Comparison of the Efficacy of Ropivacaine-Clonidine Mixture with Plain Ropivacaine for Caudal Analgesia in Paediatric Lower Abdominal Surgeries

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ABSTRACT

BACKGROUND

Caudal epidural is practised in paediatric anaesthesia with the aim of providing postoperative analgesia. To use clonidine as an adjuvant to ropivacaine through caudal space has been shown to improve analgesic efficacy of local anaesthetics. We wanted to evaluate postoperative caudal analgesia with 0.2% ropivacaine alone and its combination with clonidine.

METHODS

120 children aged between two to eight years scheduled for lower abdominal surgeries were allocated randomly into two groups. Group RO received 0.2% ropivacaine 1 mL/Kg and Group RO C received 0.2% ropivacaine 1 mL/Kg with clonidine in a dose of 2 µg/Kg. Postoperative pain was assessed using the observational pain discomfort scale (OPS) for 24 hours and rescue analgesia was administered if this score reached 11 or more.

RESULTS

The duration of analgesia was longest in children receiving clonidine and ropivacaine together (380.71 minutes vs. 270 minutes group RO) and was found to be statistically significant; $P < 0.05$. Significantly fewer doses of rescue medications were needed for subjects in group RO C. None of the subjects were treated for bradycardia or hypotension and no significant sedation was noted. No motor impairment was seen in either groups on awakening or during the next 24-hour period.

CONCLUSIONS

Caudal administration of ropivacaine with the addition of clonidine resulted in superior analgesia with longer duration with decreased demand for rescue analgesics.

KEYWORDS

Ropivacaine, Clonidine, Caudal Analgesia

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BACKGROUND

Pain is an unpleasant sensation which is experienced than expressed especially in children. Attention has focused on the problem and major philosophical shifts and technical advances have occurred in the management of pain in children over the years. Caudal epidural analgesia remains the standard of care for providing postoperative analgesia in children. Ropivacaine offers a wide margin of safety with lower potential for side effects as well as ability to produce lesser motor blockade compared to bupivacaine. This characteristic of ropivacaine is of greater benefit in paediatric population. Clonidine an alpha - 2 agonist is an attractive additive to caudal local anaesthetics because unlike opioids, clonidine enhances and prolongs the analgesic effects of local anaesthetics without causing respiratory depression, urinary retention, nausea or pruritis. Addition of clonidine to caudal epidural local anaesthetics in children improves analgesic efficacy and duration of analgesia. We undertook the study to assess the analgesic efficacy in terms of duration of analgesia of ropivacaine 0.2% with the addition of clonidine 2 µg/Kg following single shot caudal epidural block in children.

METHODS

The present study was a prospective observational study conducted in our paediatric surgery department after approval from the hospital ethical committee. 120 children in the age group 2-8 years belonging to ASA status 1 and 2 undergoing lower abdominal surgeries had been considered as the population for the study after obtaining written informed consent from the parents. Children with history of allergy to drugs including local anaesthetics, bleeding diathesis, pre-existing neurological or spinal diseases, infection at the site of puncture, sacral anomalies, and recent respiratory infection were excluded from the study.

All the patients included in the study underwent a detailed preanaesthetic check-up. The age and weight are noted. The baseline heart rate, respiratory rate and blood pressure were recorded. Milk and solids are restricted for six hours but clear fluids were allowed up to 2-3 hours prior to induction Premedication with oral midazolam 0.3 mg/Kg given half an hour before surgery. Atropine 0.02 mg/Kg and ondansetron 0.1 mg/Kg given after iv cannulation. The intraoperative monitors included electrocardiogram, pulse oximetry, non-invasive blood pressure and end tidal carbon dioxide. Intravenous access was secured with 24G or 22G cannula either with patient awake or under gas-oxygen-sevoflurane through a well-fitting mask depending on the cooperation of the child. Ringer lactate was set up and fluid administered according to the calculated requirements. Induction done with 5-7 mg/Kg of thiopentone sodium intravenously and then maintained on oxygen -nitrous oxide sevoflurane in sufficiently deep plane of anaesthesia with the patient in spontaneous ventilation. Fresh gas flow kept at 2-3 times the minute ventilation.

