A study to evaluate efficacy and safety of dexmedetomidine (1 µg/Kg) as an adjuvant to caudal ropivacaine (0.25%1 Ml/Kg) in paediatric infraumbilical surgeries

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Abstract

Aim: Clinical evaluation of efficacy and safety of dexmedetomidine used as an adjuvant to caudal ropivacaine in paediatric infraumbilical surgeries.

Materials and Method: In randomized, prospective, double blind study, 60 paediatric patients were randomly allocated into one of the two study groups of 30 each to receive caudal injection either ropivacaine (1ml/kg) + normal saline (0.5 ml) (RN) or ropivacaine (1ml/kg) + dexmedetomidine (1 µg/kg) (RD) for post operative analgesia. Pain was assessed by face, leg, activity, cry, consolability (FLACC) pain score and arousability assessed by Ramsay's sedation score.

Results: The duration of post operative analgesia in group RD was 8 hours as compared with group RN was 4 hours. The sedation scale was assessed by Ramsay's sedation score, Group RD showed better sedation and easily arousable as compared to group RN. The number of rescue analgesia was more in group RN (mean ±SD 1.69±0.66) as compared to group RD (mean ±SD 1.22±0.43), it was statistically significant with $P < 0.001$. Group RN patient significantly shows higher FLACC score compared with group RD patients.

Conclusion: Caudal dexmedetomidine 1 µg/kg with 0.25% of ropivacaine 1 ml/kg for paediatric patient undergoing lower abdominal surgeries achieved postoperative pain relief upto8 hours and the required dose of rescue analgesic was less with minimal adverse effects.

Keywords: Caudal block; ropivacaine; dexmedetomidine; children.

Introduction

Pain is an unpleasant subjective sensation which can only be experienced and not expressed, particularly in paediatric age group who completely depend on parents and care givers. Numerous methods have evolved for providing post-operative pain relief in paediatric patients. In paediatric surgeries caudal analgesia is one of the simplest and safest techniques, which reduces the administration amount of inhaled and intravenous anesthetics and attenuates stress response to surgery. A rapid smooth recovery and good immediate post operative analgesia is facilitated by caudal anesthesia. Single shot caudal block provide good quality pain relief during, immediate post operative period but after regression of block patient feels pain again. But the disadvantage of this technique using only local anesthetic is short duration of action. To avoid the risk of infection due to the placement of catheter andto prolong the duration of caudal anaesthesia many adjuvants. Like morphine, fentanyl, clonidine, ketamine and magnesium are added to local anaesthetic agents to prolong the duration of post-operative analgesia in paediatric patients.

Dexmedetomidine shows high affinity towards alpha2 adrenergic receptors. Dexmedetomidine has anxiolytic, analgesic, sympatholytic, sedative properties and without respiratory depressant effect. Dexmedetomidine also reduces both anesthetic and opioid analgesic requirement during perioperative period.

Ropivacaine is an amide local anaesthetic with long duration of action when it was used for paediatric caudal anaesthesia. It provides pain relief with less cardiotoxicity and with less motor blockade which makes it more suitable for caudal epidural analgesia especially for day care surgeries.

This study is being undertaken with the hypothesis that dexmedetomidine when given as additive at a dose of 1µg/kg to ropivacaine which prolongs the duration of analgesia when given in caudal anaesthesia in paediatric surgeries.

Materials and Method

This study was conducted from July 2016 to December 2016.This is a randomised double blinded study which included 60 children of ASA class I, of either sex, coming for various elective infra-umbilical surgical procedures such as herniotomies, circumcision, orchidopexy, perineal surgeries and minor lower extremity procedures.

The study was conducted after obtaining approval from ethical committee. Written informed consent was taken from patient guardians. Patients were randomly divided into two groups, details of the group and the drug to be given were sealed within envelopes, which was randomly picked and administered by one anaesthesiologist unrelated to study.

1. Group RN (30 patients) received caudal 1ml/kg of 0.25% ropivacaine along with 0.5 ml of Normal Saline.
2. Group RD (30 patients) received caudal 1ml/kg of 0.25% ropivacaine along with dexmedetomidine 1µg/kg, making volume to 0.5ml.

Pre-anaesthetic assessment: A detailed pre-anaesthetic evaluation including history of previous medical illness, previous surgeries, general examination and appropriate baseline investigations were carried out on the day prior to surgery and recorded. An informed and written consent was taken from the patient's guardian after explaining the anaesthetic procedure in detail.

Pre-operative fasting was done by restriction of solid food and formula feeds for 6 hours, milk for 4 hours and clear fluids for 2 hours prior to surgery. All patients were pre-medicated with syrup Promethazine 1 mg/kg, night before the surgery.

