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COMPARATIVE STUDY OF CAUDAL ROPIVACAINE AND ROPIVACAINE-CLONIDINE COMBINATION IN PAEDIATRIC UROGENITAL SURGERIES FOR POST-OPERATIVE ANALGESIA

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ABSTRACT: BACKGROUND: Addition of clonidine to ropivacaine (0.2%) can potentially enhance analgesia without producing prolonged motor blockade. The aim of the study was to compare the post-operative pain relieving quality of ropivacaine (0.2%) and clonidine mixture to that of plain ropivacaine (0.2%) following caudal block in children's. **OBJECTIVE:** In this study I examined the quality, post-operative analgesia and haemodynamics effects in children when clonidine is added to ropivacaine for urogenital surgeries in caudal anaesthesia. **MATERIAL AND METHODS:** In this clinical trial, 30 children's aged 1-10 years who were candidates for elective urogenital surgeries were studied. Induction and maintenance of anaesthesia were achieved using propofol, sevoflurane and nitrous oxide. Children were randomly divided into 2 groups in double blind fashion, and were given caudal block with 0.2% ropivacaine (1ml/kg) alone and ropivacaine plus clonidine 2mcg/kg. Haemodynamic parameters were observed before, during and after the surgical procedure. Post-operative analgesia evaluated using FLACC score and sedation was assessed using Ramsey sedation scale. Paracetamol was given orally for cases with FLACC score 4 or more. **RESULTS:** Duration of analgesia was found to be significantly longer in the group given ropivacaine plus clonidine. **CONCLUSIONS:** I concluded that addition of clonidine to ropivacaine prolongs the duration of post-operative analgesia without any respiratory or haemodynamic side-effects.

KEYWORDS: Fentanyl, Combined epidural spinal block, Visual analogue scale.

INTRODUCTION: It is defined by International Association of Study of Pain as "an unpleasant sensory and emotional experience associated with potential tissue damage". Post-operative pain relief in paediatric patients needs special attention due to their inability to express the severity and type of pain, they are suffering. Significant pain from improper analgesia will not only cause unacceptable pain during procedure, but also produces "pain memory", as illustrated by exaggerated response to vaccination as long as 6 months following surgery.¹ Caudal analgesia is a useful adjunct to general anaesthesia for lower abdominal surgeries in children as it provides postoperative analgesia and reduces perioperative narcotic requirement.² Unfortunately motor blockade resulting from caudal block may be a Cause of distress in post-operative period and may lead to delayed hospital discharge.³

Single shot caudal block with bupivacaine is the most commonly used regional technique for intra operative and postoperative pain relief in children. It has been proved that its efficacy in producing safe, reliable, efficient and long lasting analgesia.⁴ Ropivacaine is another amide local anaesthetic which has been reported to cause less motor block and less cardiotoxicity than bupivacaine, but producing similar duration of analgesia.² Some studies showed that use of ropivacaine in caudal block causes a quicker onset and longer duration of action than bupivacaine.⁵

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The main disadvantage with single shot caudal block with plain local anaesthetic is its short duration of action. To prolong the duration of analgesia and to reduce the intra and postoperative analgesic requirements many adjuncts have been investigated like Clonidine, Midazolam, S-Ketamine, Fentanyl, Dexmedetomidine etc.

Addition of Clonidine has allowed the use of lower concentration of Local anaesthetic for achieving same level of anaesthesia but increases the duration of analgesia with increasing the margin of safety and reduces the incidence of unwanted motor blockades.⁶

This study has been carried out to compare the efficacy of caudal block with ropivacaine and ropivacaine with clonidine combination in paediatric urogenital surgeries:

1. To compare the effect of Ropivacaine versus Ropivacaine-Clonidine combination for caudal block in paediatric patient, in a prospective randomized controlled study.
2. To compare duration of post-operative analgesia.
3. To evaluate the hemodynamic effects produced by both the drugs.

METHODOLOGY: After obtaining approval from the Hospital Ethics Committee and written informed consent from the patients, this single center, prospective, randomized, double blind study was conducted in the Department of Anaesthesiology MGM Medical College, Indore. A sample size of 60 patients with ASA Grade I and II aged between 01 to 10 years scheduled to undergo elective urogenital surgeries.

