Research Paper

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A comparative study of caudal bupivacaine and bupivacaine with clonidine for post-operative analgesia in paediatric patients

Medical Science

KEYWORDS : caudal, epidural, bupivacaine, clonidine

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ABSTRACT

Pain in infancy is a developmental process. Due to the underdeveloped pain pathways in the spinal cord, the threshold of stimulation and sensation of pain is low at birth and has potential impacts on increasing the central effects of pain. Primary trauma during infancy can cause long term changes in structure and function of pain pathways that continue until adulthood. Lack of pain management in children can result in morbidity and mortality This is a study of 60 patients of 2-12 years age weighing ≤ 20 kg of ASA status I & II undergoing elective infraumblical surgeries.. They were randomly divided into two groups of 30 each .Group A received 0.5% plain Bupivacaine 2mg/kg and normal saline. Group B received 0.5% Bupivacaine 2mg/kg with1 ug/kg clonidine and normal saline ,making it 1 ml/kg. We found that the duration of analgesia and sedation was higher in group B in post operative period . Need for postoperative rescue analgesics were also less in group B

Introduction

Pain is one of the most misunderstood, underdiagnosed and untreated medical problems particularly in children. It is a likely reflection of myths like the child's lack of ability to perceive pain or remember painful experiences and relative lack of knowledge about age specific aspects of physiology and pharmacology and routine pain assessment.[1]

New JACHO (joint commission on accreditation of health care organization) regards pain as the fifth vital sign and requires care givers to regularly address and assess pain. Since October 17th, 2005 focus on children's pain started with IASP's Global day against pain in children.[13]

IASP (International association for study of pain) defines pain as "An unpleasant emotional and sensory experience associated with actual or potential tissue damage or described in terms of such damage". It further states that pain is always subjective .Each individual learns the application of the word through experiences related to injury in early life, thus it emphasises the importance of early pain experiences in shaping the response to future pain. Inadequate pain relief during childhood may have long term negative effects including harmful neuroendocrine responses, disrupted eating and sleep cycles and increased pain perception during subsequent painful experiences. [11]

Post-operative pain has adverse psychological effects in child. Pain can result in restless and uncooperative patient. So, it is preferable to prevent the onset of pain rather than to relieve its existence.

Various multimodal techniques for pediatric pain relief have been designed. These involve regional anesthesia with systemic analgesics, out of which the most commonly used regional block in pediatrics is caudal epidural block.

Caudal block was first studied by Cathelin and Secard (1901) and described extensively by Kay[4] (1974), is favoured due to ease of performance and the extensive safety record in children. Other advantages of caudal block are early extubation, ambulation and decreased risk of chest infections, decreased post-operative analgesic requirements and early discharge.

One of the disadvantages of caudal block is relatively short duration of analgesia. Various additives eg. Ketamine, Neostigmine, Clonidine, Ephedrine and opioids have been used to prolong the duration of analgesia provided by single injection. Ketamine has potential risk of neurotoxicity and opioids have side effects such as nausea, vomiting and respiratory depression. [8] Clonidine, an alpha -2 adrenergic agonist is a known antihypertensive agent . Because of its sedative and analgesic effects, it is gaining popularity in anesthesiology. Clonidine produces analgesia by interacting with alpha 2 adrenergic receptors, located on superficial laminae of spinal cord and brain stem nuclei .It does demonstrate adverse effects like sedation, hypotension and bradycardia.[6,9,11,12,15] Using Clonidine makes catheter placement unnecessary for pediatric procedures, reducing the overall morbidity and cost of regional block procedure[18].

Considering the above facts, the present study was designed using Bupivacaine alone and Bupivacaine with clonidine in order to assess analgesic efficacy, duration of postoperative analgesia, hemodynamic stability, post -operative sedation and any adverse effects in children undergoing infraumblical surgeries.

Materials and method

A written informed consent was obtained from all the parents of the children who were included in this study. This study was conducted in 60 children of ASA physical status I and II, weighing less than 20 kg undergoing elective infra-umbilical surgeries like herniotomy, orchidopexy, hypospadiasis repair etc. during the period from year 2010 -2013. Patients with history or evidence of infection at back, allergy to drugs, congenital malformations of the back, pre-existing neurological or spinal diseases were excluded.

