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Effect of addition of clonidine to bupivacaine or ropivacaine on caudal efficacy and effectiveness in pediatric patients undergoing infraumblical surgery

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Abstract

Introduction: Children are not as expressive as adults, but they do feels pain equally. In the perioperative period, pain is the most alarming, upsetting and disturbing symptom for a patient. In pediatric populace, amongst the regional blocks, caudal epidurals with local anesthetics are preferred and universally practiced by anesthesiologists, but comparatively shorter period of analgesia is its major limitation. So, to improve the effectiveness of caudal epidurals, a variety of additives are used besides local anesthetics.

Materials and Method: A double-blind, prospective and randomised study was carried on 60 children falling in the age group of 1- 6 years belonging to ASA I or II, posted to undergo surgery infraumblically, were allocated randomly to one of two groups of 30 each who then received injection of 0.25% bupivacaine-clonidine(2ug/kg) or 0.25% ropivacaine-clonidine (2µg/kg) @ 1ml/kg caudally. Haemodynamic variables were documented peri-operatively. Pain was assessed using the Modified Hanallah pain score for 24 hours and complications were observed in the postoperative period.

Results: No statistically significant difference was observed when 2ug/kg of clonidine added to 0.25% bupivacaine or 0.25% ropivacaine caudally in pediatric patients, in procedures below the umbilicus with mean duration of analgesia with group BC and RC were mins respectively. Also no significant undesirable side effects like bradycardia, hypotension, urinary incontinence, nausea and vomiting were observed in either of these groups.

Conclusion: The mean extent of analgesia was equally prolonged in both the groups postoperatively. So, clonidine in a dose of 2ug/kg added to 0.25% bupivacaine or 0.25% ropivacaine for caudal analgesia, proves safe and effective method in prolonging the duration of analgesia without producing any significant side effects.

Keywords: Bupivacaine, Ropivacaine, Caudal, Infraumbilical surgery, Clonidine, Post-operative analgesia.

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Introduction

Caudal epidural block, among the regional blocks is not only frequently performed but is also the accepted procedure by majority in pediatric populace. Along with cutting the requirement of additional anaesthetics, it also decreases the traumatic response to surgery and helps in delivering a speedy and uneventful recovery.[(1)]

Major limitation following caudal anaesthesia, is its comparatively shorter length of analgesia in the postoperative period[(2)] even when amide local anesthetics like bupivacaine and ropivacaine were chosen. Although there is better separation of sensory and motor effects with ropivacaine, still it results in comparable analgesia as with bupivacaine.

A variety of additives for instance morphine, fentanyl and butorphanol, are required to enhance and lengthen the effect of caudal analgesia. Supplementation of such agents caudally with local anesthetics helped in extending the extent of block, but along with that there are number of disagreeable side effects such as nausea, vomiting, irritation, itching, urine retention, in addition they also have the likelihood to develop respiratory compromise.[(3)]

To overcome such untoward effects, non-opioid additives such as tramadol,[(2)] ketamine,[(4)] and neostigmine,[(5)] adrenaline[(6)] etc. have been used but that also with unpredictable outcome. Tramadol appreciably prolongs the length of postoperative analgesia when added caudally to bupivacaine in children.[(7)] Likewise, use of ketamine and neostigmine caudally reported to enhance the period of analgesia but are also accountable for complications such as hallucinations, nausea and vomiting which additionally limits their clinical efficacy.

Use of caudal clonidine may offer significant analgesic benefits. Clonidine is a central acting partial alpha$_2$ adrenergic agonist (220:1) α_2 to α_1. Presence of alpha$_2$ receptors in the spinal cord helps in modulating pain pathway and hence resulting in analgesia.[(8)] Clonidine helps in enhancing the intensity and extent of local anesthetics when caudally administered and reduces the additional supplementation of analgesics, attenuates requirements for anaesthetics, also helps in limiting haemodynamic changes and provide sympathoadrenal stability perioperatively.

So, in order to compare the efficacy and effectiveness of caudal bupivacaine-clonidine and ropivacaine-clonidine, we conducted a study in our

institute on pediatric patients posted for surgeries below the umblicus. We in our study, also studied complications with the use of these drug combinations.

