

Comparison of Analgesic Effect of Dexmedetomidine versus Tramadol as Adjuvants to Caudal Ropivacaine in Infraumbilical Surgeries among Pediatric Patients: A Randomized Double Blind Interventional Study

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Abstract:

Objective: To compare the postoperative analgesic effects of 0.2% ropivacaine with Dexmedetomidine (2 g/kg) and tramadol (2 mg/kg) among pediatric patients undergoing infra umbilical surgery.

Material and Methods: This hospital based, randomized double blind interventional study included 60 pediatric patients, aged 1–7 years, having American Society of Anaesthesiology grade I and II, weighing 7–25 kg, and undergoing infra-umbilical surgeries under general anesthesia. Subjects were randomly allocated into two groups to receive either: 2 mcg/kg of Dexmedetomidine or 2 mg/kg of Tramadol, as adjuvant to 0.2% of Ropivacaine. Pain intensity was assessed using the pediatric observational Children’s Hospital of Eastern Ontario Pain Scale (CHEOPS) score. Rescue analgesia was given, when the CHEOPS score was ≥ 6 . Duration of analgesia was defined as: the time period between administrations of block until rescue analgesia was given. Level of sedation was assessed by the Ramsay sedation score.

Results: Kaplan Meier analysis showed that the median time to first rescue analgesia (duration of analgesia) was significantly (p -value <0.001) prolonged with Dexmedetomidine (780 minutes; 95% CI: 760.68–799.32 minutes) as compared to Tramadol (648 minutes; 95% CI: 635.92–660.38 minutes). Mean emergence time and duration of sedation were also significantly prolonged with Dexmedetomidine as compared to Tramadol.

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Conclusion: In pediatric patients undergoing infraumbilical surgeries, Dexmedetomidine as adjuvant to Ropivacaine provides an advantage of longer post-operative analgesia and lack of opioid related adverse events associated with Tramadol.

Keywords: adjuvant, CHEOPS, Dexmedetomidine, Ropivacaine, Tramadol

Introduction

Pain refers to unpleasant sensory and emotional experiences that result from actual or potential tissue damage.¹ Alleviation of pain was defined by the society of Paediatric anaesthesia at its 15th annual meeting, in New Orleans, Louisiana (2001); irrespective of age, medical condition, treatment, or primary service response for patient care or medical institution.

Since children can only experience, not express the amount of pain, it becomes difficult to assess painful experiences in this pediatric age group. The impact of painful experiences on young nervous systems leads to significant long-term effects; including, a lower pain tolerance for months and behavioral defects.^{2,3} Providing effective post-operative analgesia has become imperative in paediatric anaesthesia, in order to improve post-operative pain management, increase patient compliance and reduce hospital readmissions, Langlade et al., 1997 made the suggestion of "managing pain before it occurs".⁴

As of recent years, the concept of proper post-operative analgesia in pediatric patients has become well established. One example is the use of intravenous opioids, which although being quite effective they have side effects; such as respiratory depression, which limits their use. This is why caudal analgesia has become one of the most prevalently used regional techniques in paediatric anaesthesia.⁵⁻⁸ Additionally, caudal anaesthesia has been shown to have minimal effect on cardiovascular hemodynamics⁹, when combined with general anaesthesia, The caudal block has been found to be very effective, and safe in children in a variety of infraumbilical surgeries.¹⁰

Besides providing good post-operative analgesia, caudal blocks also allow for a rapid recovery from anaesthesia.¹¹

Several local anaesthetic agents have been used for caudal blocks. Ropivacaine is an amino amide local anaesthetic with a better in safety profile; i.e., less CNS and cardiac toxicity as well as less motor blockade.^{12,13}