All the patients underwent a pre-anesthetic check-up the day before surgery and all the routine investigations were noted. The children were electively kept Nil by mouth for 6 hours before surgery and prior to operation a written and informed parental consent was taken. Intravenous line was secured. Standard monitors like ECG, pulse oximeter and NIBP were applied. All children were premedicated intravenously with Glycopyrrolate 0.04 mg/kg, Emset 0.1mg/kg , Midazolam 0.1mg/kg.and Ketamine 1mg/kg was given and the child was placed on his/her left lateral decubitus position. Caudal block was induced using 23-guage needle and after making sure that blood or CSF was not found in aspiration, anesthetic drug was injected. According to the drug administered the patients were randomly allocated into 2 groups:

Group A (control)	(0.5%) plain Bupivacaine 2mg/kg + Normal saline
Group B (study)	(0.5%) plain Bupivacaine 2mg/kg + 1µg/kg Clonidine + Normal saline

Total 1ml/kg anesthetic solution was injected. The site of injection was dressed and the patient was turned supine. Then patient was given Inj. Propofol 2mg/kg and LMA was positioned and fixed. Anesthesia was maintained on O_2 + N_2O + Sevoflurane.

Heart rate, blood pressure, respiratory rate and oxygen saturation were recorded before induction and immediately after caudal anesthesia and every 15 minutes during surgery thereafter. Adequate analgesia was defined as hemodynamic stability as indicated by the absence of an increase in SBP or HR of more than 20% compared with baseline value and from intra-operative requirement of inhalational agent. A decrease in MAP>30% was defined as hypotension and was treated with intravenous fluids/ Inj. Ephedrine. A decrease in HR>30% was considered as bradycardia and was treated with Inj. Atropine 0.01 mg/kg.

After completion of surgery LMA was removed after thorough oral suction.

All patients were observed for 2 hours in recovery room before returning to ward. HR, BP, RR were monitored continuously. Postoperative pain was assessed at 30 min,1, 2, 4, 6 ,8, 10, 12, 18 and 24 hours after recovery from anaesthesia using observer pain score(OPS).

Duration of analgesia (time from caudal block to first dose of rescue analgesic or OPS >= 12) was recorded. Postoperative rescue analgesia was given in form of paracetamol 10 mg/kg suppository. The time of first rescue analgesia received and total number of doses received in 12 hours were noted in all the groups postoperatively.

Patients were randomly assigned to receive either (Bupivacaine + saline) or (Bupivacaine + Clonidine +saline)in each group. All assessments were made by single **observer in double blind fashion**

OBSERVATIONAL PAIN SCORE (OPS)

BEHAVIOURAL OBJECTIVES	NONE	MODERATE	SEVERE
Facial expression	1	2	3
Crying	1	2	3
Position of legs	1	2	3
Position of torso	1	2	3
Motor restlessness	1	2	3

Sedation score was noted at 15 min, 30 min, 45 min, 1hr, 2hr, 4hr, 6hr, 8hr, 10hr and 12 hrs after recovery from anesthesia using objective score based on eye opening.

Eyes open spontaneously (score 0), eyes open in response to verbal command (score 1), eyes open in response to physical stimulus (score 2), unarousable (score 3). The incidence of adverse effects such as nausea, vomiting, respiratory depression and sedation was evaluated. Respiratory depression was defined by RR< 10 breathes / min.

All the observations were recorded and all the results were analysed. Statistically data were presented as mean +- S.D. Analysis was performed. A value of P<0.05 was considered as a statistically significant difference with unpaired students t test. Statistical software was used from Graphpad.com

Results

Mean age, weight and sex distribution in all groups were without any significant differences .

Table 1
Surgical procedures

Surgical procedures	Group A	Group B
Hypospadias repair	7	7
Hip spica + ORIF	11	10
Scrapping + STG	1	3
Circumcision	3	0
Herniotomy	8	5
Orchidopexy	0	1
Cystolithotomy	0	2
Hydrocele sac excision	0	2

Table-2 : Duration of surgery

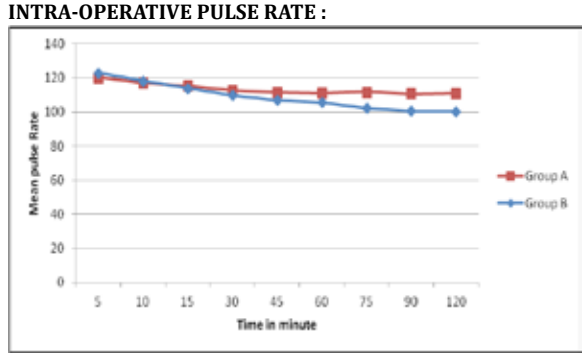
Duration (min)	Group A	Group B
0-30	1 (3.33%)	0
31-60	13 (43.33%)	16 (53.33%)
61-90	7 (23.33%)	7 (23.33%)
91-120	9 (30%)	7 (23.33%)
Mean±SD	81.5±29.91	77±28.60

Maximum surgeries 13 (43.33%) in Group A and 16 (53.33%) in Group B were of 30-60 minutes. Duration remaining almost same as seen by mean of all the groups.

