

ORIGINAL RESEARCH

A Comparative Study Between Clonidine And Dexmedetomidine Used As Adjuncts To Ropivacaine For Caudal Analgesia In Paediatric Patients

A. Naresh Babu¹, G.Harinath²

ABSTRACT

Introduction: Caudal epidural block is a simple, safe, effective and reliable technique. Different techniques, drugs, drug combinations, doses and concentrations have been tried by many anesthesiologists.

Material an Method: Study was done for a period of 1 year on 60 pediatric patients and divided into 3 groups Group R (n=20) received 1ml/kg of 0.25% ropivacaine and 0.5ml of 0.9% of saline caudally, Group C (n=20) received 1ml/kg of 0.25% ropivacaine and 1mcg/kg of clonidine made to 0.5ml by adding 0.9% of saline and Group D (n=20) received 1ml/kg of 0.25% ropivacaine and 1mcg/kg of dexmedetomidine made to 0.5ml by adding 0.9% of saline. Observed for duration of analgesia pain, sedation, pulse rate, mean arterial pressure oxygen saturation and complications associated.

Results: Dexmedetomidine as an adjunct to Ropivacaine produced the maximum duration of postoperative analgesia as compared to Clonidine as an adjunct to ropivacaine and plain Ropivacaine. In all the three groups intraoperative parameters like pulse rate, mean arterial pressure and oxygen saturation was monitored throughout the surgery and did not differ significantly from the preoperative baseline values. There were no significant complications in the postoperative period in either of the groups.

Conclusion: Addition of both clonidine and dexmedetomidine with ropivacaine administered caudally in paediatric patients significantly increases the duration of analgesia without complications.

Keywords: Ropivacaine, Dexmedetomidine, Clonidine, Caudal analgesia.

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INTRODUCTION

Pain is an unpleasant subjective sensation which can only be experienced and not expressed, especially in children. The primary reason to treat or prevent pain is humanitarian. This is even more important in children who rely completely on their parents or caregivers for their well being. The concept of postoperative pain relief and its utilization in the paediatric age group has improved dramatically over the recent years.

The various methods of providing pain relief have some side effects which prohibit their use in children for eg. Narcotics in children, because of their respiratory depression, the other analgesics which cannot be given for sometime after general anesthesia due to the fear of vomiting and aspiration, the objection to the needles in the case of parenterally administered analgesics.

The regional anaesthetic techniques significantly decrease post operative pain and systemic analgesic requirements. Caudal route was chosen for this study as it is one of the simplest and safest techniques in paediatric surgery with a high success rate. Epidural space in children favours rapid longitudinal spread of drugs and makes it effective in treating postoperative pain.

Caudal block is usually placed after the induction of general anesthesia and is used as an adjunct to intraoperative anesthesia as well as postoperative analgesia in children undergoing surgical procedures below the level of the umbilicus.¹ Caudal analgesia can reduce the amount of inhaled and IV anaesthetic administration, attenuates the stress response to surgery, facilitates a rapid, smooth recovery, and provides good immediate postoperative analgesia.¹ In order to decrease intra operative and postoperative analgesic requirements after single shot caudal epidural blockade, various additives such as morphine, fentanyl, clonidine and ketamine with local anaesthetics have been investigated.²

Ropivacaine, a long-acting amide local anaesthetic related structurally to bupivacaine, has been used for paediatric caudal anaesthesia. It provides pain relief

with less motor blockade. Literature suggests that ropivacaine is less cardiotoxic than bupivacaine, hence ropivacaine may be a more suitable agent for caudal epidural analgesia especially in day care surgery.³ Dexmedetomidine and Clonidine are alpha2 agonists. Major advantage of dexmedetomidine is that it has 1620 times greater affinity for alpha2 adrenergic receptors than clonidine and much less alpha1 effects. A major advantage of dexmedetomidine is its higher selectivity compared with clonidine for α_{2A} receptors which is responsible for the hypnotic and analgesic effects.⁴

The objective of this study is to compare the analgesic effects of Dexmedetomidine and Clonidine when added to ropivacaine for caudal analgesia in children undergoing lower abdominal surgeries.

MATERIAL AND METHODS

Prospective randomized comparative observer blinded study on 60 male paediatric patients was done. Study was done for a period from January 2014 to December 2014 admitted in our hospital.

Inclusion Criteria: ASA I and ASA II patients between 6 months to 6 years of age undergoing lower abdominal surgeries.

Exclusion Criteria: Suspected coagulopathy, infection at the site of caudal block, history of developmental delay, neurological diseases, skeletal deformities and allergy to local anesthetics.

