml/kg of 0.25 percent bupivicaine hydrochloride and 2 µm/kg clonidine intravenously and simultaneously same volume of saline caudally.

Both the groups were homogenous with reference to age, sex, weight and duration of anesthesia and surgery. Although males dominated in both groups, yet the difference in male female ratio between the groups was statistically insignificant ($p = 0.554$). Mean weight of patients in group B was 15.10 ± 5.25 kg as compared to 16.75±4.60 kg in group A($p=0.43$). Heart rate, blood pressure (systolic and diastolic) and oxygen saturation were recorded just before and after induction of

anesthesia and at 10 minute interval after caudal block till the end of surgery. No significant differences with respect to mean heart rate, blood pressure (systolic and diastolic) and oxygen saturation were noted during perioperative period between the groups. No patient required drug therapy to treat hypotension or bradycardia. No episode of oxygen saturation < 95% was recorded. Our results correlate with the study of T.G Hansen et al[17] observed no significant differences in mean arterial pressure and heart rate with the administration of 2µg/kg of clonidine (caudal or i/v) to patients undergoing subumblical surgeries. Our results also correlate with the study of Aynur Akin et al (2010)[18] who observed no significant differences in mean arterial pressure and heart rate with the administration of 2µg/kg of clonidine (caudal or intravenous) to patients undergoing subumblical surgeries. Our results are contradictory to that of Syed Hejazi M et al (2008)[19], who have reported that heart rate, systolic and diastolic blood pressures were significantly lower in clonidine bupivacaine combination group than in bupivacaine alone group. As in our study we did not use any premedication, which may potentiate the action of clonidine and the dose of clonidine used was minimal (2µg/kg), so hemodynamic variations were not observed. Furthermore it is possible that caudally administered clonidine results in less hemodynamic changes than systemically administered clonidine. In our study, the quality of analgesia postoperatively was assessed using observer pain scale at 30 minutes intervals while in recovery room and thereafter 2 hourly for 12 hours. We found patients in group A had comparable pain scores during 12 hour study period as compared to group B and the difference was statistically insignificant. (P>0.05). 16 (53.33%) patients in group A received single dose rescue analgesia as compared to only 14 (46.67%) patients in group B during 12 hour study period. Whereas 10(33.33%) patients in group A and 12 (40.00%) patients in group B received two doses of rescue analgesia during the 12 hour study period The difference was statistically insignificant between the two groups. (P<0.05). The mean duration of analgesia in group B was 404 ± 196 minutes. while in group A mean duration of analgesia was 428 ± 197 minutes. The duration of analgesia in group A and B was comparable and the difference was statistically insignificant (p=0.64). Our observation correlate with that of T.G Hansen et al (2007)[17],who in their study observed better and longer post operative analgesia with caudal or intravenous clonidine when added to caudal bupivacaine. This was confirmed by longer time of interval to first request of analgesic dose. Our observation also correlate with that of Aynur Akin et al (2010)[18],who in their study observed better and longer post operative analgesia with caudal or intravenous clonidine when added to caudal Levobupivacaine. This was confirmed by longer time to first request of analgesic dose. Our observation correlate with that of Motsch J et al (1997)[20], who in their study also observed significantly better and longer post operative analgesia with caudal clonidine and bupivacaine as compared to bupivacaine alone. This was confirmed by longer time of interval to first request of analgesic and by lower number of analgesic requirements. Lee JJ and Rubin AP (1994)[21] also observed that caudal analgesia in children with clonidine - bupivacaine combination resulted in longer duration of post operative analgesia and reduced frequency of parental opiod administration. Yildiz T.S et al (2006)[22] also observed that children undergoing elective inguinal repair receiving caudal clonidine – bupivacaine combination had increased duration of post operative analgesia without any respiratory and hemodynamic side effects. Jamali et al. (1994)[16] also observed that duration of post operative analgesia with caudal bupivacaine was significantly increased by addition of 1µg/kg of clonidine.

CONCLUSION

The duration of analgesia in group B was 404 ± 196 minutes while in group A the duration was 428 ± 197 minutes. Maximum observational pain score (OPS) scores were comparable between the two groups. The number of rescue analgesia dose requirement was comparable between the two groups. The difference was statistically insignificant (P>0.05).

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