Patients were shifted to the operating room all necessary care was taken and caudal block was performed. Postoperatively patient was observed for FLACC score to know the duration of post operative analgesia, sedation was observed with Ramsay's sedation score.

The FLACC Scale

Categories	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disoriented	Frequent to constant frown, quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to; distractible	Difficult to console or comfort

Level/Score	Clinical Description
1	Anxious, agitated, restless
2	Cooperative, oriented, tranquil
3	Responds only to verbal commands
4	Asleep, brisk response to light stimulation
5	Asleep, sluggish response to stimulation
6	Unarousable

Total dose of rescue analgesia, no. of doses of rescue analgesia and adverse effects like bradycardia, hypotension, post operative nausea and vomiting, urinary retention were noted.

Statistical analysis: Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Results

The study was undertaken to analyze demographic profile, type of surgeries done, duration of post-operative analgesia, hemodynamic changes, requirement of rescue analgesia and adverse effects.

The age distribution of patients was 3-4.9 years and 5-8 years. As shown in the Table 1, the mean age was 4.80±1.88 and 5.80±1.67 years in groups RN and RD respectively. Difference was statistically insignificant. There were 77% and 70% males in group RN and RD respectively, whereas females were 23% and 40% respectively and were statistically insignificant. The weight distribution was categorized into 3 major categories. The patients were from 0 to 9.9 kg, from 10 to 14.9 kg of age and 15 to 20 kg of weight. From Table 1 the mean weight was 12.70±2.91 and 14.33±2.55 in kilograms (kg) in groups RN and RD respectively and difference between the groups was statistically insignificant.

The lower abdominal surgery cases constituted 43.3% in group RN and 53.3% in group RD, genital surgeries 30% in group RN and 6.7% in group RD and other surgeries 26.7% in group RN and 40% in group RD. Type of surgery is statistically similar except in case of Lower Abdominal Surgery which was slightly higher in Group RD with P value of 0.091.

The heart rate is compared from baseline with an interval of every 10 minutes. There is statistical significance of both the groups after 20 minute. There is also fall in heart rate in every 10 minutes in both the groups. In Graph 1 the heart rate of both the groups are shown.

In Graph 2 systolic blood pressure (SBP) of both the groups is shown. The systolic blood pressure is compared from baseline with an interval of every 10 minutes. There is no statistical significance for both the groups. And there was a fall in systolic blood pressure during the 1st 30mins.

In Graph 3 diastolic blood pressure (DBP) of both the groups are shown. The diastolic blood pressure is compared from baseline with an interval of every 10 minutes. There is no statistical significance of both the groups.

Table 2 shows FLACC score of group RN and RD group. There is significance difference between the groups in the FLACC score measured 4th hourly in the post-operative period. Group RN patient significantly shows higher FLACC score compared with group RD patients. In group RN, patients have FLACC score of 4 in the 4th hour, where as group RD had in the 8th hour.

Table 3 shows Ramsay sedation score of group RN and RD group. There is significant difference between the groups in the Ramsay's sedation score in the post-operative period. Group RN patient significantly shows score 1 at the 10thhour where as in group RD patients have score of 2.

In Table 4 shows the number of rescue analgesia given in both the groups. It is seen clearly that less number of times analgesia was required in group RD as compared to RN, with P <0.001 which is statistically significant.

In Table 5 shows the amount of rescue analgesia given to both the groups. It is seen that the amount of rescue analgesia is needed more in group RN as compared with RD.

In Table 6 shows the adverse effects of both the groups. As compared to both the groups distribution of adverse effects are statistically similar in two groups with P=0.781 which is statistically insignificant.

Table 1: Demographic Profile

Parameters	Group RN	Group RD	P Value
Age (in yrs)	4.80 ± 1.88	5.80±1.67	0.297(>0.05)
Sex (F/M)	7/23	9/21	0.559(>0.05)
Weight	12.70±2.91	14.33±2.55	0.111(>0.05)

Table 2: FLACC Score

FLACC Score	4 hours	6 hours	8 hours	10 hours	12 hours	16 hours	20 hours	24 hours
Group RN (n=30)								
0	25(83.3%)	22(73.3%)	24(80.0%)	24(80.0%)	25(83.3%0	23(76.7%)	28(93.3%)	27(90.0%)
1	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
2	2(6.7%)	2(6.7%)	4(13.3%)	6(20%)	3(10%)	5(16.7%)	1(3.3%)	0(0%)
3	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	2(6.7%)	1(3.3%)	3(10%)
4	3(10%)	6(20%)	2(6.7%)	0(0%)	3(10%)	0(0%)	0(0%)	0(0%)
Group RD (n=30)								
0	29(96.7%)	29(96.7%)	28(93.3%)	28(93.3%)	23(76.7%)	28(93.3%)	24(80.0%)	29(96.7%)
1	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
2	1(3.3%)	1(3.3%)	0(0%)	1(3.3%)	0(0%)	0(0%)	3(10%)	1(3.3%)
3	0(0%)	0(0%)	0(0%)	1(3.3%)	5(16.7%)	0(0%)	3(10%)	0(0%)
4	0(0%)	0(0%)	2(6.7%)	0(0%)	2(6.7%)	2(6.7%)	0(0%)	0(0%)
P value	0.227	0.014*	0.212	0.103	0.151	0.009**	0.327	0.237