After induction of anaesthesia, the child was placed in lateral decubitus position vitals were checked once again. The caudal space was identified and the appropriate drug was injected as per the group using a 22G scalp vein set. The preparation of drug was done by one anaesthesiologist and the caudal block was performed by another. Group RO received test dose + 0.2% Ropivacaine 1 mL/Kg, group RO C received test dose + 0.2% Ropivacaine 1 mL/Kg mixed with clonidine 2 µg/Kg. The patients were allocated randomly to one of the two groups of 60. The maximum volume injected was 20 ml. The time of caudal block and duration of surgery was noted.

The intraoperative hemodynamic and respiratory parameters were monitored and documented every 5 min till awakening. Once vital were stable the child was shifted to recovery room. The time from discontinuation of anaesthetic to spontaneous eye opening was noted. When the child maintained good colour without oxygenation or external airway support they were transferred to post-operative ward.

Assessment was done for a period of 24 hours after caudal block. The observational pain/discomfort scale (OPS) (table 1) was used for assessment of postoperative pain.

	None	Moderate	Severe
Crying	1	2	3
Facial Expression	1	2	3
Position of Torso	1	2	3
Position of Legs	1	2	3
Motor Restlessness	1	2	3

Table 1. Pain Evaluation Score

Minimum score was taken as 5 and maximum score was taken as 15. If OPS more than 11, rescue analgesia was given. Rescue analgesia was using oral paracetamol 15 mg/Kg who had pain score equal to or more than 11 anytime for 24 hours.

Side Effects

- Sedation: The time from discontinuation of anaesthesia to spontaneous eye opening was noted.
- Motor weakness: The duration of motor block was assessed by determining when the children began to move their legs.
- Delay in micturition: The time of first micturition was noted.
- Any episode of hypotension.

RESULTS

Data were analysed using computer software, statistical package for social sciences (SPSS) version 10. Data expressed in frequency and percentage as well as mean and standard deviation. Chi ($\chi 2$) square test was used as non-parametric test to elucidate associations and comparisons of different parameters. Analysis of variance (one-way ANOVA) was performed to compare different variables. Mann Whitney's U test was used to compare different groups. For

all statistical evaluation a two tailed probability of less than 0.05 was considered significant. The age, weight and the duration of surgery in the study groups were compared using the student's t test. Table 2 shows that the groups were comparable. The average time of micturition was statistically not significant (p >0.05).

Parameters	Group	Mean	± SD	t Value	p Value
Age (years)	Ropivacaine	3.34	1.27	-0.361	> 0.05
	Ropivacaine + Clonidine	3.43	1.44		
Weight (Kg)	Ropivacaine	12.25	1.97	- 1.208	> 0.05
	Ropivacaine + Clonidine	13.05	2.07		
Duration of Surgery (Minutes)	Ropivacaine	18.49	7.22	0.365	> 0.05
	Ropivacaine + Clonidine	18.02	7.43		
Micturition (Hours)	Ropivacaine	5.10	0.55	0.256	> 0.05
	Ropivacaine + Clonidine	5.06	0.81		

Table 2. Student's t Test Comparing Different Parameters between the Two Groups

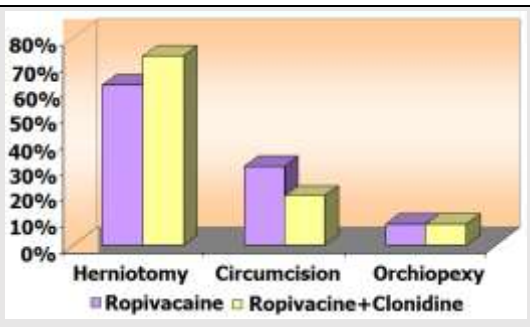

Figure 1. Distribution Based on Procedure

The two groups with respect to surgical procedure was not statistically significant after applying the chi ($\chi 2$) square test (p >0.05) figure 1. While considering the time of first analgesia in 24 hours, the mean time to requirement in the clonidine-ropivacaine (RO C) group was 6.35 hours (380.71 minutes) while it was 4.50 hours (270.00 minutes) in the Ropivacaine group (RO) and the difference was statistically significant. (Figure 2)