Prolongation of analgesia can be obtained by adding various adjuvants in varying concentrations; such as, dexmedetomidine tramadol, ketamine, neostigmine, clonidine, and nalbuphine etc, to achieve different degrees of success.¹⁴ Dexmedetomidine is a selective α_2 adrenergic agonist, with analgesic and anxiolytic properties. It is a safe and effective adjuvant for many anesthetic techniques; such as intrathecal or epidural.^{15,16} Tramadol is a centrally acting μ -opioid receptor agonist and serotonin/norepinephrine reuptake-inhibitor that is structurally related to codeine and morphine.¹⁷

This study aimed to compare the post-operative analgesia effect of Dexmedetomidine (2 $\mu\text{g}/\text{kg}$) and tramadol (2 mg/kg) added to 0.2% ropivacaine among pediatric patients undergoing infra umbilical surgeries.

Material and Methods

This hospital based, randomized double blind superiority type of interventional study was conducted in a tertiary care center, which is one of the largest tertiary care centers of Northern India, in the year 2020.

The study included: pediatric patients aged 1 to 7 years, of either gender, weighing 7 to 25 kg, with American Society of Anaesthesiology (ASA) grades I and II and undergoing infra-umbilical surgeries under general

anesthesia. Those with allergy reactions to the drugs used in this study, coagulation disorders or on anticoagulant therapy, local infection at the site of puncture for caudal anesthesia, developmental delay, neurological deficit or with vertebral deformity were excluded from this study.

The sample size was calculated at 95% confidence interval (CI) and 80.0% power to verify the expected difference of 136 ± 78.30 minutes in mean duration of analgesia in both groups; as per the findings of a published study.¹⁸

A total of 60 eligible subjects were recruited consecutively until the sample size was achieved. Subjects were randomly allocated into one of the following two groups, using the block randomization method, to ensure the equal number of subjects in both groups:

Dexmedetomidine; or Group RD: wherein, the patients received 2 mcg/kg of Dexmedetomidine (volume 0.5 ml) with 0.2% Ropivacaine 1 ml/kg, or the Tramadol group; or Group RT: wherein, the patients received 2 mg/kg of Tramadol (volume 0.5 ml) with 0.2% of Ropivacaine 1 ml/kg.

Allocation concealment was ensured using the opaque sealed envelope method for group allocation. Allocation was conducted by a person not involved directly in the research to avoid selection bias. Neither the anesthetist nor the patient was aware of the groups, or the drugs used (double blind).

All patients were subjected to standard pre-anesthetic checkups before the surgery; including, detailed history, examination, vitals, routine investigations and markers. Injections of intravenous midazolam 0.05 mg/kg and glycopyrrolate 0.005 mg/kg were used as pre-medication. Anesthesia was induced using 8.0% sevoflurane and 50.0% nitrous oxide (N_2O) in oxygen with spontaneous ventilation. Appropriate sized laryngeal mask airway was inserted after eye reflex loss and jaw full relaxation was achieved, upon which the sevoflurane concentration was reduced to 3.0% with 50.0% oxygen and 50.0% N_2O .

Afterwards, patients were placed in a lateral position and the skin of their backs was disinfected with povidone-iodine solution. Using a 22-gauge or 23-gauge needle, a single-dose caudal epidural injection was performed under aseptic conditions. The needle position was confirmed by the pop heard during penetration of the sacro-coccygeal ligament, which was confirmed by ultrasound. Caudal medication was given, depending on the group assigned after negative aspiration of blood or cerebrospinal fluid.

The study drug was prepared by an anesthetist not directly involved in the research upon opening of the envelope. It was agreed to disclose the drug to the researcher only in the event of any serious, adverse event. We recorded the time of caudal injection, and allowed the surgery to begin 10 minutes after the injection: 3.0% sevoflurane and oxygen 50.0% and nitrous oxide 50.0% were used for maintenance of anesthesia. During surgery, vital parameters were continuously monitored, and all anaesthetic drugs were discontinued after the completion of surgery.