Table 3: RAMSAY Score

Sedation score	2 hour	4 hours	6 hours	8 hours	10 hours	12 hours	16 hours	20 hours	24 hours
Group RN (n=30)									
1	0(0%)	0(0%)	0(0%)	0(0%)	1(3.3%)	0(0%)	0(0%)	0(0%)	0(0%)
2	23(76.7%)	27(90%)	22(73.3%)	26(86.7%)	26(86.7%)	22(73.3%)	23(76.7%)	29(96.7%)	27(90.0%)
3	5(16.7%)	0(0%)	4(13.3%)	3(10%)	1(3.3%)	3(10%)	5(16.7%)	0(0%)	0(0%)
4	2(6.7%)	3(10%)	3(10%)	1(3.3%)	2(6.7%)	5(16.7%)	2(6.7%)	1(3.3%)	3(10%)

5	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Group RD (n=30)									
1	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
2	30(100%)	29(96.7%)	29(96.7%)	28(93.3%)	28(93.3%)	23(76.7%)	28(93.3%)	24(80.0%)	29(96.7%)
3	0(0%)	1(3.3%)	1(3.3%)	1(3.3%)	1(3.3%)	1(3.3%)	2(6.7%)	5(16.7%)	0(0%)
4	0(0%)	0(0%)	0(0%)	1(3.3%)	1(3.3%)	5(16.7%)	0(0%)	1(3.3%)	1(3.3%)
5	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	1(3.3%)	0(0%)	0(0%)	0(0%)
P value	0.011*	0.237	0.065+	0.204	0.802	0.531	0.009**	0.052+	0.612

Table 4: No of rescue analgesia doses

No. of rescues analgesia	Group RN		Group RD	
	No	%	No	%
Nil	1	3.3	12	40.0
1	12	40.0	14	46.7
2	14	46.7	4	13.3
3	3	10.0	0	0.0
Total	30	100.0	30	100.0
Mean ±SD	1.69±0.66		1.22±0.43	

Table 5: Total Suppository Paracetamol (mg)/ Total Inj. Fentanyl (µg)

	Group RN	Group RD	P value
Total Suppo. Paracetamol (mg)	319.23±107.12	278.18±142.79	0.377
Total Inj. Fentanyl (µg)	42.00±21.68	26.00±8.43	0.056 +

Table 6: Adverse effects in two groups studied

Adverse effects	Group RN (n=30)		Group RD (n=30)	
	No	%	No	%
Nil	20	66.7	21	70.0
Yes	10	33.3	9	30.0
Brady	1	3.3	3	0.0
Hypo	2	6.7	0	30.0
PONV	4	13.3	2	0.0
UR	3	10.0	4	0.0

Discussion

Many studies have reported using opioids and other drugs in caudal block in children for optimal postoperative analgesia. Although the use of caudal opioids did prolong the duration of analgesia, it was associated with several adverse-effects like respiratory depression, urinary retention, nausea, vomiting and pruritus. So, other drugs like clonidine and dexmedetomidine are being used to improve analgesia in the postoperative period and also avoiding the side-effects associated with opioid use.

In comparison to bupivacaine, ropivacaine has a wider margin of safety, less cardiovascular or neurological toxicity, less motor blockade and similar duration of action. Hence, it can be used safely in paediatric patients for the regional anesthesia and analgesia.

In the present study, caudal block using ropivacaine alone and ropivacine along with dexmedetomidine was used and the study was conducted in 60 children in the age group of 0 to 10 years of ASA grade I coming for various elective infraumblical surgeries.

In the present study, there was no significant difference in the two groups with regard to age, weight and sex. The mean age was 4.80±1.88 years in group RN and 5.80±1.67 years in group RD. The mean weight was 12.70±2.91 kg in group RN and 14.33±2.55 kg in group RD. In both the groups' males were more (> 70%). This could be due to inclusion of surgeries like herniotomy, orchidopexy and circumcision in our study.

In 2002, Deng XM et al[14] studied the effect of caudal analgesia in children undergoing hyospadiasis repair, where all patients were males (100%). We have used face, leg, activity, cry, consolability (FLACC) score[15,16] in our study which is a valid, objective and reliable method of pain assessment in children between 0 to 10 years.