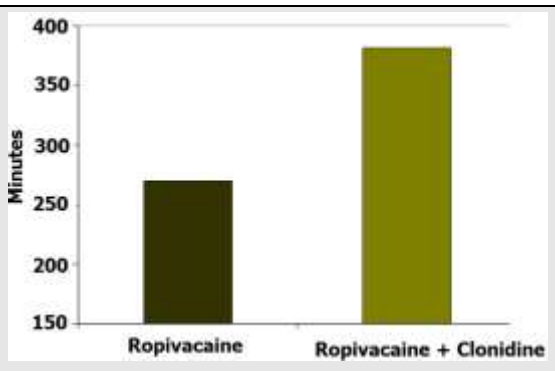

Figure 2. Time for First Analgesia (Minutes)

Table 3 compared the heart rate between the two groups during preoperative, immediate post-operative, post-operative 2 hours, 4 hours and 6 hours found that mean heart rate was statistically not significant during preoperative and immediate postoperative period which may be due to atropine premedication .The comparison of mean heart rate were statistically significant during 2nd, 4th and 6th hours, a fall in heart rate for RO C group were observed. Bradycardia is defined as heart rate of less than 60/minute. None of the patients showed bradycardia.

Heart Rate (Nos. /Min.)	Group	Mean	± SD	t Value	P Value
Pre-Operative	Ropivacaine	106.97	8.27	0.746	> 0.05
	Ropivacaine + Clonidine	105.78	9.60		
Immediate Post-Operative	Ropivacaine	105.44	7.49	-0.399	> 0.05
	Ropivacaine + Clonidine	105.98	7.69		
Post-Operative - 2 Hours	Ropivacaine	104.21	7.59	2.226	< 0.05
	Ropivacaine + Clonidine	101.30	7.05		
Post-Operative - 4 Hours	Ropivacaine	103.75	7.14	3.292	< 0.01
	Ropivacaine + Clonidine	99.30	7.99		
Post-Operative - 6 Hours	Ropivacaine	104.05	7.37	4.287	< 0.001
	Ropivacaine + Clonidine	97.9 0	8.66		

Table 3. Comparison of Heart Rate between the Two Groups at Different Hours of Observations

Systolic BP (mmHg)	Group	Mean	± SD	t Value	P Value
Pre-Operative	Ropivacaine	94.75	2.70	-0.772	> 0.05
	Ropivacaine + Clonidine	95.21	3.89		
Immediate Post-Operative	Ropivacaine	92.87	2.35	2.489	< 0.05
	Ropivacaine + Clonidine	90.98	5.55		
Post-Operative - 2 Hours	Ropivacaine	92.19	2.66	3.805	< 0.001
	Ropivacaine + Clonidine	89.87	4.03		
Post-Operative - 4 Hours	Ropivacaine	92.24	3.02	4.879	< 0.001
	Ropivacaine + Clonidine	89.22	3.87		
Post-Operative - 6 Hours	Ropivacaine	92.43	3.08	6.694	< 0.001
	Ropivacaine + Clonidine	88.57	3.38		

Table 4. Comparison of Systolic BP between the Two Groups at Different Hours of Observations

From table 4, it was observed that preoperative systolic blood pressure between two groups was not statistically significant whereas comparison of mean BP in two in the immediate postoperative and postoperative 2nd, 4th & 6th hours was found to be statistically significant which may be due to quality of analgesia with clonidine. Hypotension was defined as a 20-30% reduction from baseline systolic BP. None of the patients had hypotension.

