Comparative Study of Caudal Ropivacaine Combined with Ketamine and with Midazolam for Analgesic Efficiency in Pediatric Infraumbilical Procedures

Dr Nikulbhai Jivanbhai Prajapati[1], Dr. Hardul Vasantkumar Modi[2], Dr Akshaykumar Vinodbhai Pandya[3]

[1,2]*Associate Professor, Department of Anesthesia, Nootan Medical College and Research Center, Visnagar, Gujarat, India*
[3]*Assistant Professor, Department of Anesthesia, Nootan Medical College and Research Center, Visnagar, Gujarat, India*

Corresponding author: Dr Akshaykumar Vinodbhai Pandya, Department of Anesthesia, Nootan Medical College and Research Center, Visnagar, Gujarat, India

Conflict of interest: No! Conflict of interest is found elsewhere considering this work.
Source of Funding: There was no financial support concerning this work

KEYWORDS

Pediatric anesthesia, caudal block, ketamine, ropivacaine, postoperative pain.

ABSTRACT

Background: Postoperative pain management in pediatric patients undergoing infraumbilical surgeries can be challenging. Caudal epidural analgesia with local anesthetics like ropivacaine is commonly used, but adjunct medications like ketamine and midazolam are often added to enhance analgesic efficacy.
Aim: To compare the analgesic efficacy of caudal ropivacaine combined with ketamine versus ropivacaine combined with midazolam in pediatric patients undergoing infraumbilical surgeries. **Material and Methods:** A prospective, randomized study was conducted with pediatric patients aged 2-12 years undergoing elective infraumbilical surgeries. Group A received caudal ropivacaine + ketamine, and Group B received ropivacaine + midazolam. Postoperative pain scores, opioid consumption, and adverse effects were assessed at various time points.
Results: Group A demonstrated significantly lower pain scores at 1, 4, and 8 hours postoperatively and required less opioid consumption compared to Group B. No significant differences were observed at 24 hours. Both combinations had similar safety profiles, with mild sedation and nausea observed in both groups.
Conclusion: Caudal ropivacaine combined with ketamine provides superior early postoperative pain relief and reduces opioid consumption compared to ropivacaine with midazolam in pediatric infraumbilical surgeries.

Introduction

Effective postoperative pain management in pediatric patients is crucial for ensuring comfort, reducing stress, and promoting faster recovery after surgery. In pediatric infraumbilical surgeries, managing pain remains a challenge, as children may experience significant discomfort postoperatively. One of the most common techniques for managing pain in these patients is caudal epidural analgesia, which involves the administration of local anesthetics, such as ropivacaine, to block pain transmission from the lower abdominal region.[1] Ropivacaine is a long-acting local anesthetic that has gained popularity for use in pediatric anesthesia due to its safety profile and

effective analgesia, with fewer central nervous system and cardiac side effects compared to other anesthetics like bupivacaine.[2]

In an attempt to enhance the analgesic effects of ropivacaine, adjunct medications such as ketamine and midazolam are often included in the anesthetic regimen. Ketamine, a glutamate receptor antagonist, is known for its potent analgesic and opioid-sparing effects.[3] Its addition to ropivacaine in pediatric caudal anesthesia has been shown to provide prolonged pain relief and reduce opioid consumption.[4] On the other hand, midazolam, a benzodiazepine, is often used to augment the sedative and anxiolytic properties of anesthesia and is hypothesized to have an analgesic effect as well.[5]

Despite the widespread use of these adjuncts, studies comparing the analgesic efficacy of caudal ropivacaine combined with ketamine versus ropivacaine combined with midazolam are limited. Therefore, this study aims to evaluate and compare the analgesic efficacy of these two combinations in pediatric patients undergoing infraumbilical surgeries. The primary objective is to determine which combination provides superior pain relief, prolongs the duration of analgesia, and minimizes the need for additional analgesics postoperatively. This study also seeks to assess the safety profile of these combinations by monitoring adverse effects during the perioperative period.

Material and Methods

Study Design and Setting:

This study is a prospective, randomized, double-blind, controlled trial conducted at a tertiary care center in Gujarat, India. The study was conducted from January 2023 to December 2024. Ethical approval for the study will be obtained from the institutional review board (IRB), and informed consent will be obtained from the guardians of all enrolled pediatric patients.

Inclusion and Exclusion Criteria:

Inclusion criteria for this study include:

- Pediatric patients aged 2 to 12 years undergo elective infraumbilical surgeries (e.g., hernia repair, circumcision, appendectomy).
- ASA (American Society of Anesthesiologists) physical status I or II.
- Parental consent for participation in the study.

Exclusion criteria include:

- Allergies to ropivacaine, ketamine, or midazolam.
- Known history of systemic diseases (e.g., cardiovascular, respiratory, or neurological disorders).
- Patients requiring emergency surgery or those with contraindications to regional anesthesia.
- Patients with cognitive impairment or those unable to follow postoperative instructions.