They were randomly divided into two equal groups, Group A and group B; each patient underwent a thorough pre-anaesthetic check-up prior to surgery. Premedication syrup Midazolam 0.5mg/kg was given 1 hour prior to surgery. Inj. Glycopyrolate 0.004mg/kg intramuscular administered half an hour prior to surgery. Anaesthesia was induced with Inj. Propofol 2-3mg/kg and Inj. Suxamethonium chloride 2mg/kg. Appropriate sized endotracheal tube was inserted. Anaesthesia was maintained with 70% nitrous oxide in oxygen and sevoflurane 2%, with intermittent positive pressure ventilation. After induction patients received caudal block with Inj. Ropivacaine (0.2%) 1ml/kg+0.5ml Normal saline (Group A) and Inj. Ropivacaine (0.2%) 1ml/kg with Inj. Clonidine 2mcg/kg diluted to 0.5ml with Normal saline (Group B) in left lateral position using a 23-gauge short bevel needle under aseptic conditions.

No intraoperative sedatives or opioids were administered.

Heart rate (HR), Systolic blood pressure (SBP), and Peripheral arterial saturation (SPO₂) were recorded before the induction of anaesthesia and every 5min after the placement of caudal anaesthesia till the end of surgery.

During surgery, adequate analgesia was defined by hemodynamic stability, as indicated by the absence of an increase in SBP or HR by >15% of pre incision baseline values. Sevoflurane concentration was maintained between 2-3%. An increase in HR or SBP within 25 minutes of skin incision indicated failure of caudal anaesthesia.

If the recordings increased by >15%, the child received a rescue opioid (Fentanyl 2mcg/kg initially and subsequently 0.5mcg/kg as directed by hemodynamic variables), because analgesia was considered inadequate. They were excluded from the study.

Fluid therapy was standardized during and after surgery. During surgery, children received lactated Ringer's solution 4 ml/kg/hr, whereas 5% Dextrose in 0.45% NaCl was infused at 4 ml/kg/hr in the postoperative period. An intraoperative decrease of SBP or HR by >30% was defined

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as hypotension or bradycardia, respectively, and was treated by fluid bolus, (10ml/kg), ephedrine (0.01mg/kg IV), or atropine (.02mg/kg IV) as necessary.

Each patient was observed for 2 hour in the recovery room before being transferred to paediatric surgery ICU. HR and SPO₂ were monitored continuously, and SBP was monitored every 5 min. When the child was awake in the recovery room, pain, sedation scores, respiratory rate, SBP, and HR were assessed. Assessments were repeated every 2hrs, 4hrs, 6hrs, 8hrs, 10hrs, 12hrs, 14hrs after recovery from anaesthesia.

Postoperative pain was assessed with FLACC score.

The visual analogue scale (10cm horizontal scale) could not be used in our study because it was not well understood by all children in the study. If the FLACC pain score was 4 or more, syrup paracetamol 15mg/kg was administered. The duration of analgesia (From the time of caudal injection to the time at which FLACC score was 4 or more) was also recorded.

Parameter	Finding	Points
Face	No particular expression or smile	0
	Occasional grimace or frown withdrawn, disinterested	1
	Frequent to constant quivering chin, clenched jaw	2
Leg	Normal position or relaxed	0
	Uneasy, restless, tense	1
	Kicking or legs drawn up	2
Activity	Lying quietly, normal position, moves easily	0
	Squirming, shifting back and forth, tense	1
	Arched, rigid or jerking	2
Cry	No cry (Awake or sleep)	0
	Moans or whimpers occasional complaints	1
	Crying steadily, screams or sobs, frequent complaints	2
Consolability	Content relaxed	0
	Reassured by occasional touching hugging or being to, distractable	1
	Difficult to console or comfort	2
FLACC score to assess post-operative analgesia		

Sedation score was assessed using Ramsey's sedation scale as follows:

1. Anxious and agitated or restless or both.
2. Co-operative, oriented and calm.
3. Responsive to commands only.
4. Exhibiting brisk response to glabellar tap or loud auditory stimulus.
5. Exhibiting a sluggish response to light glabellar tap or loud stimulus.
6. Unresponsive.

Complication such as postoperative nausea and vomiting (PONV), respiratory depression, urinary retention, hypotension and bradycardia were also noted. Respiratory depression was defined as a decrease in SPO₂ of less than 95% requiring supplementary oxygen.

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Hypotension was defined as systolic arterial pressure plus twice the age in years and associated with altered peripheral perfusion.

Bradycardia was defined by as HR below 80 beats per min for age 1 year and 60 beats per min for ages above 1 year. Delayed anaesthetic emergence was defined as 20 min elapsing from the end of surgery to exiting the operation theatre.