Parameters	Ropivacaine			Ropivacaine + Clonidine			Mann-Whitney U	P Value
	Mean	Median	±SD	Mean	Median	±SD		
Pain Score @ 1st hour	4.97	5	0.18	5.00	5	0.00	1921.500	>0.05
Pain Score @ 2nd hour	5.00	5	0.00	5.00	5	0.00	1984.500	>0.05
Pain Score @ 4th hour	6.40	6	0.55	5.29	5	0.49	385.000	<0.001
Pain Score @ 8th hour	8.05	8	0.66	7.59	7	0.64	1382.500	<0.01
Pain Score @ 12th hour	8.84	9	0.51	8.54	8	0.46	1621.000	<0.05
Pain Score @ 24th hour	9.84	10	0.72	9.15	9	0.71	1516.000	<0.05
No. of Doses of Paracetamol Taken	2.68	3	0.47	1.65	2	0.63	517.500	<0.001
Sedation Score: Immediate Post-Operative	1.86	2	0.43	1.81	2	0.50	1888.500	>0.05
Sedation Score: Post-Operative - 6 Hours	2.86	3	0.35	2.67	3	0.48	1706.500	>0.05

Table 5. Mann Whitney U Test Comparing the Two Groups

The observational pain discomfort score (OPS) was assessed at 1, 2, 4, 8, 12 and 24 hours after caudal block. The pain score (table 5) at the 1st and 2nd hour was not significant whereas in the 4th hour it was found to highly

significant between the two groups. The score was found to be significant in the 8th, 12th and 24 hours which may be attributed to the superior analgesia by clonidine.

Comparison of mean values of sedation score in the immediate postoperative and postoperative 6th hours was not statistically significant during the two observations in between groups. (Table 5). The requirement of rescue medications needed was more in the RO group and was found to be statistically significant.

DISCUSSION

The lower incidence of cardiovascular side effects and neurotoxicity as well as ability to produce lesser motor blockade has made ropivacaine a safer choice as compared to bupivacaine for caudal epidural anaesthesia for day care surgeries. To avoid variation in the duration of surgery and anaesthesia ASA1 and ASA2 patients undergoing elective lower abdominal surgeries were included in the study. Since the spread of analgesia is unpredictable & failure rate is high in children older than 8 years, children belonging to 2 to 8 years of age group were alone included in the study. All patients were given same premedication and test drug.

Ropivacaine produces lesser postoperative motor blockade as compared to bupivacaine when used in lower concentration. Da Conceicao and colleagues[1,2] have identified moderate motor blockade in the early postoperative period when ropivacaine 0.25-0.375% is used. Ivani G et al,[3,4] Khalil S[5,6] et al used 0.2% of ropivacaine for caudal block for sub umbilical surgeries provided better post-operative analgesia and duration with fewer motor effects. However, Khalil S et al[5] and Luz G et al[7] reported that a concentration of 0.1% and 0.15% for caudal block to be insufficient to produce intraoperative analgesia. No reports of systemic toxicity of ropivacaine has so far been reported in children although caudal administration of 2.8 mg/Kg (Koinig H et al)[8] results in plasma levels which are comparable to the maximal tolerated levels in awake adult volunteers (Knudson et al).[9] The reduction of total amount of ropivacaine will thus further reduce the risk of systemic toxicity even if an inadvertent intravascular injection takes place. Thus in this study a concentration of 0.2% was selected. There was no motor blockade probably due to the lower concentration of ropivacaine used.