Study groups were divided into:

Group R (n=20): Patients who received 1ml/kg of 0.25% ropivacaine and 0.5ml of 0.9% of saline.

Group C (n=20): Patients who received 1ml/kg of 0.25% ropivacaine and 1mcg/kg of clonidine made to 0.5ml by adding 0.9% of saline.

Group D (n=20): Patients who received 1ml/kg of 0.25% ropivacaine and 1mcg/kg of dexmedetomidine made to 0.5ml by adding 0.9% of saline.

In all the children age, I.P. no., body weight and baseline vital parameters were recorded. History regarding previous anesthesia, surgery, any significant medical illness, medications and allergy were recorded. Complete physical examination and airway assessment were done. Following laboratory investigations were done: blood grouping typing, haemoglobin%, blood sugar, urea, serum creatinine, serum electrolytes and urine analysis.

After getting the institutional ethical committee approval and written informed consent from parents, the patients were randomly allocated into three groups. On the day of surgery patients were shifted to the operation theatre. All the patients were premedicated after securing appropriate sized IV cannula with midazolam 0.03mg/kg and atropine

0.02mg/kg 10 min prior to induction. Routine monitors (ECG, Pulse oximetry, NIBP) will be attached and baseline vital parameters like mean arterial pressure (MAP), heart rate (HR), and arterial oxygen saturation (SPO2) will be recorded. IV drip started with Isolyte-P at a calculated rate according to the body weight. Anesthesia will be induced with thiopentone sodium and succinyl choline and the patients will be intubated with an appropriate sized portex endotracheal tube. Caudal block for all the patients was performed after induction of general anesthesia and before the start of the surgery. After induction oxygen: nitrous (30:50) and sevoflurane will be used throughout the surgery. The patients will be positioned in left lateral position. Under strict aseptic precautions, a 23G needle will be introduced into caudal space and either ropivacaine with saline (Group R) or ropivacaine with clonidine (Group C) or ropivacaine with dexmedetomidine (Group D) will be administered. At the end of surgery residual neuromuscular blockade will be reversed by appropriate dose of neostigmine and atropine and tracheal extubation performed.

The following parameters will be observed at every 10min in the first hour and there afterwards at every 2 hours after surgery.

Pain was assessed by CRIES scale. A score of 0 signifies excellent analgesia whereas a score of 10 indicates ineffective analgesia.

CRIES SCALE

CRIES SCALE FOR POSTOPERATIVE PAIN			
	0	1	2
Crying	No	High-pitched	Inconsolable
Requires SpO ₂ >95%	No	FiO ₂ <30%	FiO ₂ <30%
Increased vital signs	Heart rate and blood pressure equal to or less than preoperative values	Less than 20% of preoperative values	Greater than 20% of preoperative values
Expression	None	Grimace	Grimace/grunt
Sleeplessness	No	Awakens frequently	Awake

Sedation was assessed by 4 point scale-

1. Barely arousable (sleep needs shaking or shouting to arouse)
2. Asleep (eyes closed, arousable with soft voice or light touch)
3. Sleepy (eyes open but less active and responsive)

4. Awake

- Pulse rate, Mean arterial pressure and respiratory rate
- Side effects like nausea, vomiting, pruritis.
- Duration of postoperative analgesia will be defined as the time between the injection of drug caudally to the first administration of postoperative analgesia.

Rescue analgesia will be administered when CRIES score >4. Failure of caudal block was defined as any increase in HR or MAP > 20% than preincision values.⁴

Data was analysed using SPSS version 15.0 computer software. Numerical variables were presented as mean and standard deviation (Mean±SD). Comparison between the groups were performed by the Kruskal-Wallis One Anova.

RESULTS

Present clinical study consists of 60 patients, aged between 6 months to 6 years, who are randomly chosen and divided into three groups. Present clinical study was conducted on ASA Grade-1 paediatric patients who were undergoing infraumbilical surgical procedures, from January 2014 to December 2014 admitted in our hospital. Group R,C and D include 20 patients in each group, Statistical analysis in present study data is expressed as mean and standard deviation where it is appropriate. The statistical analysis was done by Kruskal-Wallis One Anova. Probability value less than 0.001 was considered as statistically significant. Table-1 shows the difference between the R,C,D groups was not statistically significant ($P > 0.05$). The difference of weight between the groups was not statistically significant ($f = 0.190$, $d.f. = 59$ and $P > 0.05$). Table-2 shows the preoperative, intraoperative and postoperative haemodynamic changes between the groups were comparable and were not statistically significant and therapeutic interventions were not required. Table-3 shows that after 2 hours, most of the patients of all the groups had sedation score 2 whereas after six hours, maximum number of patients had sedation score 3 (in all the groups). At twelve hours, patients of all the three groups mostly had sedation score 4. The mean sedation scores in the post operative period between the groups were comparable but not statistically significant ($P > 0.05$). Table-4 shows that there was a significant difference between the groups in the CRIES Score measured 2nd hourly in the postoperative period. Group R patients achieved significantly higher CRIES SCORE compared with Group C and Group D patients. Whereas as significant number of patients achieved a CRIES