A follow up study was undertaken to detect any adverse neurological outcome in the study population. This follow up consisted of a questionnaire to parents (Any movement abnormality, child complaining of any abnormal sensation, such as pain {any sort of pain, without an obvious injury or lesion}, paresthesia or weakness, any loss of bladder or bowel function, dislike for outdoor sports) and a physical examination, which consisted of observations of movements, tests of motor power, reflexes, position, vibration, and temperature sense. Tests for position, vibration, and temperature were performed in children who could comprehend the directions given to them.

Elective urogenital surgeries were included in our study to avoid the type, nature, and duration of pain associated with different types of surgery. Moreover, all cases were performed by the same surgical team to minimize the differences in tissue handling. Observations are analyzed using independent unpaired 't' test, relevance test for equality of variance and; t; test for equality of means.

OBSERVATION AND RESULTS:

Age (Years)	Group A	Group B
1-3 yrs	9	9
4-6 yrs	9	10
7-9 yrs	7	6
10-12 yrs	5	5
Mean +/- SD	5.61 +/- 3.04	5.44 +/- 2.99

Table 1: Age distribution

As per Table 1, the mean age distribution in group Ropivacaine and Ropivacaine with Clonidine are almost same without any significant difference.

Sex	Group A	Group B
Male	27	27
Female	3	3

Table 2: Sex distribution

Both groups have equal gender ratio, hence avoiding the statistical significance

Surgery	Group A	Group B
Herniotomy	12(40%)	13(44%)
Circumcision	8(27%)	7(23%)
Urethroplasty	4(13%)	6(20%)
Orchidopexy	6(20%)	4(13%)

Table 3: Surgical procedures in group A

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Duration	Group A	Group B
0-29mins	3	5
30-59 mins	27	25
60-89 mins	0	0
Mean +/- SD	34.89 +/- 5.49	33.34 +/- 6.35

Table 4: Duration of surgery

	2hrs	4hrs	6hrs	8hrs	10hrs	12hrs	14hrs
FLACC 0	18	0	0	0	0	0	0
FLACC 1	10	2	0	0	0	0	0
FLACC 2	0	12	0	0	0	0	0
FLACC 3	0	6	6	0	0	0	0
FLACC 4	0	10	24	30	30	30	30

Table 5: Duration of analgesia FLACC score in Group A (Ropivacaine)

By the end of 6 hours 26 patients have attained the score of ≥ 4 .

	2hrs	4hrs	6hrs	8hrs	10hrs	12hrs	14hrs
FLACC 0	30	22	7	0	0	0	0
FLACC 1	0	6	10	11	5	0	0
FLACC 2	0	2	8	10	9	0	0
FLACC 3	0	0	5	6	11	3	0
FLACC 4	0	0	0	3	5	27	30

Table 6: Duration of analgesia FLACC score in Group B (Ropivacaine + Clonidine)

By the end of 14 hours all the patients have attained the score of ≥ 4

Hemodynamic variables	Pre op	Intra op	Post op
Mean PR	102	93	91
MAP	83	82	83
Mean SPO ₂	98	98	98

Table 7: Hemodynamic variables in Group A

Hemodynamic Variables	Pre op	Intra op	Post op
Mean PR	103	94	93
MAP	80	79	80
SPO ₂	98	98	98

Table 8: Hemodynamic variables in Group B

	Group A	Group B	P value
Time to first analgesia	5.74±2.95hrs	12.34±4.23hrs	< 0.001

Table 9: Total Duration of Analgesia

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Total duration of analgesia in Group A is 5.7hrs.

In group B it is 12.2hrs with significant prolonged post-operative analgesia in Group B.

DISCUSSION: Ropivacaine, in comparison to bupivacaine, has a wide range of safety, less motor blockades, less cardiovascular toxicity with equal duration of analgesia in ambulatory setting in paediatric patients.

Like opioids, clonidine also enhances the effects of local anaesthetics without increasing the incidence of side effects in its usual dose (1-2mcg/kg). Clonidine compared to opioids is much more selective α_2 adreno receptors, which might permit its application for sedation and analgesia without the unwanted effects like nausea, vomiting, constipation, itching, respiratory depression and urinary retention. Clonidine, in comparison to opioids has a unique dose dependent sedation (Easily arousable). These properties render clonidine suitable for sedation and analgesia during whole perioperative period.