PREOPERATIVE VITALS (Mean±SD)	Group A	Group B	P value
Pulse	112.73±11.66	112.4± 10.70	>0.05
BP	97.93± 6.73	93.13± 6.33	<0.05

Table 3 shows that there was no significant difference in preoperative pulse rate (p value >0.05) but there was reduced BP in Group B (93.13±6.33) as compared to Group A (97.93±6.73) which was statistically significant (p value <0.05).

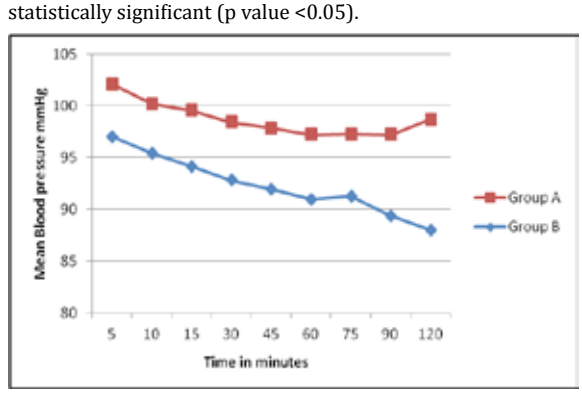
INTRA-OPERATIVE PULSE RATE :



Graph 1 shows there was no significant difference in intra-operative pulse rate (p value >0.05).

INTRA-OPERATIVE BLOOD PRESSURE

Graph shows there was reduction in mean BP in Group B (92.31±2.85) as compared to Group A (97.59±3.99) which was statistically significant (p value <0.05).



Graph 2 Mean intraoperative Blood Pressure

POST-OPERATIVE PULSE RATE: Graph 3 shows that mean pulse rate decreased in Group B (105.32±1.37) as compared to Group A (112.61±0.57) in post-operative period which was statistically significant (p value <0.05).

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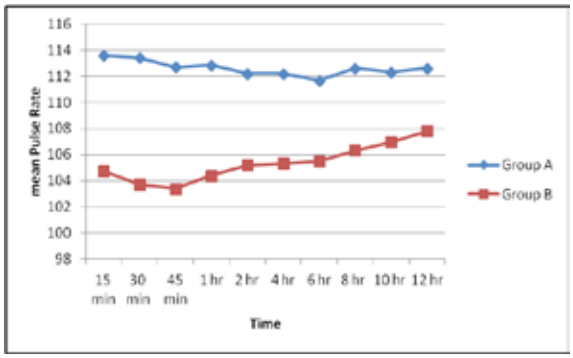
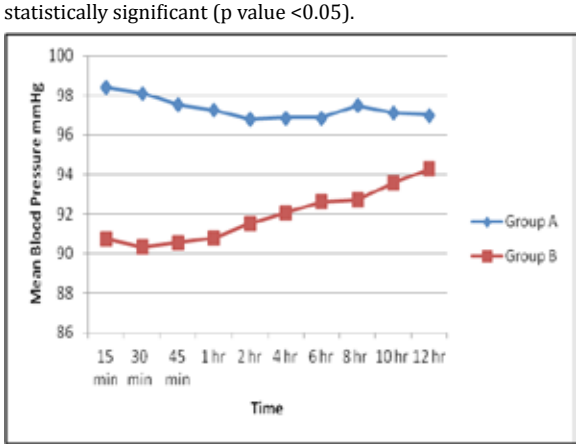


Graph-3 Mean post-operative Pulse Rate

POST-OPERATIVE BLOOD PRESSURE Graph -4 shows there was reduction in mean BP in Group B (91.92±1.36) as compared to Group A (97.33±0.55) in post-operative period which was statistically significant (p value <0.05).