Materials and Method

A double-blind, prospective and randomised study was carried on 60 children falling in the age group of 1-6 years belonging to class I or II of American society of anesthesiology(ASA), posted to undergo surgery of infraumblical region, after getting approval from hospital ethics committee and written consent from the parents. Children with known neurological compromise, local sepsis at the site of injection, bleeding diathesis, hypersensitivity to local anesthetics, deformity of sacrum or tubercular spine, those on blood thinners were excluded from the study group. Thereafter, according to 60 coded slips in an opaque envelope, patients were assigned randomly to one of two groups.

Group BC(n=30): Received bupivacaine 0.25% with clonidine (2µg/kg) @1ml/kg.

Group RC(n=30): Received ropivacaine 0.25% with clonidine (2µg/kg) @1ml/kg.

Before surgery, pre anaesthetic checkup was done thoroughly and patients advised fasting according to age as per the fasting protocols. Next morning, in pre recovery area, premedication with syrup midazolam @0.5mg/kg was given 30 minutes before surgery, thereafter, patient was shifted to operating room. Following the placement of monitors, induction with halothane and nitrous oxide in oxygen via Jackson and Rees circuit. On deepening, good intravenous line secured and after that maintenance all the way through the procedure was done using facemask with O_2 + Nitrous oxide+ Halothane.

Once the child deepens with inhalational agents, lateral decubitus position was made and aseptically using 24 gauge intravenous needle, caudal block was given. Confirmation of the correct space was done with 'whoosh test'. After ensuring no blood or cerebrospinal fluid, drug mixture was introduced in the space.

On procedural completion, patient was placed supine and surgeon allowed to perform on achieving caudal efficacy which was defined as lack of limb movements or significant(>20%) change in heart rate(HR) and/or respiratory rate(RR) on applying forceps at the site of incision 5 minutes after placement of caudal anaesthesia and every 2 minutes thereafter upto 15 minutes. Similarly, caudal effectiveness score was used to check the quality of block. Intraoperatively, parameters monitored were SpO_2, noninvasive blood pressure(NIBP), heart rate, respiratory rate and noted at 5 minutes interval throughout the procedure. Modified Hanallah pain scale[(1)] was used to assess postop pain relief and sedation score to observe sedation intensity in which grade 1-asleep i.e. no arousle with vocal response; 2-asleep, arousable through vocal contact; 3-drowsy not sleeping; 4-attentive/aware. Duration of motor block was noted till the child started leg movements. Also, additional requirement of analgesic doses in first 24 hours period following surgery was recorded.

On completion, the study groups were decoded. Data thereafter was compiled and the results were analyzed statistically, for parametric statistics Student's paired t- test, ANOVA and Posthoc tests were used and for non-parametric records, Chi square test used. Statistical significance was given to the value if $p < 0.05$.

Observations & Results

In order to evaluate the efficacy and effectiveness of addition of clonidine combined with bupivacaine or ropivacaine, the present study was performed on 60 ASA I & II in age group of 1- 6 years scheduled for infraumblical surgery. Comparable results were obtained when demographic profile with regards to age, sex and weight in group BC and group RC was considered. No statistically significant difference was found and is clearly evident from the Table 1.

Table 1: Comparison of demographic profile

	Group BC	Group RC	Statistical analysis
SEX(M/F)	26/4	27/3	NS
Age(years)	2.70±1.74	2.21 ±1.14	NS
Weight	13.25±3.79	13.65±3.26	NS

Also, when surgical procedure performed and surgery duration in minutes were compared, no statistical significant difference was witnessed in both the groups.

Baseline parameters were recorded and as seen in Table 2 no significant differences was seen on intergroup comparisons.

Table 2: Comparison of baseline haemodynamic parameters

Haemodynamic parameters	Group BC	Group RC	Intergroup comparison
Mean HR beats/min	117.25±6.95	116.05±9.23	NS
Mean SBP mmHg	100.80±10.19	100.45±8.69	NS
Mean DBP mmHg	53.70±7.95	52.35±6.12	NS
Mean RR breaths/min	32.09±5.24	28.70±4.21	NS
Mean SpO2	99.35±.74	99.50±.68	NS

Fig. 1, elucidates the results of heart rate between both the groups in the intraoperative period and no statistical difference was observed.($p>0.05$)