The various route of administration of clonidine is there, oral dose available as a 0.1mg tablets maximum up to 0.2-0.7mg. The intravenous route has been found to be effective in hypertensive crisis. (150-300mcg), transdermal patches and the epidural administration clonidine is rapidly absorbed into the spinal CSF compartment, peaking 30-60min after injection. One of the major advantages of clonidine over other sedatives is its respiratory effect, which are minimal in adults and children.

S. J. Singh Bajwa et al (2010)⁷ administered clonidine in dose of 2mcg/kg as adjuvant with 0.25% ropivacaine caudally. They found that the mean duration of analgesia was significantly higher in the group receiving ropivacaine clonidine mixture 13.4 ± 3.4 hours than group receiving ropivacaine alone 8.5 ± 3.4 hours ($p < 0.05$).

Akhilandeswari Manickam et al (2012)⁸ compared clonidine 1 mcg/kg with ropivacaine 0.1% to the ropivacaine 0.1% and 0.2% for caudal analgesia in paediatric patients and conclude that addition of clonidine to 0.1% ropivacaine caudally significantly increases the quality and duration of analgesia as compared to plain 0.1% ropivacaine while avoiding motor blocked that occurs with 0.2% ropivacaine. The patients stayed hemodynamically stable with no side effects. The mean duration of analgesia was 4.06 ± 1.66 hours in ropivacaine 0.1% group, 9.87 ± 1.39 hours in clonidine ropivacaine group and 6.48 ± 1.29 hours in ropivacaine 0.2% group. The prolongation of duration of analgesia was significant in both groups clonidine and ropivacaine 0.2% when compared to ropivacaine 0.1% administered group.

In Our Study: 60 paediatric patients (1-10yrs) posted for elective urogenital surgeries were taken:

- The group didn't differ demographically (Table: 1).
- Types of surgeries were comparable (Table: 2).
- Received equal volume of drug according to weight.
- Received equal concentration of ropivacaine.
- Hemodynamic variables were stable in both the groups.
- FLACC score was analysed using "student t" test.
- The mean duration of analgesia in Group A is 5.74 hours \pm 2.95 hours (95% CI).
- The mean duration of analgesia in Group B is 12.34 hours \pm 4.23 hours (95% CI) with a P value of <0.001 .

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Group A patients achieved a statistically significant higher FLACC score compared to Group B patients. The pre-operative, intra-operative and post-operative hemodynamic variables between these groups were comparable (Table 7 and Table 8) and there was no statistically significant difference and therapeutic interventions were not recorded.

No episodes of clinically significant postoperative complication such as post-operative nausea, vomiting, respiratory depression, urinary retention, pruritus, hypotension and bradycardia were observed.

The results of our observation show that in addition to prolonged post-operative analgesia, clonidine has a favourable safety profile and stable hemodynamics, which are in concordance with the reports published by other several other authors.

- Group B had better quality sleep with easily arousable of sedation

K Adate et al (2010)⁹ compared two different concentration of ropivacaine 0.1% and 0.2% with fixed dose of clonidine 2mcg/kg as an adjuvant for paediatric caudal block in 60 ASA-I children and showed that the incidence of agitation following sevoflurane anaesthesia was significantly lower with clonidine ($P < 0.05$). Ropivacaine 0.1% group had similar quality of intra and post-operative analgesia without residual motor block as that of Ropivacaine 0.2% with clonidine. Mean duration of analgesia was significantly longer in both groups (22.50 ± 5.71 hours and 21.37 ± 6.87 hours) with $P < 0.001$. No statistically significant difference in hemodynamic was found between the groups. In 2012, Akhilandeshwari Manickam et al.⁸ compared in a randomized double blind study, the postoperative analgesia, wide margin of safety and degree of motor block by the ropivacaine 0.1% with clonidine 1mcg/kg, ropivacaine 0.1% and 0.2% for caudal anaesthesia in children after induction with general anaesthesia.

Sixty children with 3 different groups, 1-6 years ASA I & II scheduled for subumbilical surgeries were included in the study. All children received different concentration of ropivacaine 0.1% with clonidine, plain ropivacaine 0.1% and 0.2%. Post-operative duration of analgesia, FLACC (Face, Legs, Activity, Cry, Consolability), sedation by Ramsey sedation scale and residual motor block by Bromage scale were recorded. Paracetamol suppository administered rectally for cases with FLACC > 3 . The age, weight, and the duration of surgery in the study groups were compared. The duration of analgesia was significantly longer in group B (0.1% ropivacaine with clonidine 590.25 min.) compared to groups A (243 min.) and C (388 min.) and none of children had motor blockade in group A and B.