score of 4 at 6th hour compared with 0 patients in Group C and Group D patients. Majority of Group C patients had CRIES score of 4 at 14th hour and that of Group D patients had CRIES score of 4 at 18th hour. Table-5 shows that no episodes of clinically significant postoperative complications such as PONV, respiratory depression, urinary retention, pruritis, hypotension and bradycardia were observed

DISCUSSION

Motor blockade resulting from caudal block is very distressing to children in the postoperative period and delays hospital discharge. Ropivacaine in comparison to bupivacaine, has a wider margin of safety, less motor blockade, less cardiovascular / neurological toxicity and similar duration of analgesia. It can be safely used for regional anesthesia and analgesia in the ambulatory setting in paediatrics.¹⁻⁸

Regional techniques including the caudal block, avoid most of the problems and it is possible to achieve analgesia with minimum of drug dose and complications. Caudal block is easy to perform and has been found to be very effective in children, specially in infraumbilical surgery like herniotomy.⁹ Several local anesthetic agents (eg. Bupivacaine, ropivacaine etc.) have been used for caudal block. Adjuvants like opioids (morphine,¹⁰ butorphanol, etc.) clonidine, midazolam and ketamine are added to local anaesthetic agents to increase the duration of analgesia, decrease the individual dose of the drug and thereby decreasing the side effects. Like clonidine,^{11,12} dexmedetomidine also enhances the effects of local anaesthetics without increasing the incidence of side effects.¹³ A major advantage of dexmedetomidine is its higher selectivity compared with clonidine for α_2A receptors which is responsible for the hypnotic and analgesic effect. Dexmedetomidine, although currently available for i.v. use only, has been successfully administered epidurally for postoperative analgesia in humans in clinical trials.

El-Hennawy et al.⁴ administered Dexmedetomidine and Clonidine both in a dose of 2 μ g/kg as adjuvant with 0.25% Bupivacaine caudally. They found that duration of analgesia was significantly higher in the group receiving bupivacaine-dexmedetomidine mixture [median (95% confidence level): 16 (14-18) hrs] bupivacaine-clonidine mixture [median (95% confidence level): 12(3-21) hrs] than the group receiving bupivacaine alone [median (95% confidence level): 5 (4-6) hrs]. In our study we found that ropivacaine and dexmedetomidine mixture had a mean 14.13 hrs (CI 12.97 – 15.28), ropivacaine and

Demographic characteristics	R group		C group		D group		Total	
Age in months								
6-12	4	20	1	5	6	30	11	18.3
13-24	1	5	4	20	1	5	6	10
25-36	2	10	5	25	4	20	11	18.3
37-48	2	10	2	10	3	15	7	11.7
49-60	3	15	3	15	1	5	7	11.7
61-72	8	40	5	25	5	25	18	30
Total	20	100.0	20	100.0	20	100.0	60	100
Mean ±SD	49.35±24.85		45.60±20.36		39.55±24.31		44.83±23.22	
Significance	P>0.05							
Weight in kgs								
	No	%	No	%	No	%	No	%
0-5	1	5	0	0	1	5	2	3.3
6-10	7	35	6	30	9	45	22	36.7
11-15	10	50	9	45	4	20	23	38.3
16-20	2	10	5	25	6	30	13	21.7
21-25	0	0	0	0	0	0	0	0
Total	20	100	20	100	20	100	60	100
Mean ±SD	12.14±3.95		12.88±3.29		12.33±4.49		12.45±3.89	
Significance	P > 0.05							

Table-1: Comparison of demographic characteristics between the groups

	Variables	R group		C group		D group		‘f’	Significance (p)
		Mean	SD	Mean	SD	Mean	SD		
Pre- op	PR	94.5	7.22	98.00	6.87	99.10	7.60	1.86	P > 0.05
	MAP	78.70	4.50	76.80	4.54	75.80	4.50	2.12	P > 0.05
	SPO2	99.40	0.598	99.70	0.47	99.40	0.59	1.92	P > 0.05
Intra-op	PR	92.14	7.34	91.07	6.34	88.11	6.98	1.89	P > 0.05
	MAP	73.14	4.10	71.74	3.56	70.03	2.70	4.30	P > 0.05
	SPO2	99.53	0.51	99.57	0.52	99.53	0.53	0.16	P > 0.05
Post-op	PR	92.42	7.172	91.06	5.32	88.85	7.07	1.58	P > 0.05
	MAP	76.79	4.830	73.55	3.21	71.43	2.60	5.96	P > 0.05
	SPO2	99.11	0.748	98.94	0.80	99.17	0.69	1.44	P > 0.05

Table-2: Comparison of haemodynamic variables between the groups.

