www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i6.72

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Comparative Study of Plain Bupivacaine and Bupivacaine with Clonidine for Caudal Epidural in Paediatric Patients

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Abstract
Aims and Objectives: *To compare perioperative haemodynamic changes and complications, the quality and duration of post operative analgesia, total number of rescue analgesic doses required and degree and duration of sedation post operatively in each group.*
Material and Method:*70 children of ASA grade I or II aged 5-10 years, undergoing elective infraumbilical surgies were randomly allocated to group A(n=35)(0.25% plain bupivacaine 1 ml/kg+1 ml normal saline) and group B(n=35)(0.25% bupivacaine 1 ml/kg + clonidine 1mcg/kg in 1 ml normal saline). Post operative pain scores, duration of analgesia, total number of rescue analgesic doses required, haemodynamic changes, perioperative complications and degree and duration of sedation were recorded. Pain score was assessed using OPS score,*
Results: *The mean duration of analgesia in postoperative period was more in group B(9.20 ±0.76) hours as compared to Group A (4.9 ± 1.23) hours ;P<0.05.The children in group B had lower pain scores as compared to group A which was statistically significant. 100% patients in group A required two or more than two doses of rescue analgesic whereas in group B 85% patients required single dose of rescue analgesic and 12% patients required two doses of rescue analgesic in first 12 hours post operatively. Mean sedation scores were higher in group B as compared to group A*
Conclusion: *Addition of clonidine (1 mcg/kg) to bupicaine (0.25% 1 ml/kg) to caudal epidural block prolongs the duration of analgesia in paediatric patients.*
Keyword: *Paediatric patients, caudal epidural block, bupicaine and clonidine, postoperative analgesia.*

Introduction

The IASP (International Association For The Study Of Pain) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such. Surgery is a form of premedicated injury to body which leads to stimulation of free nerve endings and specific nociceptors leading to intraoperative and postoperative pain. Pain has adverse effects on the patients moral as well as various physiological functions of the body. So adequate control of postoperative pain is essential for good out come as well as it is one of the factors which reduce the hospital stay. Pain relief can be achieved by various methods like systemic opioids, NSAIDs, central neuroaxial block, peripheral nerve block and infiltration of wound by local anaesthetics. Historically children have

been under treated for pain and for painful stimuli because of wrong notion that they neither suffer or feel pain nor respond to or remember the painful experience to the same degree that adults do. An unproved safety and efficacy of the analgesics and worries about the risk of opioid induced respiratory depression added more reasons for the under treatment of pain in children The society of paediatric anesthesia at its 15th annual meeting at NEW ORLEANS LOUISINA (2001) clearly defines the alleviation of pain as a basic human right irrespective of age, medical condition, treatment, service response for the patient care or medical institution. Caudal epidural block is used in paediatric patients for providing postoperative analgesia because it is not possible to perform surgery in children with only caudal block as children are very uncooperative so either general anaesthesia or heavy sedation has to be given. Heavy sedation may sometimes lead to respiratory depression so we chose general anaesthesia with caudal block for postoperative analgesia. Limitation of caudal block is the short duration of action of bupivacaine which is four to six hours. To prolong the duration of caudal block various additives such as opioids, clonidine, ketamine, midazlom and neostigmine are used. Clonidine an alpha-2 adrenergic agonist agonist when used in caudal block produces analgesia by interacting with the alpha-2 adrenergic receptors located on superficial laminae of spinal cord and brain stem nuclei. Clonidine has adverse effects like ypotension, bradycardia and sedation. So we designed the present study to compare bupivacaine alone and bupivacaine with clonidine in caudal block to compare the duration and quality postoperative analgesia and any adverse effects in the perioperative period.

Materials and Methods

The study was conducted on 70 children of ASA grade I or II aged 5-10 years of either sex, undergoing elective infraumbilical surgies.

Exclusion criteria were:

1. Infection at the site of caudal block
2. Coagulopathy
3. Congenital spinal deformities
4. Allergy to local anaesthetics.