A total of **100 patients** were enrolled in this study, with **50 patients** assigned to each treatment group. Sample size calculation is based on the primary outcome measure of postoperative pain scores (using the Visual Analog Scale, VAS) with an alpha level of 0.05 and a power of 80%. The sample size is calculated to detect significant differences in the analgesic efficacy between the two groups.

Study Groups:

Participants were randomly assigned to one of two treatment groups using computer-generated randomization:

1. Group A (Ropivacaine + Ketamine): Patients in this group received 1 mL/kg of 0.2% ropivacaine combined with 0.5 mg/kg of ketamine via caudal epidural injection.

2. Group B (Ropivacaine + Midazolam): Patients in this group received 1 mL/kg of 0.2% ropivacaine combined with 0.1 mg/kg of midazolam via caudal epidural injection. Both anesthesiologists and patients' guardians were blinded to the group assignment. The doses of ropivacaine, ketamine, and midazolam were chosen based on previous studies that had shown effective analgesia with minimal side effects (Bavbek et al., 2015; O'Brien et al., 2018).

Procedure

Preoperative assessment was conducted to ensure eligibility. All patients received a standard preoperative preparation, including zero per os (NPO) status, as per institutional protocols. General anesthesia was induced using standard anesthetic agents, and patients were placed in a prone position. A caudal block was performed under aseptic conditions using a 22-gauge needle, and the appropriate medication mixture (ropivacaine + ketamine or ropivacaine + midazolam) was injected into the epidural space.

Postoperatively, patients were monitored in the recovery room, and pain levels were assessed at 1, 4, 8, and 24 hours using the Visual Analog Scale (VAS). Additional pain relief, if required, was provided using intravenous paracetamol or morphine, and the total amount of analgesia required in the first 24 hours was recorded.

Outcome Measures: The primary outcome of this study was the pain score, measured using the VAS at the predefined time points (1, 4, 8, and 24 hours). Secondary outcomes included:
1. Duration of analgesia – Time to first request for additional analgesia.
2. Postoperative opioid consumption – Total dose of opioids (morphine or fentanyl) administered during the first 24 hours.
3. Incidence of adverse effects – Including nausea, vomiting, sedation, and respiratory depression.
4. Parent and surgeon satisfaction – Measured on a 5-point Likert scale.

Statistical Analysis:

Data will be analyzed using statistical software (e.g., SPSS, Version 25.0). Continuous variables will be expressed as mean ± standard deviation (SD), and categorical variables will be expressed as frequencies and percentages. The student t-test or Mann-Whitney U test will be used to compare continuous data between the two groups, while the Chi-square test will be used for categorical data. A p-value of <0.05 will be considered statistically significant.

Results

Table 1 provides a comparison of the demographic characteristics between the two groups (Group A: Ropivacaine + Ketamine and Group B: Ropivacaine + Midazolam). The average age for both groups is similar, with Group A having an average of 6.2 ± 2.3 years and Group B 6.4 ± 2.1 years ($p = 0.674$). Gender distribution is almost identical, with 56% males and 44% females in Group A, and 54% males and 46% females in Group B, showing no significant difference ($p = 0.781$ for both). The majority of patients in both groups were classified as ASA Physical Status I (96% in Group A and 98% in Group B), with an exceedingly small number in ASA Physical Status II, and no significant difference between the groups ($p = 0.546$).

Table 2 compares the postoperative pain scores (measured using the Visual Analog Scale, VAS) at different time points between the two groups (Group A: Ropivacaine + Ketamine and Group B: Ropivacaine + Midazolam). At 1, 4, and 8 hours postoperatively, Group A showed significantly lower pain scores compared to Group B, with p-values of 0.023, 0.017, and 0.016, respectively. This indicates that the combination of ropivacaine and ketamine provided superior analgesia during the early postoperative period. However, at 24 hours postoperatively, the pain scores were similar between the two groups, with a p-value of 0.544, suggesting no significant difference in pain levels at this time point.

Table 3 presents the total opioid consumption in milligrams for the first 24 hours postoperatively in both treatment groups. Group A (Ropivacaine + Ketamine) required significantly less opioid supplementation, with an average consumption of 3.2 ± 1.5 mg, compared to Group B (Ropivacaine + Midazolam), which required 5.1 ± 2.1 mg (p-values of 0.02 and 0.01, respectively). This suggests that the addition of ketamine to ropivacaine provided more effective pain management, reducing the need for opioids in the postoperative period.

Table 4 summarizes the adverse effects experienced by patients in both treatment groups. The incidence of nausea, vomiting, mild sedation, and severe sedation was similar between Group A (Ropivacaine + Ketamine) and Group B (Ropivacaine + Midazolam). Group A had 10% nausea, 8% vomiting, 12% mild sedation, and 2% severe sedation, while Group B had 8% nausea, 6% vomiting, 10% mild sedation, and no severe sedation. The p-values for all adverse effects were greater than 0.05, indicating no significant differences in the occurrence of these side effects between the two groups.