In 2012, Arpita Laha et al.¹⁰ In prospective, double blind, randomised study 30 ASA I children aged 3-11 years scheduled for infraumbilical surgeries were randomly allocated to receive a caudal block of either plain ropivacaine 0.2% (1ml/kg) or a mixture of ropivacaine with clonidine 2 mcg/kg. The combination of clonidine and ropivacaine was associated with an improved quality of post-operative analgesia CHEOPS (Childrens Hospital Eastern Ontario Pain Scale) compared to plain ropivacaine without causing any significant degree of postoperative sedation or prolongation of motor block.

CONCLUSION: Ropivacaine is a newer amide type local anaesthetic drug with significantly enhanced safety profile and a propensity to block sensory fibres more readily than motor fibres. For these reasons this has become a drug of choice of interest for day care surgeries.

Clonidine is an agonist of α_2 adrenergic receptors safer than opioids.

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The present study was conducted in 60 paediatric patients aged 1-10yrs, with ASA grade 1&2 physical status, planned for elective urogenital surgeries.

Group A patient's received 0.25% Ropivacaine 1ml/kg + 0.5 ml normal saline

Group B patient's received 0.25% Ropivacaine 1ml/kg + 2mcg/kg Clonidine diluted to 0.5 ml with normal saline.

Caudal Clonidine 2mcg/kg with 0.25% Ropivacaine 1 ml/kg for paediatric urogenital surgeries achieved significant post-operative pain relief up to 12 hours, which resulted in a better quality of sleep and aduration of arousable sedation. Also, there was no necessity for any supplemental analgesic and the hemodynamics too was stable. No episodes of clinically significant postoperative complications were observed.

Hence, we find clonidine to be safe and effective adjuvant for caudal analgesia in paediatric patients.

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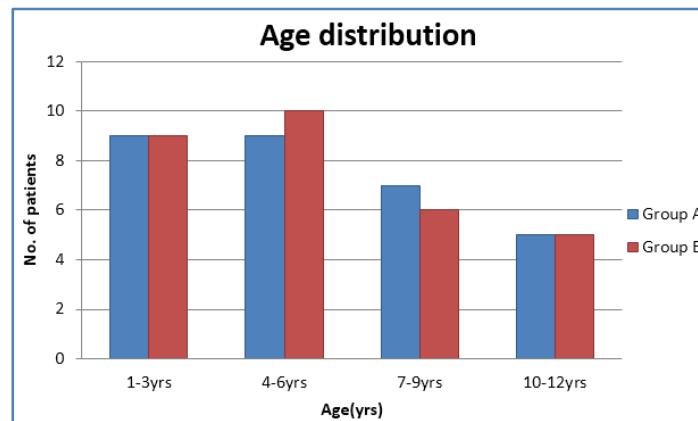


