ORIGINAL RESEARCH PAPER

Anaesthesiology

EFFICACY OF CLONIDINE AS AN ADJUVANT TO BUPIVACAINE FOR CAUDAL ANALGESIA IN CHILDREN UNDERGOING SUB UMBILICAL SURGERY

KEY WORDS: Caudal, Bupivacaine, Clonidine, Children

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ABSTRACT

Study is done on caudal epidural block using bupivacaine alone and bupivacaine with clonidine combination was conducted in 60 children in the age group of 1 to 8 years of ASA grade I and II coming for various elective sub-umbilical surgeries which include herniotomy , circumcision,orchidopexy, perineal surgeries.Theywere divided into two groups of 30 each. Group A received caudal bupivacaine 0.25% (1ml/kg). Group B received caudal bupivacaine 0.25% (1ml/kg) with clonidine (1 g/kg).The main parameters studied were hemodynamic changes, duration of post-operative analgesia and incidence of side-effects. Both the groups were comparable with respect to age, sex and weight distribution. Post-operative analgesia was assessed by using Paediatric Objective Pain scale.The mean duration of post-operative analgesia was 252 ± 40.7 min in group A and 433.5 ± 60.2 min in group B, thereby reducing the requirement of analgesics in group B in the post-operative period.There was no significant difference between the two groups with respect to haemodynamic parameters.

Caudal epidural block is one of the most common regional anaesthetic techniques used in children. It is generally considered a simple and safe procedure and its main disadvantage is the short duration of action, even with the use of long acting local anaesthetic agents such as bupivacaine.[1] Bupivacaine has short duration of action about 4-6 hrs when administered as a single shot technique. Several adjuncts such as opioids , ketamine, midazolam, clonidine and neostigmine have been used with bupivacaine to prolong its action & thus extend the duration of post operative analgesia provided by the 'single shot' caudal technique.[2,3,4]

Clonidine, an alpha 2 agonist has extensively been used in neuraxial blocks and peripheral nerve blocks to prolong the action of bupivacaine. It is one of the most commonly used additives with bupivacaine for caudal analgesia in children.[5]

Clonidine has been shown to produce analgesia without causing significant respiratory depression after systemic, epidural or spinal administration. Although epidural clonidine may also cause hypotension, bradycardia and sedation in higher doses, serious adverse effects are uncommon in the dose range normally used in children(1-2 μg/kg).[1]

Clonidine action is similar to local anaesthetic action and its interaction with local anaesthetics have been explained with three possible mechanisms.First, clonidine blocks Aδ & C fibers as a consequence of an increase in potassium conductance in isolated neurones, thus intensifying local anaesthetic conduction block. Secondly, clonidine may cause local vasoconstriction thus decreasing the local spread and removal around neural structures. This effect is mediated by drug action on post synaptic alpha$_2$ receptors, although there is little evidence of this mechanism with clinical doses. Thirdly, clonidine combined with spinal local anaesthetics or used in peripheral blocks intensifies and prolongs analgesia.[6]

The role of clonidine in improving and prolonging the analgesia produced by caudal bupivacaine is highly variable in different published studies. Also the duration of post operative analgesia using caudal clonidine bupivacaine mixtures is also highly variable[5]

With this in mind, we conducted this study to assess the efficacy of clonidine in prolonging the action of bupivacaine when used for caudal epidural analgesia in children undergoing infra umbilical surgeries.

METHODS:

Keeping the confidence limit at 95% and power of study at 80%, the minimum sample size required in each group is 21. We have included 30 patients in each group for better validity of result.(http://www.openepi.co m/SampleSi ze/SS M ea n. htm)

After obtaining institutional ethical committee approval and informed consent. A prospective randomised double blind controlled study is planned in 60 patients of ASA 1 & ASA 2 physical status aged between 1 to 8 years scheduled to undergo elective surgery. Patients satisfying all the above criteria will be enrolled in the study and will be randomly allocated into two groups:
Group A(n=30) Patients receiving 1 ml/kg 0.25% bupivacaine in normal saline

Group B(n=30) Patients receiving 1 ml/kg of 0.25% bupivacaine with 1 μg/kg of clonidine in normal saline.

Children with sacral spine abnormalities, local site infection & coagulation abnormalities.Patients with haematological diseases, neurologic, psychiatric disease, severe renal and hepatic derangement.excluded from the study.