All children were kept nil by mouth for 6 hours before surgery. In operative room electrocar-diogram, NIBP and pulse oximeter were connected. Intravenous line was secured and Inj Ringer lactate was started. All children were premedicated with Inj.Glyopyrolate 0.04 mg/kg iv and Inj.Ondansetron 0.1 mg/kg.P atients were induced wit Inj.thiopentone sodium 6 mg/kg and endotracheal intubation was facilitated with Inj. suxamethonium chloride 2 mg/kg. Anaesthesia was maintained with O_2+N_2O with Sevoflurane and Inj vecuronium bromide 0.08 mg/kg loading dose and 0.02 mg/kg maintenance dose.

After induction caudal block was performed under strict aseptic precautions in lateral decubitus position with 23 G hypodermic needle.

According to the drug administered patients were randomly allocated to group A(n=35)(0.25% plain bupivacaine 1 ml/kg+1 ml normal saline) and group B(n=35)(0.25% bupivacaine 1 ml/kg + clonidine 1mcg/kg in 1 ml normal saline).

Heart rate, blood pressure and oxygen saturation were before induction, just after caudal block and every 15 min thereafter. At te end of the surgery, reversal of neuromuscular blockade was done by Inj.neostigmine 0.08 mg/kg and Inj neostigmine 0.05 mg/kg and patients were extubated.

At 30 min, 1,2,4,6,8,10 and 12 hours postoperatively vital parameters, Observer pain score (OPS score), Sedation score and any adverse effects were recorded.

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

Duration of analgesia was defined as the time from caudal block to first dose of rescue analgesic or OPS>=12.

Sedation score was assessed by objective score as follows: Eyes opening spontaneously (score 0),

eyes opening in response to verbal command (score 1), eyes opening in response to pysical stimulus (score 2), unarousable (score 3).

Results

Table-1: Demographic data

Variables	Group A	Group B
Age in years		
Mean	7.65	7.51
SD	2.01	2.12
Weight in kg		
Mean	22.52	23.05
SD	2.15	2.10
Sex ratio		
M:F	31:4	32:3

Table-2: Duration of surgery

Duration(min)	Group A	Group B
0-30	0	0
31-60	11	13
61-90	13	13
91-120	11	9
Mean	87.75	81.75
SD	26.33	25.98

Table-3: Surgical procedures:

Surgery	Group A	Group B
Inguinal hernia	7	8
Orchidopexy	8	7
Hypospadias & urethral fistula repair	15	15
Cystolithotomy	3	3
Extrophy bladder repair	2	2

There was no significant difference between the two groups in terms of age, weight, sex, duration or type of surgery. (P value>0.5) (unpaired t-test). The type of surgeries included inguinal hernia repair, hypospadias and urethral fistula repair, cystolithotomy, orchidopexy, extrophy bladder repair and were equally distributed between the two groups.

Table-4: Haemodynamic data

Preoperative vitals (Mean±SD)	Group A	Group B	P value
Pulse	114.8±13.09	116±10.6	NS
BP	94±8.72	90.3±6.56	NS

Intraoperative vitals (Mean±SD)	Group A	Group B	P value
Pulse	115±2.61	110±3.3	NS
BP	88±0.67	89.1±0.69	NS

Postoperative vitals (Mean±SD)	Group A	Group B	P value
Pulse	115±4.08	111±0.49	NS
BP	88.7±0.66	89.5±0.37	NS

There was no significant different between preoperative, intraoperative and postoperative heart rate and blood pressure between the two groups.

Table-5: Mean duration of caudal analgesia in hours:

	Group A	Group B	P value
Mean duration of analgesia	4.9±1.23	9.20±0.76	<0.0001

The mean duration of analgesia was significantly higher in group B than in group A which was statistically significant.

Table: 6 No of rescue analgesic required:

No of rescue analgesic	Group A	Group B
0	0	0
1	0	30(85.71%)
2	7(20%)	5(12%)
3	20(57.14%)	0
4	8(22.85%)	0

In group A all patients required two or more than two rescue anlgesics whereas in group B 85% patients required single dose of rescue analgesic and 12% required two doses of rescue analgesic.