The emergence time was the time between discontinuation of anesthetics and the opening of the eyes upon verbal command. Based on the pediatric observational Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) score¹⁹; with a score range of 4–13, each patient's pain intensity was assessed hourly until 6 hours, then 3 hourly till 12 hours and every 6 hours till 24 hours, up until the first dose of rescue analgesia was administered. Paracetamol 20 mg/kg (intra-venous) was administered as rescue analgesia when the CHEOPS score was ≥ 6 . The duration of analgesia is the time between the administration of the block and the administration of rescue analgesia when the CHEOPS score reaches ≥ 6 . Ramsay sedation score was used to assess sedation levels.²⁰

Ethical approval was obtained from the Institutional Ethics Committee (No.735/MC/EC/2020), with CTRI registration (CTRI/2021/02/030958). Written informed

consent was obtained from parents or guardians (the legally authorized representative) of all the patients before inclusion into the study (Figure 1).

Statistical analysis: Quantitative data were summarized as mean and standard deviation and analyzed using Student “t-test,” while the median and interquartile range of ordinal variables were calculated and analyzed using the “Mann-Whitney U test”. Frequencies and percentage were analyzed using chi square test. Kaplan meier curve analysis, with log rank test was performed to compare time to first rescue analgesia between the two groups. A “p-value” <0.05 was taken as statistically significant. SPSS trial version 22 was used for analysis.

Results

The mean age of subjects in Group RD was 4.5±1.80 years, and in Group RT it was 3.95±1.93 years. Both the groups were comparable in relation to their baseline characteristics; such as age, gender, ASA grade, type of surgery and duration of surgery (Table 1). Duration of

analgesia, mean emergence time, and duration of sedation was significantly prolonged with Dexmedetomidine as compared to Tramadol (Table 2). Kaplan meier analysis (Figure 2) showed that the median time to first rescue analgesia (duration of analgesia) was significantly prolonged (p-value<0.01) by Dexmedetomidine (780 minutes; 95% CI: 760.68–799.32 minutes) as compared to Tramadol (648 minutes; 95% CI: 635.92–660.38 minutes).

The CHEOPS was similar (non-significant) in both groups, up until 5 hours as follows: at EOS (p-value=1.08), at 1 hour (p-value=1.023), at 2 hours (p-value=0.317), at 3 hours (p-value=0.317), at 4 hours (p-value=0.317), at 5 hours (p-value=0.317). The score was significantly lower in Group RD as compared to Group RT at 6 and 9 hours (p-value<0.001) (Figure 3). The sedation score was significantly lower in Group RD, at EOS (p-value=0.04), at 1 hour (p-value<0.01), at 3 hours (p-value<0.01), at 4 hours (p-value=0.03) and at 5 hours (p-value<0.04) as compared to the RT group (Figure 4).