Clonidine an alpha-2 agonist, produces analgesia without significant respiratory depression after systemic, epidural or intrathecal administration. Clonidine as analgesic is more pronounced after neuraxial injection, which suggests spinal mode of action and makes this route of administration preferable. Klimscha et al[10] studied the effectiveness of caudal clonidine in children in potentiating the postoperative analgesic effect, found that addition of clonidine 1-2 µg /Kg to bupivacaine 0.25% significantly prolonged the median duration of analgesia compared to plain bupivacaine. Ivani G et al[3,4] studied the effectiveness of clonidine in prolonging the duration of analgesia even with a lower concentration of ropivacaine (0.1%). The time between caudal block and the need for supplemental analgesia was 125 minutes and 222 minutes in the 0.2% ropivacaine only group and 0.1% ropivacaine-clonidine (2 µg /Kg)group respectively in their study.

The addition of clonidine 2 µg / kg to 0.2% ropivacaine prolonged the duration of caudal block more than with 0.2% ropivacaine alone (mean duration of analgesia 380.71 minutes vs 270 minutes).Significantly fewer doses of analgesics were required over the first 24 hours by RO C group compared to RO group This study confirmed the findings of the study by Klimscha et al[10] and Ivani G et al.[3,4] An effective postoperative analgesia means a co-operative child with less emotional and hemodynamic stress and rapid recovery with less hospital stay.

Lee et al[11] and Ivani et al[3,4] in two independent studies using clonidine 2 µg / kg have shown increased sedation. Sedation was also noticed in a study by Motsch[12] and colleagues using 5 µg / kg clonidine in sub umbilical surgeries. In our study sedation was noted in RO C group and sedation causing obstructive apnoea and oxygen desaturation was not seen because of lower concentration used. However, the sedation scores were not statistically significant between the two groups as all the patients were easily arousable which is consistent with another study by Ivani G and Bergendahl H et al.[13] The sedative effects in children reflected the improved quality of analgesia offered by clonidine

Neuraxial clonidine administration can cause bradycardia due to parasympathetic predominance and inhibition of preganglionic sympathetic fibres resulting in hypotension. Klimscha et al[10] Eisenach J et al[14] observed decreases in mean arterial pressure following caudal block using local anaesthetics and clonidine at a dose of 1 and 2 µg /Kg. These differences occur within 20 minutes of caudal blockade and return to baseline within 1 hour of blockade, did not vary significantly from those seen with local anaesthetics alone.

In the present study there was a significant difference in heart rate between the two groups but none showed bradycardia may be due to atropine premedication used in patients. There was significant difference in systolic blood pressure between the two groups from baseline values but none of the patients had hypotension which is consistent with the findings of Jamali et al,[15] Klimscha et al[10] and Sukhminder Jit Singh Bajwa et al.[16] This showed the superior analgesia provided by clonidine and caudal block.

Neuraxial clonidine prolongs the motor blockade of local anaesthetics and can delay micturition. Koinig et al[8] in his study with 0.5% ropivacaine compared 0.25% ropivacaine, showed significant delay in micturition in the 0.5% group possibly due to higher concentration. Studies of Jamali S et al,[15] Klimscha et al,[10] Sukhminder Jit Singh Bajwa et al[16] on ropivacaine and clonidine did not show any delay of recovery of bladder function. These effects were minimal in the present study because of the use of low concentration of ropivacaine.

Sukhminder Jit Singh Bajwa et al[16] in his study on caudal ropivacaine and clonidine had three patients who had post-

operative vomiting, one in the ropivacaine only group and two patients from the ropivacaine-clonidine group. This was attributed to the effects of general anaesthesia and was not found to be statistically significant. In the present study there was no similar incidents in both the groups. This could be attributed to ondansetron premedication 0.1 mg/Kg intravenous prior to caudal block in both the groups.

None of the patients showed respiratory depression in the present study which was consistent with the findings of Jamali S et al,[15] Klimscha et al[10] and Sukhminder Jit Singh Bajwa et al[16] on ropivacaine and clonidine.

CONCLUSIONS

Clonidine appears to be an attractive adjuvant to local anaesthetics for prolonging postoperative analgesia without much adverse effects. In conclusion, the present study demonstrates that for caudal blockade, the addition of clonidine 2 µg/Kg to ropivacaine significantly prolongs the duration of analgesia without any significant clinical adverse effects.

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