Table-7: Mean OPS Score:

Post operative duration	Group A (Mean±SD)	Group B (Mean±SD)	P-value
30 min	5.3±0.66	5±0	>0.05(NS)
1 hr	7.15±1.23	6.35±0.59	>0.05(NS)
2 hr	10.4±2.01	6.9±0.85	<0.0001(Significant)
4 hr	11.3±2.72*	8.3±0.92	<0.0001(Significant)
6 hr	8.2±2.67	10±0.79	<0.05(Significant)
8 hr	11.7±2.11	11.3±1.33	<0.05(Significant)
10 hr	8.5±3.28	11.8±3.40*	<0.05(Significant)
12 hr	12.1±1.96	7.1±2.83	<0.05(Significant)
Mean OPS Score	9.33±2.43	8.52±2.59	<0.05(Significant)

***Time to fist rescue analgesic.**

There was no significant difference in OPS score in immediate post operative period. Thereafter, in Group- A OPS reached to 11.3±2.72 at 4 hours

(significantly more) .In Group B OPS remained below 12 till 10 hours and were not given rescue analgesic till that time ,which was statistically significant from 4 hours to 10 hours .

Table-6: Mean postoperative sedation score:

Postoperative duration	Group A (Mean±SD)	Group B (Mean±SD)	P-value
15 min	1.25±0.44	1.55±0.6	>0.05(NS)
30 min	1.1±0.31	1.35±0.49	<0.05(Significant)
45 min	1.05±0.22	1.55±0.51	<0.05(Significant)
1 hr	1.15±0.37	1.4±0.5	<0.05(Significant)
2 hr	0.8±0.52	1.25±0.55	<0.05(Significant)
4 hr	0.75±0.55	1.2±0.7	<0.05(Significant)
6 hr	0.05±0.22	1.2±0.7	<0.05(Significant)
8 hr	0.05±0.22	1.25±0.7	<0.05(Significant)
10 hr	0.05±0.22	0.05±0.22	>0.05(NS)
12 hr	0.05±0.22	0.05±0.22	>0.05(NS)

Table shows that the mean sedation scores are higher in Group B compared to Group A till eight hours post-operatively and are statistically significant. In immediate post operative period Sedation score was 1.55± 0.6 in Group B, which means patients were sedated but arousable. After eight hours the mean sedation scores in both the groups are almost same and statistically not significant. Patients were not deeply sedated (unarousable Score -3), during the study period in group B.

Table-7: Postoperative complications: s

Postoperative complication	Group A	Group B
Nausea/Vomiting	3(8.57%)	10(28.57%)
Respiratory depression	0	0

In group B 28.57% patients had nausea/vomiting and group A 8.578% patients had nausea /vomiting. There were no other complications in both the groups.

Discussion

Clonidine is an $\alpha_2$adrenoreceptor agonist, the analgesic action of intrathecal or epidural clonidine results from direct stimulation of pre and post synaptic $\alpha_2$adrenoreceptors in the dorsal grey matter of spinal cord thereby inhibiting the release of nociceptive neurotransmitters. This effect correlates with the concentration of Clonidine in the cerebrospinal fluid but not that in the plasma.

The present study was undertaken to assess the efficacy and safety of Clonidine with Bupivacaine in paediatric patients undergoing infraumbilical surgeries under caudal analgesia.

Sharpe et.al[12] speculated that small volume of Bupivacaine (0.5ml/kg) may not be enough to deliver clonidine upto the spinal cord leaving only direct action on the nerve routes in caudal area. These findings suggest that the addition of Clonidine 2µg/kg to low volume of caudal anaesthetics has limited clinical benefit in paediatric patients undergoing circumcision. Also Joshi W[6] in their study did not recommend the addition of 2µg/kg Clonidine to 0.125% Bupivacaine 1 mg/kg.

The dose of Clonidine for epidural administration is 1-5µg/kg. We chose a dose of 1µg/kg in our study as there were studies (Klimsha et al[17].) showing that showing 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.

We chose the OPS score to evaluate post-operative pain as it is easy to use, is validated and gives an objective evaluation.

Demographic Data

There were no statistically significant difference in age, body weight and gender distribution in both the groups.

Surgical Procedure and Duration of Surgery

Majority of patients had infraumbilical surgical procedures like inguinal hernia, hypospadias, orchidopexy and extrophy bladder repair and were equally distributed in both the groups. Duration of surgery was also similar in both the groups and was statistically not significant.

Intra and Post-Operative Pulse Rate and Blood Pressure

The finding of haemodynamic changes are as shown by other workers (Motsch et al.[18], Aruna parameswari et al.[2],Upadhyay L[9] and Archna Koul et al.[1]) .There was no significant decrease in heart

rate and blood pressure from the baseline with the use of clonidine with bupivacaine in caudal anaesthesia.