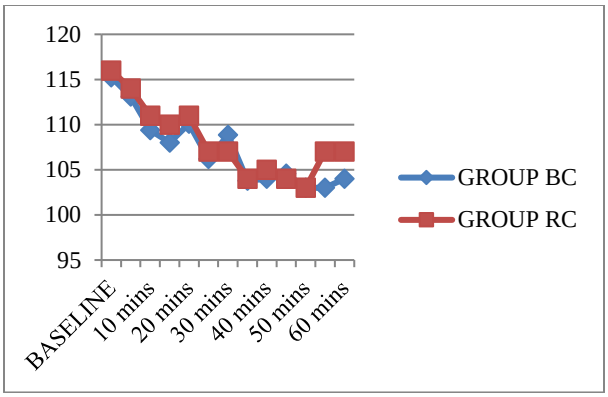

Fig. 1: Mean intraoperative heart rate

Fig. 2, 3 demonstrates the mean systolic and diastolic blood pressure in group BC and RC and parallel inclination was observed in both the groups in terms of blood pressure at different intervals during surgery intraoperatively, further suggesting that difference was not statistically significant in group BC and RC.

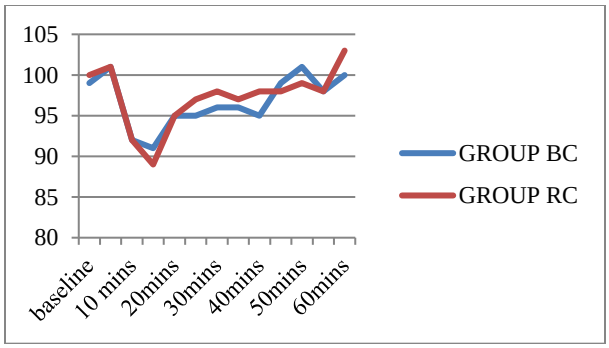

Fig. 2: Mean systolic blood pressure

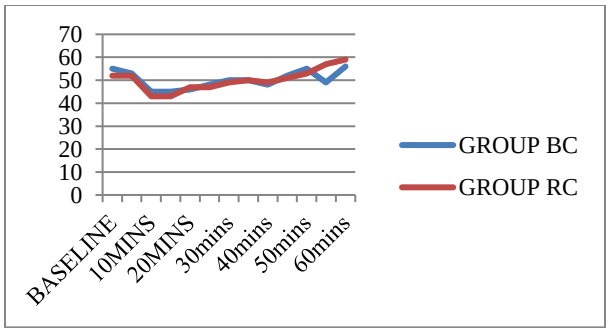

Fig. 3: Mean diastolic blood pressure

The analgesic duration was defined as the time from caudal injection until pain score ≥4. The entire extent of analgesia in group BC and RC was 617.25±202.03 minutes and 687.07±192.27 minutes and this dissimilarity was statistically not worth mentioning (Table 3).

Table 3: Total duration of postoperative analgesia in 24 hours period

Total duration of analgesia in mins	Group 2	Group 3	Statistical analysis
	664.50±185.93 (11.07±3.09)	719.00±226.45 (11.9±3.77)	NS

Data are Mean±SD NS: non significant (p>0.05) HS: highly significant (<0.001)

Quality of pain relief among the study groups was evaluated using modified hanallah pain score, time to first rescue analgesia and total analgesic requirement in the postoperative period. The mean pain score in group BC and group RC increased at around 8 - 10 hours in the ward; thereafter, the pain score started reducing with rescue analgesia and remained mild. On intergroup comparisons, there was no statistical significance between group BC and RC at any given time. (Fig. 4)

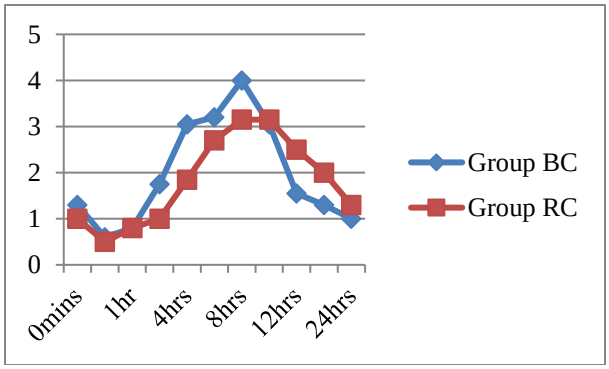

Fig. 4: Mean modified hanallah pain score

Table 4, is showing the total number of analgesic doses required postoperatively. It is evident from the above observation that not all the patients demanded rescue analgesic doses.