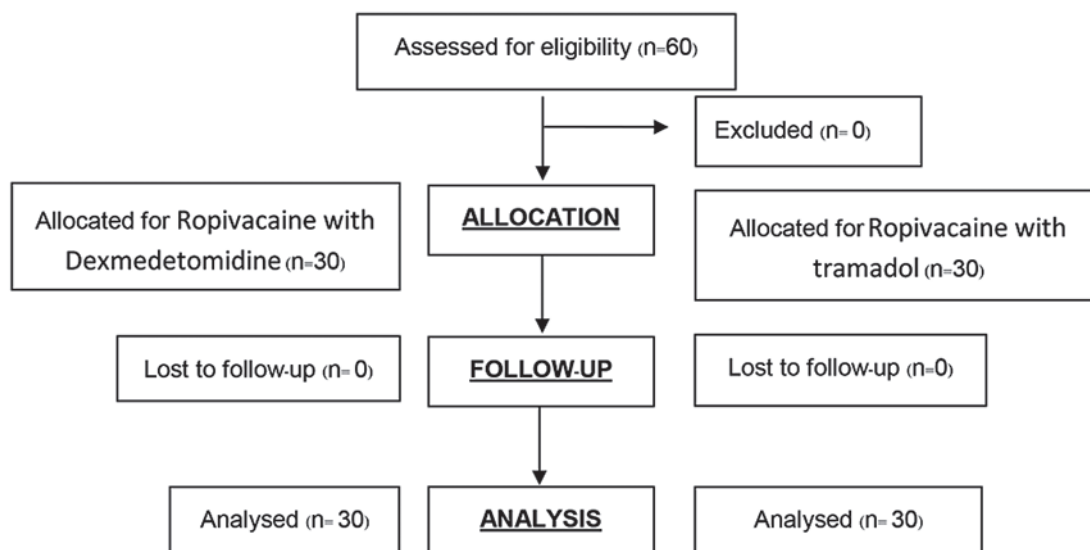


Figure 1 Consort flow chart of the study

Among the study groups, there was no statistically significant (p -value >0.05) difference in intraoperative heart rate or mean arterial pressure (Figures 5, 6). A total of 2 patients in Group RD and 3 patients in Group RT experienced nausea or vomiting (p -value >0.05).

Discussion

Caudal epidural analgesia is the safest and most reliable technique in children; however, it has a short duration of action after a local, single shot anesthetic injection.²¹ To overcome this limitation, various adjuvants have been

used to increase the duration and quality of caudal epidural analgesia.²² This study compared the effectiveness of Dexmedetomidine versus Tramadol as adjuvants to caudal Ropivacaine in infra-umbilical surgeries in pediatric patients. In our study, the mean age of patients in Group RD and Group RT were 4.5 ± 1.80 and 3.95 ± 1.93 years, respectively (p -value >0.05). The majority of cases, in both groups, were male (83.3% in Group RD and 90.0% in Group RT). The age, gender, weight, ASA grading, duration and type of surgery are comparable in both study groups, which helped in eliminating any possible confounding.

Table 1 Baseline characteristics of the study groups

		Group RD	Group RT	p-value
Age (mean \pm S.D.)	In years	4.5 \pm 1.8	3.95 \pm 1.93	0.25
Gender	Male	25 (83.3%)	27 (90.0%)	0.704
	Female	5 (16.7%)	3 (10.0%)	
Weight (mean \pm S.D.)	In kg	14.73 \pm 3.32	13.63 \pm 3.43	0.210
ASA	Grade I	14 (46.7%)	13 (43.3%)	1.000
	Grade II	16 (53.3%)	17 (56.7%)	
Type of surgery	Circumcision	9 (30.0%)	8 (26.7%)	0.66
	Hydrocele	8 (26.7%)	6 (20.0%)	
	Herniotomy	10 (33.3%)	12 (40.0%)	
	Orchidopexy	3 (10.0%)	4 (33.3%)	
Duration of surgery (mean \pm S.D.)	In minutes	55 \pm 7.63	47.66 \pm 11.7	0.06

S.D.=standard deviation, ASA=American Society of Anaesthesiology, RD=Ropivacaine with Dexmedetomidine, RT=Ropivacaine with Tramadol

Table 2 Duration of analgesia, duration of sedation and emergence time compared across the study groups (minutes)

	Group RD	Group RT	p-value
Duration of analgesia (median with IQR)	780 (95.0% CI: 760.68–799.32)	648 (95.0% CI: 635.92–660.38)	<0.001
Duration of sedation (mean \pm S.D.)	4.86 \pm 0.81	4.1 \pm 0.6	<0.001
Emergence time (mean \pm S.D.)	420.56 \pm 13.6	314.46 \pm 10.3	<0.001

S.D.=standard deviation, ASA=American Society of Anaesthesiology, RD=Ropivacaine with Dexmedetomidine, RT=Ropivacaine with Tramadol, IQR=interquartile range