Time in hours	R group		C group		D group		‘f’	Significance
	Mean	SD	Mean	SD	Mean	SD		
2 hours	2.30	0.657	2.20	0.523	2.30	0.657	0.176	P > 0.05
4 hours	2.65	0.813	2.75	0.851	2.65	0.813	0.098	P > 0.05
6 hours	3.05	0.686	3.00	0.725	3.10	0.718	0.099	P > 0.05
8 hours	3.35	0.745	3.25	0.786	3.30	0.733	0.088	P > 0.05
12 hours	3.55	0.686	3.45	0.759	3.60	0.681	0.232	P > 0.05

Table-3: Comparison of mean sedation score in the post operative period between the groups.

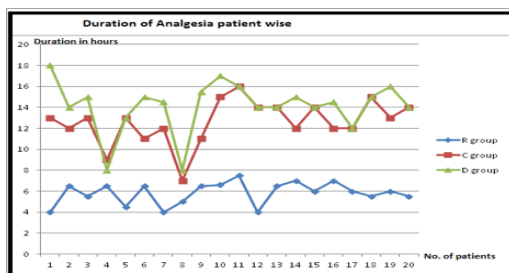


Figure-1: Duration of analgesia in all patients in the study

Clonidine mixture had a mean 12.60 hours (CI 11.62-13.58) duration of analgesia than ropivacaine alone, which had 5.83 hrs (CI 5.33 – 6.33). Saadawy et al¹⁴ compared caudal bupivacaine 0.25% with dexmedetomidine 1µg/kg and caudal bupivacaine alone and showed that the incidence of agitation following sevoflurane anaesthesia was significantly lower with dexmedetomidine (P<0.05); The duration of analgesia was significantly longer with dexmedetomidine (P<0.001). Upadhyay and Colleagues,¹⁵ they

CRIES score in R group					
Time	Score-0	Score-1	Score-2	Score-3	Score-4 and above
2 hrs	13	5	2	0	0
4 hrs	0	1	14	2	3
6 hrs	0	0	0	9	11
8 hrs	0	0	0	0	20
12 hrs	0	0	0	0	0
14 hrs	0	0	0	0	0
18 hrs	0	0	0	0	0
20 hrs	0	0	0	0	0
CRIES score of C group					
2 hrs	20	0	0	0	0
4 hrs	9	10	1	0	0
6 hrs	0	14	4	2	0
8 hrs	0	2	11	6	1
12 hrs	0	0	1	9	10
14 hrs	0	0	0	3	17
18 hrs	0	0	0	0	20
20 hrs	0	0	0	0	20
CRIES score of D					
2 hrs	20	0	0	0	0
4 hrs	14	4	2	0	0
6 hrs	9	6	4	1	0
8 hrs	0	9	7	2	2
12 hrs	0	3	7	7	3
14 hrs	0	0	2	9	9
18 hrs	0	0	0	0	20
20 hrs	0	0	0	0	20

Table-4: CRIES score in groups children in post operative period

	R Group	C Group	D Group
PONV	2	1	2
Respiratory depression	Nil	Nil	Nil
Urinary retention	1	1	1
Hypotension	Nil	1	1
Bradycardia	Nil	1	2

Table-5: Postoperative Complications

used 1µg/kg of clonidine as adjuvant with 0.25% bupivacaine in children undergoing infraumbilical surgery and observed a significant prolongation of postoperative analgesia without any significant incidence of side effects. In our study, we used clonidine in the dose of 1µg/kg along with 0.25% ropivacaine and did not observe significant incidence of side effects like bradycardia and hypotension.

Lee et al.¹⁶ AP administered clonidine in a dose of 2µg/kg along with local anaesthetic agent in children undergoing orthopaedic surgery in their study. They observed higher incidence of bradycardia and hypo-

tension associated with 2µg/kg dose of clonidine. Klimscha et al.¹⁷ also reported that analgesic efficacy does not seem to be enhanced by increasing the dose of clonidine from 1µg/kg to 2µg/kg. In another study conducted by Schnaider et al.¹⁸, addition of clonidine 2µg/kg or dexmedetomidine 2µg/kg to ropivacaine 0.75% (20ml) administered into epidural space in patients undergoing upper abdominal surgery caused a 25% decrease in systemic systolic pressure in clonidine group and 30% decrease in dexmedetomidine group. In our study observed that the magnitude of haemodynamic changes between the groups were similar. There was no significant differences in the incidence of side effects like pruritis and nausea and vomiting. No episodes of respiratory depression or urinary retention were noted. Sedation scores were comparable between all the groups.