A prospective randomised double blind study is planned. The study solutions will be prepared by an anaesthesiologist not involved in the patients care. Patient and anaesthesiologist who will deliver the caudal epidural analgesia will be blinded by the study solutions. All pre-anaesthetic evaluation of the patients will be carried out by the anaesthesiologist a day before the surgery. All patients who belonged in the inclusion criteria, a written informed valid consent taken by their parents.Twenty minutes before the surgery all patients received midazolam 0.5-0.75 mg/kg orally. In the operation theatre, a good peripheral intravenous access will be secured using 22 G or 24 G iv cannula depending on the age of the patient. Baseline non-invasive blood pressure, pulse rate, electrocardiograph, pulse oximetry will be recorded. All patients will receive Berilyte-P or Ringer Lactate as preloading solution before the block depending on the age group. Intravenous fluids will be given as per calculated fluid requirement and operative loss requirement.

All patients airway management will be left to the discretion of the attending anaesthesiologist with either the facemask, laryngeal mask airway or endotracheal tube with or without skeletal muscle relaxants. Patients will be put in lateral decubitus position after induction and a single shot caudal block will be performed under aseptic precautions using a 23G hypodermic needle. Patients in Group A will receive 0.25% isobaric bupivacaine 1 ml/kg in normal saline and Group B will receive 1 ml/kg of 0.25% bupivacaine with

1μg/kg clonidine in normal saline. One millilitre of clonidine contains 150 μg/ml which is diluted with 9 ml saline in a 10 ml syringe. For each child two syringes are prepared : one syringe contained the diluted clonidine(15 μg/ml) to give a dose of 1 μg/kg (a total volume of 0.07 ml/kg), and the other contained the same volume of normal saline.

Baseline pulse rate, respiratory rate, non invasive blood pressure will be recorded.

Post-operative analgesia is assessed by Paediatric Objective Pain Scale **(Table 1).**

TABLE 1: PAEDIATRIC OBJECTIVE PAIN SCALE

Observation criteria	Criteria	Points
Blood pressure	+/- 10% of preoperative value >20% of preoperative value >30% of preoperative value	0 1 2
Crying	Not crying Crying but responds to tender loving care Crying with no response to tender loving care	0 1 2
Movement	None Restlessness Thrashing	0 1 2
Agitation	Asleep Mild Hysterical	0 1 2
Posture	No special posture c/o mild pain (can not localise) Moderate pain (can localise) verbally or by pointing or adopts position with legs drawn up and moves hand to painful stimuli or tries to protect it.	0 1 2

The assessment was done for a period of 24 hours after caudal block. These assessments were made at 1,2,3,4,8,12 and 24 hours after caudal block.

Duration of analgesia will be recorded as the time interval from the completion of anaesthesia to the time when the patient complains of pain. In the post anaesthesia care unit, the necessity for rescue medicine was decided by the pain score. Rescue medication was administered when the OPS score was greater than or equal to 6. Rescue analgesia was administered as paracetamol suppository (15mg/kg). During surgical procedure adverse effects like vomiting, hypotension(defined as systolic BP less than 70 mm/Hg), bradycardia(heart rate less than 80 beats/minute) and respiratory depression (defined as O_2 saturation less than 93%, requiring oxygen via face mask) will be recorded.

Sedation will be assessed by four point sedation score**. (Table 2)**

TABLE 2: 4-POINT PATIENT SEDATION SCORE

1	Asleep, not arousable by verbal command
2	Asleep, arousable by verbal command
3	Drowsy/ not sleeping
4	Awake/ alert

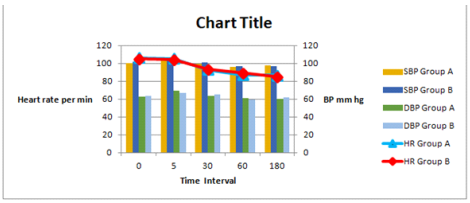
RESULTS

Analysis of patient results revealed no differences in the demo graphic characteristics of the two groups **(Table 3).**Demo gra phic parameters age,weight, gender are equally divided in the two groups. The types of surgeries included herniotomy, circumcision, orchidopexy,and anorectal surgeries.There was no significant difference in hemodynamic parameters shown in (**graph 1)**

Table 3: Demographic parameters

parameter	Group A(30)	Group B(30)	N
Age	5.7+/-1.5	5.57+/- 1.28	0.39
Weight	15.4+/-2.31	15.13+/-2.3	0.98
Gender	26 (male) 4 (females)	28(male) 2 (females)	0.38