Graph-4 Mean Post-operative Blood Pressure

Table- 4-Mean duration of caudal analgesia in hours

	Group A	Group B	P-value
Mean duration of caudal analgesia Mean±SD	4.54±1.17	10±1.15	<0.0001 (significant)

The duration of caudal analgesia was defined from the time of caudal injection to the time, the child first complained of pain or the time of first post-op rescue analgesic required. Table-4 shows the duration of post operative caudal analgesia in both the groups. This duration was significantly prolonged by addition of Clonidine to Bupivacaine

Table-5 Mean OPS Score (post-operative)

Post-operative duration	Mean ± SD (n=30)		P-value
	Group A	Group B	
30 min	5.36±0.66	5.06±0.25	<0.05
1hr	7.2±1.42	6.33±0.60	<0.05
2hr	9.93±1.85	6.96±0.80	<0.05
4hr	11.23±2.50	8.38±0.96	<0.05
6hr	7.86±2.55	10.03±0.92	<0.05
8hr	8.73±1.43	10.36±1.56	<0.05
10hr	9.26±1.76	11.93±3.40	<0.05
12hr	11.03±2.23	6.43±1.30	<0.05
Mean OPS Score	8.82±0.63	8.18±0.96	<0.0001

Table 5 shows the OPS score in post operative period. There was no significant difference in OPS score in immediate post operative period. Thereafter, in Group A OPS reached to 11.23 ± 2.50 at 4 hours (significantly more). In Group B, OPS remained below 11 till 10 hours and were not given rescue analgesic till that time, which was statistically significant from 4 hours to 10 hours.

Table-6: No of Rescue Analgesics required

No. of Rescue Analgesia required In 12 hours	Group A	Group B
0	0	1 (3.33%)
1	8 (26.66%)	29 (96.66%)
2	22 (73.33%)	0

Table-6 shows that Group B required less number of rescue analgesics as compared to Group A. In Group A, 22 (73.33%) patients required 2 rescue analgesic within 12 hours. In Group B, 29 (96.66%) patients required single rescue analgesic.

Table-7 Mean post-operative sedation Score

Post-op duration	Mean ± SD		p-value
	Group A	Group B	
15 min	1.1±0.30	1.5±0.57	<0.05
30 min	1.1±0.30	1.43±0.50	<0.05
45 min	1.1±0.30	1.4±0.49	<0.05
1hr	1.1±0.30	1.36±0.5	<0.05
2hr	0.83±0.46	1.2±0.55	<0.05
4hr	0.6±0.56	1.26±0.44	<0.05
6hr	0.03±0.18	1.43±0.56	<0.05
8hr	0.03±0.18	0.03±0.18	<0.05
10hr	0.03±0.18	0.06±0.25	>0.05
12hr	0	0.03±0.18	>0.05
Mean sedation score	0.59±0.51	1.09±0.55	<0.0001

Table-7 shows that the mean sedation score was higher in Group B (1.09±0.55) compared to Group A (0.59±0.51) till ten hours post-operatively and was statistically significant.

Table-8 Post -operative complications

Post-op complication	Group A	Group B
Nausea and vomiting	3(10%)	9(30%)
Respiratory depression	0	0
Bradycardia	0	0
Hypotension	0	0

Table-8 shows that the incidence of nausea vomiting was higher in Group B compared to Group A. There was no event of fall in spo2 and respiratory rate noted in either of the groups.

Discussion

Caudal epidural analgesia is one of the most popular and commonly performed regional blocks in pediatrics anesthesia. It is a reliable and safe technique that can be used with general anesthesia for intra and post-operative analgesia in pediatric patients undergoing lower abdominal and limb surgeries.

The awareness of pain relief in pediatric patients is increasing in both neonates and children. The past decade has witnessed many advances in the understanding and treatment of pain in children. The use of adjuncts can effectively help in reduction of the dose and an increase in duration of the local anesthetic agents. Our study was undertaken to assess the efficacy and safety of clonidine with bupivacaine in paediatric patients undergoing lower abdominal and lower limb surgeries under caudal analgesia.

The duration of study was 12 hours to assess the maximum duration of analgesia provided by clonidine and bupivacaine combination. Klimscha W et al [14] carried out a similar study but the major drawback of their study was the limited time of post operative assessment because of early discharge (6 hours). There

was no such limitation in our study

Klimscha[14] showed that increasing the dose from 1µg/kg to 2µg/kg did not enhance the analgesic effect of Clonidine but increased the incidence of side effects like respiratory depression, bradycardia and hypotension ,however we took clonidine in dose 1µg/kg in our study.

Lee[11], Klimscha[14],Jamali S[10] chose the OPS score to evaluate post-operative pain. We also used the OPS score as it is easy to use, is validated and gives an objective evaluation.

Patients in our study were demographically similar in both groups.