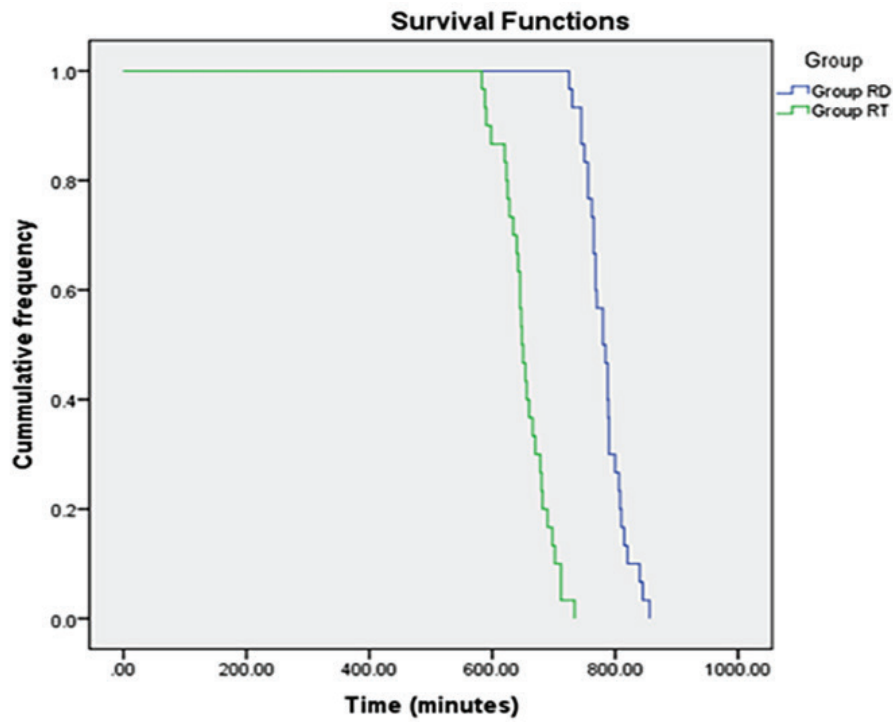


Figure 2 Kaplan Meier analysis for time to first rescue analgesia

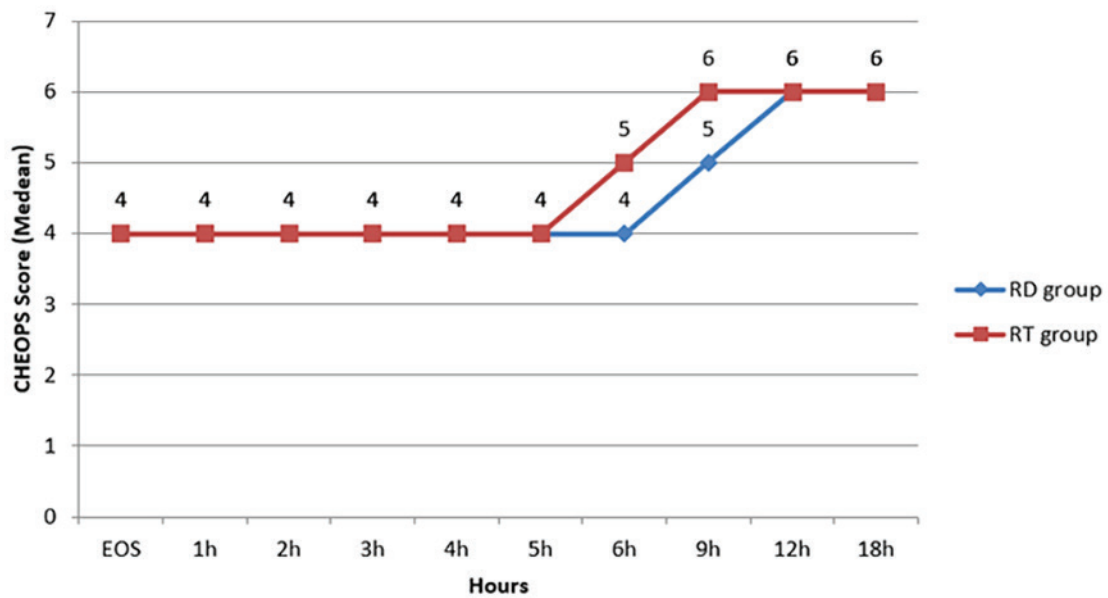


Figure 3 Children’s Hospital of Eastern Ontario Pain Scale (CHEOPS) score trend among the study groups