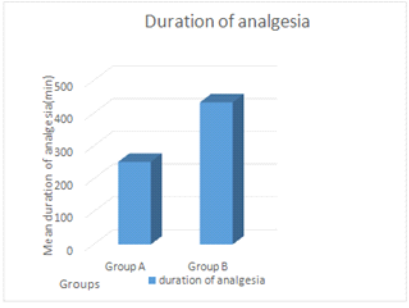
Graph 1



The distribution of subjects in the two study groups according to pain score ≥6 and requirement of rescue analgesia at various monitoring intervals.The Paediatric Objective Pain Score was below 6 at the end of first and second hour in both the groups and did not require any analgesia. At the end of third hour, 1(3%) of the patients in group A had a pain score of ≥6 whereas none of The patients had a score of ≥6 in group B, which was found to be statistically insignificant ($p > 0.05$).At the end of fourth hour, 14(47%) of patients in group A had a pain score of ≥6 and only 1(3%) in group B had similar pain score. It was statistically highly significant ($p<0.01$)

The mean duration of analgesia was 250.33 ± 41.4 min in group A with a range of 180 to 355 min. In group B, the mean duration of analgesia was 433.5 ± 60.2 min with a range of 265 to 530 min. The difference in the mean duration of analgesia was statistically highly significant ($p<0.001$). as shown in **Graph 2**

Graph 2



The sedation score at the end of first, second and third hour was less than 3 in both the groups and the children were sleeping but responding to verbal commands. At the end of fourth 9(30%) of patients in group A and 29(27%) of group B had a score of <3 (p value 0.001) At the end of 8th hour 0 in group A and 14(46%)of patients in group B respectively had a score of ≤3, indicating a significant difference (p value <0.01)in the sedation score between the groups at that time. At the end of 12 and 24 hour, all the patients in group A were awake and alert.

There was no incidence of hypotension, bradycardia, dural or vessel puncture and respiratory depression in the two groups.

DISCUSSION

In this study, caudal epidural block using bupivacaine alone and bupivacaine with clonidine combination was conducted in 60 children in the age group of 1 to 8 years of ASA grade I and II coming for various elective infra-umbilical surgeries which include herniotomy , circumcision, orchidopexy, perineal surgeries.

our study indicates that Clonidine as an additive in a dose of 1µg/kg to caudal Bupivacaine 0.25%. prolongs duration if analgesia.

Parameshwari et al[5]and Meghnani et al[7] Jamali et al[8] have used similar dose of clonidine 1µg/kg to bupivacaine 0.25% 1ml/kg.Both these studies have concluded that addition of clonidine prolongs the duration of analgesia without any side effects.

We used Inj. Glycopyrrolate 0.04mg/kg iv and oral midazolam as pre-medication in all children. We wanted to keep premedication uniform to avoid confounding effects of the premedication in assessment of post-operative analgesia. Patient was induced with oxygen and nitrous oxide and sevoflurane in increasing concentration either on spontaneous respiration or controlled ventilation with ET intubation with Jackson and Reis circuit and then caudal block was performed in left lateral position. This ensured that the child is motionless during the procedure to avoid the complications like dural puncture, intravascular puncture or breakage of needle, resulting in high success rate.

Caudal block was performed with 23G short hypodermic needle. All patients were monitored for 24 hours postoperatively for duration of analgesia and side effects. In present study we have used peadiatric objective pain score post operatively for assessment of pain. If the score was more than 6 at any interval for more than 2 consecutive interval of 10minutes, supplementary analgesia with rectal Paracetamol (15mg/kg) was administered.

Concentration of Bupivacaine we have used is 0.25% Bupivacaine 1ml/kg was similar to many studies. Armitage[9] has recommended 0.25% Bupivacaine in a dose of 0.5ml/kg for lumbo-sacral, 1ml/kg for thoraco-lumbar, 1.25ml/kg for mid-thoracic level of block and the plasma bupivacaine levels were always below 1.2µg/ml, which was below toxic levels.

Gunter et al[10] have studied caudal anaesthesia in 1-8 years children with six different concentrations of Bupivacaine. They have concluded that the patients receiving 0.125% Bupivacaine had a higher pain score on arrival to PACU than did those patients receiving 0.2% . They have concluded that the higher concentration of Bupivacaine causes motor weakness and delayed discharge.