It does not require patient participation. If the pain score is more or equal to 4, supplementary analgesic with paracetamol suppository (15 mg/kg) / injection fentanyl (1 µg /kg) IV was given. Group RD had a postoperative analgesia of 8 hours as compared to group RN where only 4 hours of postoperative analgesia which was seen statistically significant. Group RN achieved higher FLACC score compared with RD patients.

El-Hennawy et al[17] confirmed the superiority of caudal dexmedetomidine 2 µg/kg over plain bupivacaine 0.25% (1 ml/kg) in a double blind study of 6 months-6 years of age, undergoing below umbilical surgeries. The mean duration was significantly longer in dexmedetomidine group (14-18 hours) compared with those receiving plain bupivacaine (4-6hours).

VG Anand and co-workers[1] confirmed the superiority of caudal dexmedetomidine 2 µg/kg over plain ropivacine 0.25% (1 ml/kg) in a randomized double blind study. Their study inferred that caudal dexmedetomidine 2µg/kg with 0.25% ropivacaine 1ml/kg achieved significant postoperative pain relief of 15 hours, which resulted better quality of sleep and prolonged duration of arousable sedation.

The sedation scale was assessed by Ramsay's sedation score. Patients were considered sedated with score 2-3. There was a significant difference between the two groups in the Ramsay's sedation score in the post-operative period. Group RN patient significantly showed score 1 at the 10th hour where as in group RD patients has score of 2 throughout the post – operative period for 24 hours. This shows that group RD has better sedation with better arousal.

Vijay G Anand and co-workers[1] found that addition of dexmedetomidine resulted in a better quality of sleep and a prolonged duration of arousable sedation.

In the present study, heart rate and blood pressure of all the patients were monitored at regular intervals.

The mean baseline heart rate was similar in both groups before the administration of caudal block. The mean baseline rate was 126.53±20.29 beats per minute in group RN and 120.50±26.11 beats per min in group RD. There was significant fall in heart rate after 10 minutes which showed 115.27±19.06 and 107.23±16.46 beats per minute. Due to effect of caudal block at 20 minutes the heart rate dropped to 97.07±13.56 beats per minute in group RD and increase in heart rate 104.63±24.86 beats per minute in group RN. Bradycardia was observed in group RD and was treated with atropine and decrease in volatile agents.

The mean baseline systolic blood pressure was 115.17mm Hg in group RN and 113.97mmHg in group RD. There was a gradual fall in the systolic blood pressure in group RD till 30 minutes to 98.98 mmHg.

The mean baseline diastolic blood pressure was 73.60mm Hg in group RN and71.50 mmHg in group RD. The diastolic blood pressure was stable in both group RN and RD and was statistically insignificant.

Arora MK and co-workers[18] reported hemodynamic effect in the form of hypotension. In their study hypotension treated in 6 out of 30 patients with ionotropes.

Vijay G Anand[1] and EL-Hennaway AM[17] reported no significant change in hemodynamics.

In our study the rescue analgesia used was paracetamol suppository (15 mg /kg) / injection fentanyl (1 µg/kg) IV in both the groups. If FLACC score was more than 4 or more rescue drug was given. Over a postoperative period of 24 hours the number of times given rescue analgesia was seen. The number of rescue analgesia was more in group RN (mean ± SD 1.69±0.66) as compared to group RD (mean ± SD 1.22±0.43), it is statistically significant with $P < 0.001$.

In our study the amount of suppository paracetamol in group RN (mean ±SD 319.23±107.12) as compared to group RD (mean ± SD 278.18±142.79), it was statistically significant with P value 0.377. Injection fentanyl was also used in group RN (mean ±SD 42.00±21.68) as compared to group RD (mean ± SD 26.00±8.43), it was statistically significant with P value 0.056. Hence it reflects that the duration of rescue analgesia by dexmedetomidine is not only longer but also reduces the need for rescue analgesia in 24 hour postoperative period.

Urinary retention, post – operative nausea and vomiting (PONV), were the adverse effects observed in both RN and RD groups. Bradycardia was observed in 3 subjects in group RD. Both the groups distribution of adverse effects are statistically similar, in two groups with P=0.781 which is statistically insignificant. But in Arora MK and co-workers[18] reported hemodynamic effect in the form of hypotension. In their study hypotension was seen in group B 6 out of 30 patients which were treated with ionotropes.

Conclusion

Caudal dexmedetomidine 1 µg/kg with 0.25 % of ropivacaine 1 ml/kg for paediatric patient undergoing lower abdominal surgeries achieved postoperative pain relief upto8 hours and the required dose of rescue analgesic was less with minimal adverse effects.

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