Majority of patients had surgical procedures like inguinal hernia, hypospadias, circumcision, lower limb surgeries and was comparable between two groups

Motsch J et al[18] found that Intra-operative hemodynamic responses did not differ between the groups but during emergence from general anesthesia children in the clonidine group had significantly lower heart rates and blood pressure compared to children in the control group.

In our study, the mean pre-operative systolic BP in group A and B was (97.93±6.73) mmHg and (93.13± 6.33) mmHg respectively which was statistically significant. The mean pre-operative pulse rate was (112.73±11.66) per minute in Group A and (112.4± 10.70) per minute in Group B which was not statistically significant.

The mean Intra-operative systolic BP in group A and group B was (97.59±3.99) mmHg and (92.3±2.85) mmHg respectively which was statistically significant. The mean intra-operative pulse rate was (113.5± 3.35) per minute and (109± 7.92) per minute respectively which was not statistically significant again.

The mean post-operative BP in group A and B was (97.33±0.55) mmHg and (91.92±1.36) mmHg respectively, the mean post-operative pulse rate was (112.61 ±0.57) per minute and (105.32±1.37) per minute in Group A and Group B respectively which was statistically significant.

Thus, this study shows that addition of 1 µg/kg of Clonidine to Bupivacaine reduces both heart rate and Blood Pressure.

Our study confirms the finding of hemodynamic changes as shown by Motsch [18]. There was decrease in heart rate and blood pressure from the baseline with the use of clonidine with bupivacaine in caudal anesthesia.

Duration of analgesia means time from caudal block to first dose of rescue analgesic i.e. OPS >= 12 or the child complaints of pain.

In children a mixture of 0.25% bupivacaine with 1-2 µg/kg clonidine has shown to improve the duration and quality of analgesia provided by caudal block. Although results vary widely, the duration of analgesia provided range from 6.3 hours to 16.5 hours for 1µg/kg clonidine to 5.8 hours and 10.25 hours for 2µg/kg clonidine. Study by Motsch et al[18] has shown a mean duration of analgesia of 20.9±7.4 hours in children receiving caudal clonidine with bupivacaine but a dose of 5µg/kg of clonidine was used. The wide variation in the duration of action of clonidine in the various studies could be due to: doses of clonidine used, differences in premedication and volatile anesthetic used, type of surgery, indications for rescue analgesia, assessment of pain and statistical analysis.

In our study, this time was found to be 4.54±1.17 hours for the plain bupivacaine group and 10±1.15 for the Bupivacaine + clonidine group respectively (p value< 0.0001 significant) which was similar to Lee et al where it was 5.2±1.2 hrs in plain bupivacaine and 9.8±2.1 hrs in bupivacaine- clonidine group.

Our results were also similar to that of Aruna Parameswari [2]and Upadhay[15] where the mean duration of analgesia was significantly longer in group-B (Bupivacaine + clonidine) 593.4±423.3 minute than in group- A (Bupivacaine) 288.7±259.1 minute.

In our study, the clonidine group required significantly less number of rescue analgesics as compared to plain bupivacaine group. In plain bupivacaine group 22(73.33%) patients required 2 rescue analgesic within 12 hours. In clonidine group 29 (96.66%) patients required single rescue analgesic in agreement with studies by Lee[11], Aruna [2], Archna Koul[1] and Jamali S[10].

At OPS Score of 12, patient needs rescue analgesic. This score was reached at 4 hours in Group A (11.23±2.50) and at 10 hours in Group B (11.93±3.40) in agreement with the study by Lee[11] , Klimscha[14], Jamali S[10]

In our study the period of sedation was significantly longer in children who received clonidine. The greater analgesic effect of clonidine might be mistaken for sedation. Hence it cannot be concluded that the longer duration of sedation was caused entirely by the sedative effect of clonidine.

In the immediate post- operative period mean Sedation score was 1.09±0.55 in Group B which means patients were sedated but arousable and 0.59±0.51 in Group A. After ten hours the mean sedation scores in both the groups were almost same and were statistically not significant. The duration of sedation was very similar to the respective duration of caudal analgesia correlating with the studies of Lee[11], Archana Koul[1], Klimscha[14].

We have not observed decrease in respiratory rate and fall in Spo_2 requiring oxygen supplementation comparable with studies of Lee[11] and Upadhay[15].

So we **conclude and recommend** that the addition of caudal clonidine 1µg/kg to bupivacaine (0.5%) 2mg/kg with total volume 1ml/kg significantly prolongs the duration of post-operative analgesia without an increase in adverse effects in patients undergoing infraumbilical surgeries.

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