In our study, we have used a single dose of 0.25% Bupivacaine (1ml/kg) since all the patients in our hospital were monitored for 24 hours post operatively.

In our study we have used Clonidine as an additive in a dose of 1µg/kg to caudal.Several adjuvants have been used to prolong the duration of analgesia of bupivacaine for caudal analgesia in children.[2,3,4] The use of opioids is associated with an increased incidence of pruritus and post-operative nausea and vomiting[4] .The advantage of clonidine is that it prolongs the duration of analgesia without an increase in the incidence of respiratory depression, pruritus and urinary retention which are commonly seen with neuraxial opioids.

Cook et al[2] and Lee et al[11] used Clonidine (2 µg/kg) with Bupivacaine 0.25% (1ml/kg) caudally in children aged 1-10 years orchidopexy and orthopaedic surgery respectively. There is increase duration of sedation with (2µg/kg) Clonidine. To avoid this we have used Clonidine in a dose of 1µg/kg.

Klimschaet al[12] demonstrated that in small children (mean age of 3years) undergoing day care hernia repair, they have found that increasing dose of Clonidine from 1 to 2 µg /kg did not enhance the analgesic effect of Clonidine .Therefore we have used caudal Clonidine in a dose of 1 µg/kg.

Sharpe et al[13] concluded that addition of caudal Clonidine 1 µg/kg in one group and 2 µg/kg in other group to small volume of Bupivacaine 0.125%(0.5ml/kg) does not significantly prolonged the duration of analgesia. Low volume may not be enough to deliver the Clonidine up to the spinal cord, leaving only direct action on nerve routes in the caudal area. Hence in our study we have decided to use caudal Clonidine 1 µg/kg to Bupivacaine 0.25% 1ml/kg.

In our study there was no significant change in haemody namic parameters during intraoperative and post operative periods. Mosch et al[14] found that there is fall in heart rate and BP in first 3 hours of surgery in children receiving (5 µg/kg)which is relatively higher dose as compared to control group.

Pain assessment is the most important and critical component of pain management. Assessing pain in children is an ever challenging as well as a difficult task, mainly because so far no reliable, universal method of assessing and measuring child's pain is available. In our study, we have used Paediatric Objective Pain scale which is a valid, objective and reliable method of pain assessment in children between 1 to 8 years. If the pain score is more or equal to 6 at 2 consecutive intervals of 10 minutes, supplementary analgesic with rectal paracetamol (15 mg/kg) was given.

There was no incidence of pain score ≥ 6 at the end of 1stand 2ndhour in either groups. At the end of 3rd hour, 1(3%) of children in group A and none of the children in group B had a pain score of ≥ 6. It was not statistically significant($p>0.05$).

At the end of 4thhour 14(46%) of children in Group A and only 1(3%) of children in group B had pain score > 6, which is highly significant ($p<0.01$).The duration of analgesia was significantly prolonged in bupivacaine-clonidine group(433.5±60.2 min) compared to bupivacaine alone group (252.±60.2 min)in our study. ($p<0.00001$).results are similar to other studies[6,7,8,11]

The duration of analgesia achieved by the addition of clonidine to bupivacaine varies widely in different studies. This may be the result of a number of factors: like dose of clonidine used; differences in premedication and volatile anaesthetics used; type of surgery; indications for rescue analgesia; assessment of pain(FACES scale, VAS scale, FLACC scale, CHEOPS scale)

The addition of clonidine to bupivacaine in our study, did not result in an increase in the incidence of side effects. The main side-effects of epidurally administered clonidine are bradycardia, hypotension and sedation. In our study, bradycardia or hypotension warranting treatment did not occur. Sedation, as mentioned earlier, correlated well with the duration of analgesia.

In our study, 3 of the children in group A and 2 of them in group B had an episode of vomiting which was treated with Inj. Ondensetron (0.05 – 0.08 mg/kg) IV. The incidence of vomiting was comparable in both the groups, 9% and 6% in group A and B respectivelyssThere was no evidence of dural puncture, intravascular or intraosseous injection of drug during the procedure motor weakness or urinary retention after caudal block.

CONCLUSION

The present study demonstrated that caudal admin istr ation of bupivacaine 0.25%
(1ml/kg) with clonidine (1µg/kg) resulted in

a. Superior analgesia
b. Longer duration of action compared with 0.25%bupi vacaine (1ml/kg) alone.
c. Without any significant difference in the hemodynamic parameters

d. The incidence of side-effects except vomiting

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