In present study , the mean preoperative systolic BP in group A and B was (94±8.72)mm of Hg and (90.3±6.56)mmof Hg respectively, the mean preoperative pulse rate was(114.8±13.09)per min. and (116.4±10.6)per min. respectively ,which is not statistically significant.

The mean Intraoperative systolic BP in group A and group B was (88± 0.67)mm of Hg and (89.1±0.69) mm of Hg respectively ,the mean intraoperative pulse rate was (115±2.61) per min and (110±3.3)per min. respectively , which is not statstically significant.

The mean postoperative BP in group A and B was (88.7±0.66) mm of hg and (89.5± 0.37) mm of hg respectively , the mean postoperative pulse rate was (115±4.08) per min and (111±0.49) per min respectively , which is not statistically significant.

Thus our study confirms that addition of 1 µg/kg of Clonidine to Bupivacaine does not have significant effect on the patients hemodynamic status.

Duration of Analgesia

Study by Motsch et al[18] has shown a mean duration of analgesia of 20.9±7.4 hours in paediatric patients 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 anaesthetic used, type of surgery, indications for rescue analgesia, assessment of pain and statistical analysis.

Aruna Parameswari et al.[2] observed that the mean duration of analgesia was significantly longer in group-B(Bupivacaine + clonidine) 593.4±423.3 min than in group- A (Bupivacaine) 288.7±259.1 min.Patients in group B had lower pain scores and requirement of rescue medications.

Upadhyay L[9] also observed the duration of analgesia in Group A (Bupivacaine) was 5.59±0.633 hrs and in Group B(Bupivacaine + clonidine) was 10.333±0.836 hrs respectively $p<0.05$(significant).

Duration of analgesia means time from caudal block to first dose of rescue analgesic when OPS≥12 or the child complaints of pain.

In paediatric patients 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.

In our study ,this time was found to be (4.9 ± 1.23) hours for the plain bupivacaine group Versus (9.20 ±0.76) hours for the Bupivacaine + Clonidine group respectively(p value< 0.0001 significant) .

Our results were similar to that of Aruna Parameswari et al.[2] and Upadhyay L[9].

Number of Rescue Analgesics in the First 12 Hour Post-Operative Period

In our study the clonidine group required significantly less number of rescue analgesics as compared to plain bupivacaine group. In plain bupivacaine group all patients required 2 or more than 2 rescue analgesic doses within first 12 hours . In clonidine group 85% patients required single dose of rescue analgesic and 12% required 2 rescue analgesic doses. This is in agreement with studies by J.J.Lee et al.[16], Aruna Parmeswari et al.[2] and Archna Koul et al.[1]

Mean OPS Score

At OPS Score of 12, patient needs rescue analgesic. This score was reached at 4 hours in Group A(mean 11.3±2.67) and at 11 hours in Group B (mean 11.8±3.4).This is in agreement with the study by Aruna Parameswari et al.[2] who reported higher FLACC scores in plain bupivacaine group.

Sedation Score

J.J.Lee et al.[16], Archna Koul et al.[1], Klimscha et al.[17] found the period of sedation was significantly longer in paediatric patients who received clonidine. Our study is in agreement with them. However it is difficult to distinguish between sedation and analgesia, as we noticed that all paediatric patients were asleep provided they were comfortable and they became restless or awake only when they were in pain. The greater analgesic effect of clonidine might be mistaken for sedation and vice versa. Hence it cannot be concluded that the longer duration of sedation was caused entirely by the sedative effect of clonidine. Moreover, the addition of clonidine did not delay significantly recovery from anaesthesia.

In our study the immediate post- operative period Sedation score was 1.55± 0.6 in Group B, which means patients were sedated but arousable. After eight hours the mean sedation scores in both the groups was almost same and statistically not significant. Patients were not deeply sedated (unaruosable Score -3), during the study period. The duration of sedation was very similar to the respective duration of caudal analgesia.

Post-Operative Complications

Joshi W[6] reported the incidence of nausea and vomiting was higher in paediatric patients who received clonidine. In our study 10 (28.57%) paediatric patients in clonidine group complained of nausea vomiting compared to 3(8.57%) in plain bupivacaine group.

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