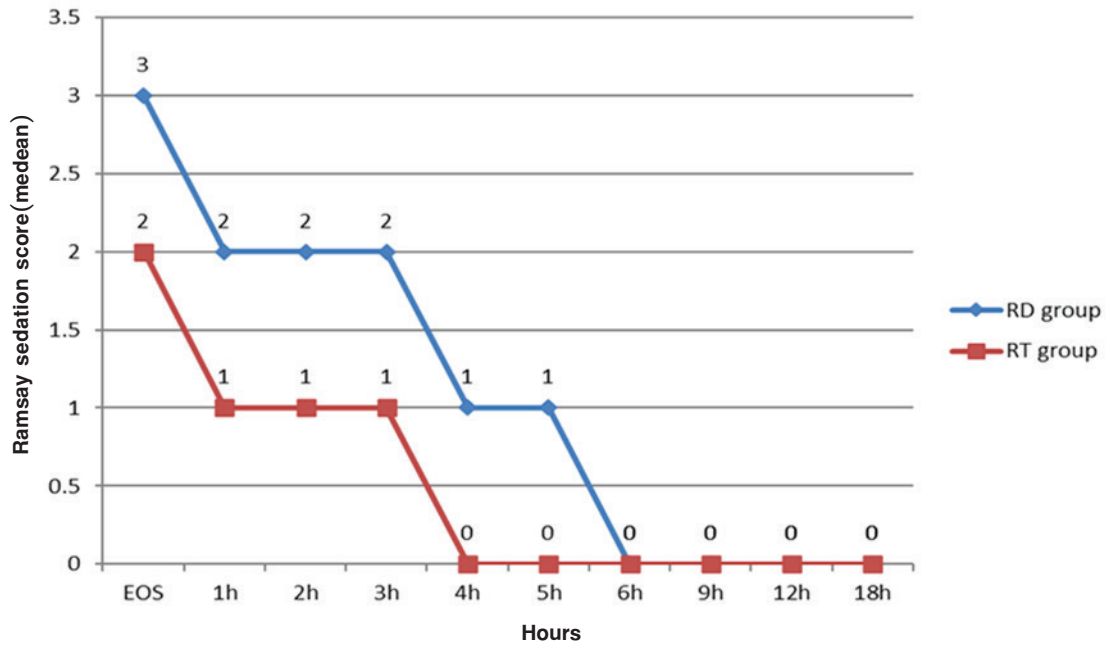


Figure 4 Comparison of median sedation score among the study groups

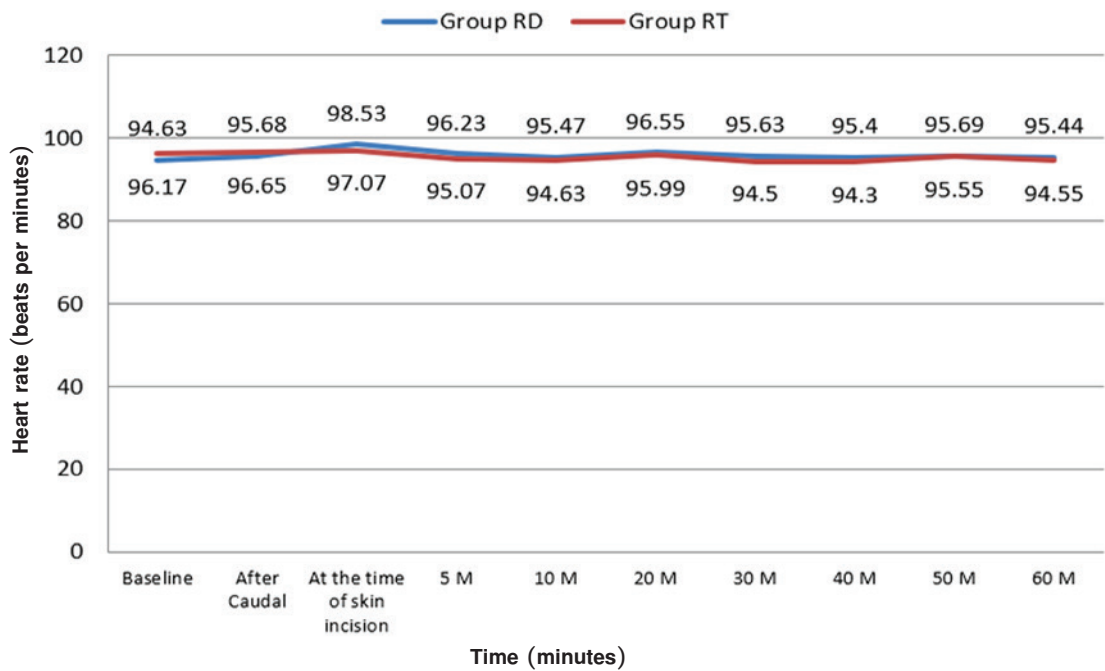


Figure 5 Comparison of heart rate among the study groups

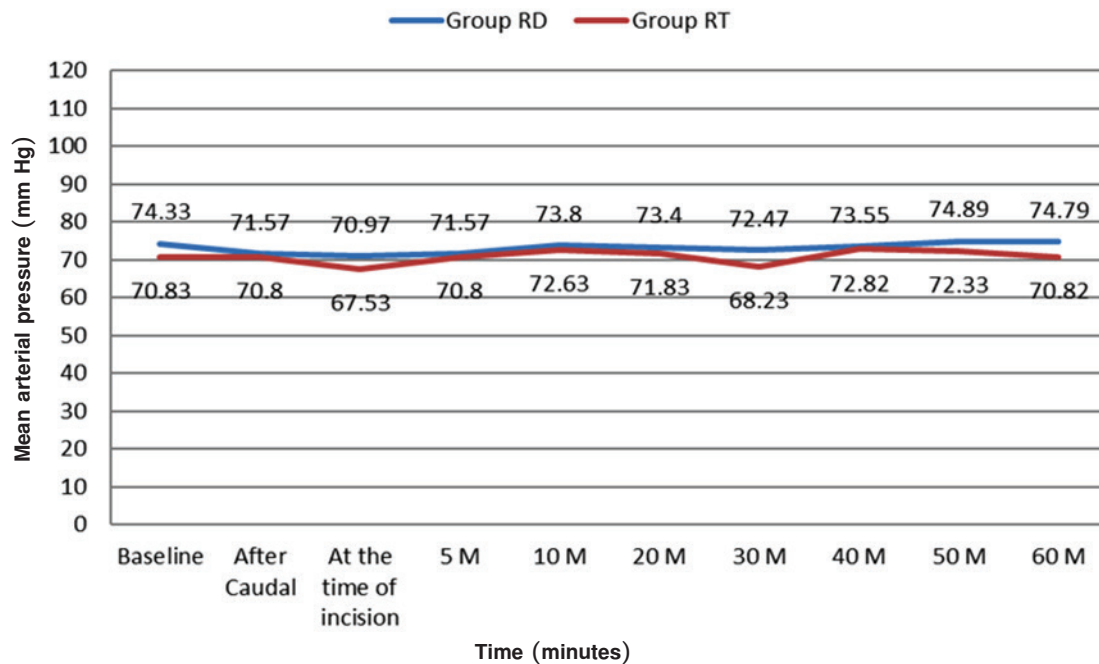


Figure 6 Comparison of mean arterial pressure among the study groups

No significant difference was found in intraoperative heart rate, systolic, diastolic and mean arterial blood pressure between the two groups. These results are similar to a study conducted by Keshari et al.²³, as in showing no significant difference between the two groups concerning hemodynamic parameters. Gupta et al.¹⁸ also found that the intra and post-operative haemodynamic variables between the groups were comparable and therapeutic interventions were not required. This shows that both the adjuvants offer similar hemodynamic stability.