CONCLUSION

In all the three groups intraoperative parameters like pulse rate, mean arterial pressure and oxygen saturation was maintained throughout the surgery and did not differ significantly from the preoperative baseline values. There was no significant difference between the mean sedation scores. There were no significant complications in the postoperative period in either of the groups. To conclude addition of both clonidine and dexmedetomidine with ropivacaine administered caudally in paediatric patients significantly increases the duration of analgesia.

REFERENCES

- Deng XM, Xiao WJ, Tang GZ, Luo MP, Xu KL. The Minimum Local Anesthetic Concentration of Ropivacaine for Caudal Analgesia in Children. *Anesth Analg* 2002; 94:1465-8.
- Birbicer H, Doruk N, Cinel I, Atici S, Avlan D, Bilgin E, Oral U. Oral. Could adding magnesium as adjuvant to ropivacaine in caudal anaesthesia improve postoperative pain control? *Pediatr Surg Int* 2007;23:195-198.
- Manjushree Ray, S. K. Mondal, A. Biswas. Caudal analgesia in paediatric patients: Comparison between Bupivacaine and Ropivacaine. *Indian J. Anaesth.* 2003;47:275-278.
- El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boullis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. *British Journal of Anaesthesia* 2009;103: 268-74.
- Ivani G, De Negri P, Conio A. Ropivacaine-clonidine combination for caudal blockade in

- children. *Acta Anaesthesiol Scand* 2000;44: 446-449.
6. De Negri, P., Ivani, G., Visconti, C., De Vivo, P. How to prolong postoperative analgesia after caudal anaesthesia with ropivacaine in children: s-ketamine versus clonidine. *Paediatr Anaesth* 2001;11:679-83.
 7. Tan JS, Choo SM, Chiu JW. Caudal Ropivacaine Versus Bupivacaine for Paediatric Day-case Circumcision Procedures. *The Internet Journal of Anaesthesiology* 2000;4:20-25
 8. vani G, De Negri P, Lonnqvist PA, L'Erario M, Mossetti V, Difilippo A, Rosso F. Caudal anaesthesia for minor pediatric surgery: a prospective randomized comparison of ropivacaine 0.2% vs levobupivacaine 0.2%. *Paediatr Anaesth*. 2005;15:491-4.
 9. Gehdoo RP. Postoperative Pain Management in Paediatric Patients. *Indian J Anaesth* 2004; 48:406-11.
 10. Gupta SD et al. Caudal epidural bupivacaine alone versus bupivacaine- low dose morphine combination in paediatric infra umbilical surgeries for post operative analgesia.
 11. Eisenach JC, De Kock M, Klimscha W. Alpha sub 2 –Adrenergic Agonists for Regional Anaesthesia: A Clinical Review of Clonidine (1984-1995). *Anesthesiology*:S1996 : 85: 655-674.
 12. Hansen TG, Henneberg SW, Walther-Larsen S, Lund J, Hansen M. Caudal bupivacaine supplemented with caudal or intravenous clonidine in children undergoing hypospadias repair: a doubleblind study. *British Journal of Anaesthesia* 2004;92:223-7.
 13. Tatsushi Yoshitomi. Dexmedetomidine Enhances the Local Anesthetic Action of Lidocaine via an α 2A Adrenoceptor. *Anesth Analg* 2008; 107:96-101.
 14. Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, Afifi W. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. *Acta Anaesthesiol Scand*. 2009, 53:251-6.
 15. Upadhyay K.K, Prabhakar T, Handa R, Beena Haridas. study of the efficacy and safety of clonidine as an adjunct to bupivacaine for caudal analgesia in children. *Indian J. Anaesth*.2005; 49:199-201
 16. Lee JJ, Rubin AP. Comparison of a bupivacaine –clonidine mixture with plain bupivacaine for caudal analgesia in children. *Br J. Anaesth* 1994; 72: 258-62.
 17. Klimscha W, Chiari A. The efficacy and safety of clonidine/bupivacaine combination in caudal blockade for paediatric hernia repair. *Anesth Analg* 1998; 86:54-61.
 18. Schnider TW, Minto CF. Predictors of onset and offset of drug effect. *Eur J Anaesthesiol*. 2001;23:26–31.