Fig. 1

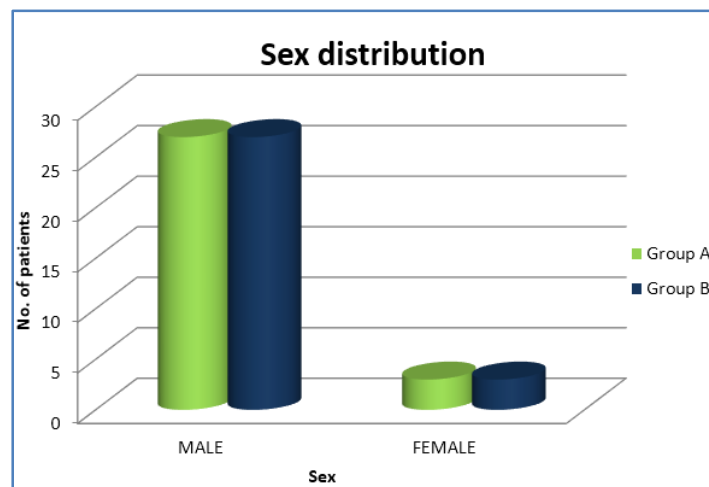


Fig. 2

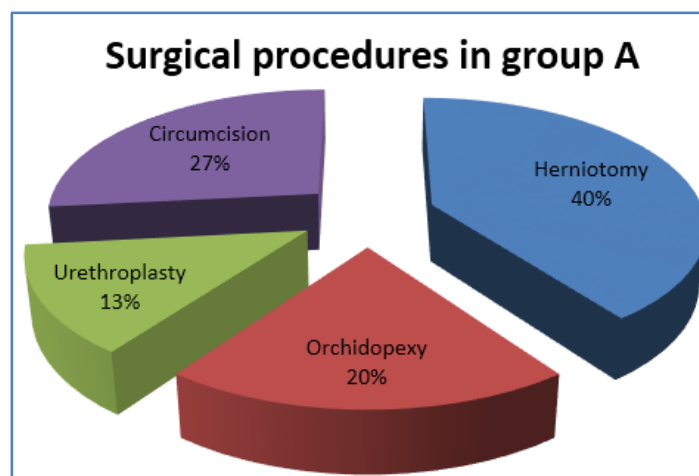


Fig. 3

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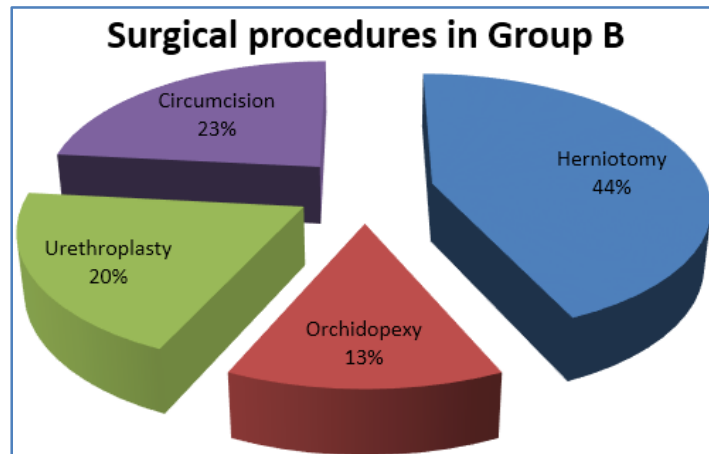


Fig. 4

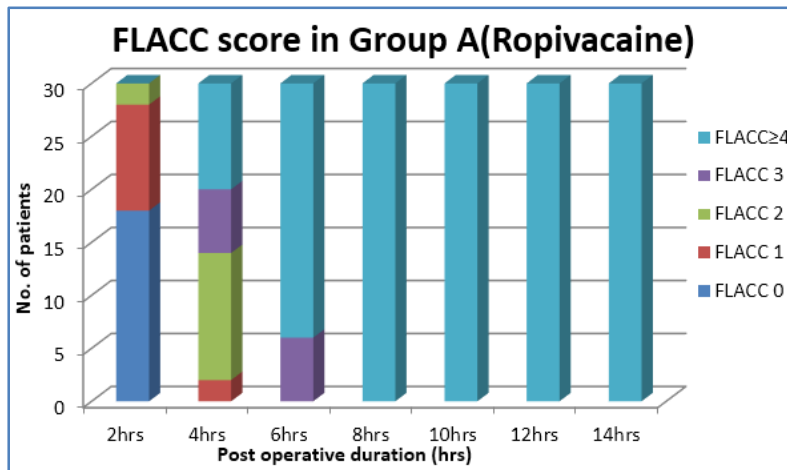


Fig. 5

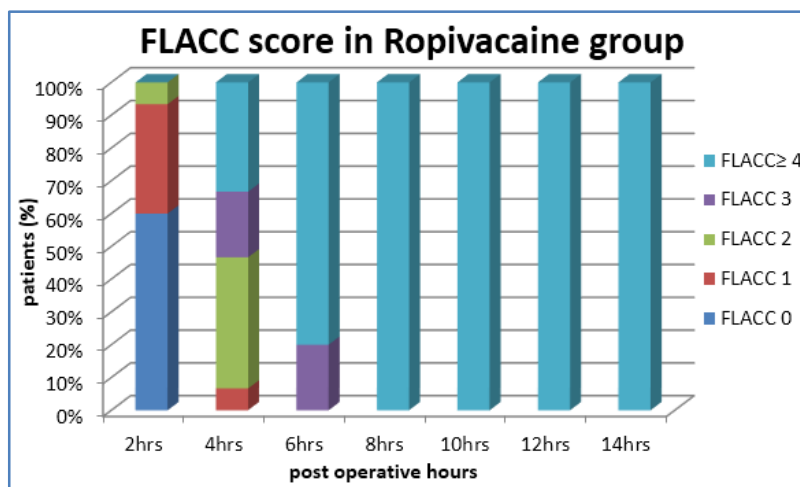


Fig. 6

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