The mean duration of analgesia in our study was prolonged in Group RD (718±31.88 minutes) as compared to Group RT (653±33.59 minutes). Gupta et al.¹⁸ also reported mean duration of analgesia to be significantly higher in the RD group (780.29±71.21 minutes) as compared to the RT group (654.20±78.38 minutes) (p-value<0.001). Another similar study, by Senthamizh et al.²⁴, also observed that caudal dexmedetomidine (2 mcg/kg) significantly prolonged duration of analgesia (750.29±71.29 minutes) when

compared with caudal tramadol 2 mg/kg (674.2±78.38 minutes) in paediatric urogenital surgeries. Similarly, Sneha et al.²⁵ also observed that caudal dexmedetomidine 2 mcg/kg significantly prolonged duration of analgesia (1075±159 minutes) when compared with caudal tramadol 2 mg/kg (762±168 minutes) in paediatric urogenital surgeries. Various other studies have also reported prolonged duration of analgesia with different doses of dexmedetomidine; ranging from 14 to 18.5 hours.²⁶⁻²⁹

In our study, the median CHEOPS score increased significantly with time in both groups. On intergroup comparison, the CHEOPS score was found to be significantly lower in Group RD. The lower pain scores, as determined by the CHEOPS score, has been reported by Imani et al.³⁰ In their study they revealed the addition of dexmedetomidine (2 mcg/kg) to ropivacaine 0.2% reduced analgesic consumption after lower abdominal surgery in children, without affecting adverse events.

Jarineshin et al.²⁸ also demonstrated enhanced analgesic effects with dexmedetomidine (2 mcg/kg) as compared to fentanyl (2 mcg/kg) when used as an adjuvant in caudal block with bupivacaine 0.25%; administered after induction of general anesthesia in children undergoing elective hernioplasty, without causing considerable adverse effects nor hemodynamic changes.

Dexmedetomidine enhances the effects of local anaesthetic via α_2A receptor mediated sedation, hypnosis, analgesia, sympatholysis and neuroprotection³¹, without increasing the incidence of side effects.^{32,33}

Duration of Sedation was significantly prolonged by the addition of Dexmedetomidine as compared to Tramadol. Past studies have also reported improved sedation on addition of dexmedetomidine as a caudal adjuvant.^{18,26,27} Children in the Dexmedetomidine group were asleep; however they were easily arousable.

The mean emergence time of Group RD (4.86 ± 0.81 minutes) was significantly longer than Group RT (4.096 ± 0.60 minutes), as has been similarly reported by other studies.^{18,24}

We did not encounter any significant post-operative adverse effects; such as, bradycardia, hypotension, shivering, nausea or vomiting in our study. Findings of similar studies indicate that Dexmedetomidine provides for the advantage of minimal adverse events.^{27,24}

Limitation and generalizability

Because of time and resource limitations, this RCT was conducted at one center (a single center study), with small representatives of the population. The study was conducted at one of the largest tertiary care hospitals of Rajasthan state, which has a large catchment area, so the sample for the study corresponds to the large population of Rajasthan; leading to good generalizability.

Conclusion

Dexmedetomidine (2 mcg/kg) is superior than Tramadol (2 mg/kg) in providing post-operative analgesia, when used as an adjuvant to 0.2% Ropivacaine in pediatric patients undergoing infraumbilical surgeries.

Conflict of interest

No

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