No significant complications were observed apart from one case of urinary retention in group BC.

Table 4: Total number of doses of rescue analgesia consumed in 24 hours

No. of doses required (syrup paracetamol)	Group BC	Group RC
0	8	9
1	22	21
2	5	4

Discussion

Our study indicates that addition of caudal clonidine 2 µg/kg to bupivacaine 0.25% and ropivacaine 0.25%, prolongs the analgesic duration significantly suggesting that clonidine- local anesthetic mixture reduced the analgesic requirement. Similar to our study, Koul et al and Parmeshwari et al also demonstrated that with clonidine addition to bupivacaine, duration of analgesia[9,10] was prolonged significantly. Similarly Bajwa et al and Neogi at al concluded that as compared to plain ropivacaine, clonidine addition to ropivacaine prolonged the total interval of analgesia significantly.[11,12] Although, the duration of analgesia was enhanced in both groups with the use of clonidine, but no significant difference was observed in our study, when both the groups were compared.

Sharpe et al and Cook et al witnessed much less increase in the mean duration of analgesia on addition of clonidine to local anaesthetics which is contrasting to our study reslts and this contrary may be attributed to lesser amount of bupivacaine (0.5ml/kg) was utilized by Sharpe et al and no use of midazolam as premedicant by Cook et al[13,14]

In our study, in order to avoid factors interfering with analgesia requirement or haemodynamic variables in both the groups, we selected the patients who were undergoing the same surgical procedure, using oral midazolam as pre-medication in all the patients, same pattern of induction and Modified hanallah pain scorewere used in both study groups to assess the caudal efficacy and effectiveness using clonidine along with bupivacaine or ropivacaine. Also, number of doses of rescue analgesia required in 24 hour postoperative period were noted.

Post-operatively, for a period of 24 hours, our patients were monitored so as to calculate the average number of doses of rescue analgesia required by both the groups. Contrasting results to our study were elicited by Koul A et al and Klimsha W et al and that may be due to fact that only a six-hour period was observed by the observer post-operatively[9,6] and thereafter following that period, parents assessed further.

Mean heart rate, Systolic and diastolic blood pressure were compared intraoperatively with the baseline values in our study, and a dip in HR and BP between 10-35 mins was found suggesting the onset of effect of clonidine but the difference when compared statistically with baseline, it turned out to be non significant. Similar to our study, Koul A et al reported comparable results. It is reported that clonidine in a dose of 1-5 µg/kg in children can be used without significant clinical respiratory or haemodynamic effects[9] Motsch and colleagues reported that although complications such as bradycardia and hypotension appear to be less evident in children when compared with adults, still they are dose-dependent.[16]

Patients under study groups, remained asleep for longer duration and the level of sedation can be contributed by both effect of clonidine and prolonged analgesia. Lee et al in concordance to our study also established comparatively prolonged duration of sedation in postoperative period following caudal bupivacaine with clonidine 2 µg/kg than with bupivacaine alone (mean 9.1 h vs 5.8 h).[15] Additionally, Klimscha et al and Motsch et al witnessed increase in the sedation score in the group were clonidine was used caudally with local anesthetic as part of the anaesthetic technique.[6,16] Whereas, Sharpe et al in contrary to our study, did not find much sedation in recovery room in clonidine receiving groups.[13] This difference in sedation possibly can be explained with the use of lower concentrations of caudal clonidine by the above authors.

None of the two groups observed any complications like nausea, vomiting, pruritis, erythema, hallucination. Urinary retention i.e. time to first micturition >6 hours, was seen in a single patient for which catheterization was not required. Cook et al and Klimscha et al also did not notice any significant complications similar to our observations.[6,14]

Conclusion

The mean extent of analgesia was equally prolonged in both the groups postoperatively and on intergroup comparison no statistical considerable difference was experienced. So, clonidine in a dose of 2ug/kg added to 0.25% bupivacaine or 0.25% ropivacaine for caudal analgesia, during infraumbilical surgery, proves safe and effective method in prolonging the duration of analgesia without producing any undesirable side effects. Hence, either of these drug combination can be choosen for prolongation of analgesia.

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