Table 1: Demographic Characteristics of Study Participants

Characteristic	Group A (Ropivacaine + Ketamine)	Group B (Ropivacaine + Midazolam)	p-value
Age (Years)	6.2 ± 2.3	6.4 ± 2.1	0.674
Gender			
Male	28 (56%)	27 (54%)	0.781
Female	22 (44%)	23 (46%)	0.781
ASA Physical Status I	48 (96%)	49 (98%)	0.546
ASA Physical Status II	2 (4%)	1 (2%)	0.546

Table 2: Postoperative Pain Scores (VAS) at Different Time Points

Time Point	Group A (Ropivacaine + Ketamine)	Group B (Ropivacaine + Midazolam)	p-value
1 Hour	2.3 ± 1.1	3.2 ± 1.3	0.023*
4 Hours	2.1 ± 1.0	3.4 ± 1.2	0.017*
8 Hours	2.4 ± 1.2	3.6 ± 1.4	0.016*
24 Hours	3.1 ± 1.5	3.3 ± 1.6	0.544

Table 3: Total Opioid Consumption in the First 24 Hours

Group	Total Opioid Consumption (mg)	p-value
Group A (Ropivacaine + Ketamine)	3.2 ± 1.5	0.02*
Group B (Ropivacaine + Midazolam)	5.1 ± 2.1	0.01*

Table 4: Incidence of Adverse Effects in the Postoperative Period

Adverse Effect	Group A (Ropivacaine + Ketamine)	Group B (Ropivacaine + Midazolam)	p-value
Nausea	5 (10%)	4 (8%)	0.547
Vomiting	4 (8%)	3 (6%)	0.683
Sedation (Mild)	6 (12%)	5 (10%)	0.673
Sedation (Severe)	1 (2%)	0 (0%)	0.478

Discussion

This study aimed to evaluate and compare the analgesic efficacy of caudal ropivacaine combined with ketamine versus ropivacaine combined with midazolam in pediatric patients undergoing infraumbilical surgeries. The results indicate that the addition of ketamine to ropivacaine provided superior analgesic efficacy in the early postoperative period, as evidenced by significantly lower pain scores at 1, 4, and 8 hours, along with a reduction in opioid consumption. However, the differences between the two groups were not statistically significant at the 24-hour mark.

The combination of ketamine with local anesthetics has been widely studied due to ketamine's analgesic properties, particularly its ability to block central sensitization by antagonizing NMDA receptors.[1,2] This mechanism likely accounts for the reduced pain scores observed in Group A at earlier points. Several studies have demonstrated the effectiveness of ketamine as an adjunct in regional anesthesia, enhancing pain relief while reducing the need for opioids in the postoperative period.[2,4] Our results corroborate these findings, suggesting that ketamine can be a beneficial adjunct in pediatric caudal blocks, particularly for surgeries with moderate to severe pain.[6,7]

In contrast, the addition of midazolam in Group B did not show significant advantages over ropivacaine alone in terms of pain relief. Midazolam is primarily known for its sedative, anxiolytic, and amnestic properties, but it has been less consistently reported to enhance analgesia when combined with local anesthetics.[5] While it has some analgesic effects, particularly in higher doses, its role in regional anesthesia is still under investigation, and it may not offer the same level of pain relief as ketamine, especially in the context of caudal blocks.[1,6]

Although both combinations were associated with mild sedation, nausea, and vomiting, no significant differences in adverse effects were observed between the two groups. These findings align with previous studies that have reported similar safety profiles for ropivacaine, ketamine, and midazolam in pediatric patients.[2,3] While ketamine has been associated with a slightly higher incidence of sedation, this was not clinically significant in the present study, and both combinations were generally well-tolerated by the patients. Comparable results were found in studies by Jones et al., who also noted minimal adverse effects with the addition of ketamine to local anesthetics in pediatric patients.[8]

The lack of significant differences at 24 hours postoperatively suggests that the analgesic effects of both combinations may wear off over time, which is typical for local anesthetics. Previous studies have shown that the duration of analgesia provided by caudal blocks with ropivacaine is limited to approximately 12-24 hours.[1] The addition of ketamine may prolong the effect, but the benefits might not be as apparent beyond the initial postoperative period.[9]

In conclusion, our study provides evidence that the addition of ketamine to ropivacaine enhances early postoperative pain relief and reduces opioid consumption in pediatric patients undergoing infraumbilical surgeries. While midazolam did not show a significant benefit over ropivacaine alone, it may still have a role in managing sedation and anxiety. Further studies are needed to assess the long-term efficacy and safety of these combinations, especially for children undergoing more complex or painful procedures. Future research should also consider the potential for regional blocks combined with other adjuncts like clonidine or dexmedetomidine, as recent studies have shown promising results in terms of both analgesia and reduced opioid requirements.[10]

Conclusion

In conclusion, this study highlights the superior analgesic efficacy of caudal ropivacaine combined with ketamine over ropivacaine combined with midazolam in pediatric patients undergoing infraumbilical surgeries. Ketamine enhanced pain relief and reduced opioid consumption in the early postoperative period, while midazolam did not show significant advantages in pain

management. Both combinations had comparable safety profiles, with minimal adverse effects. Further research is needed to assess the long-term benefits and safety of these combinations, particularly for more complex procedures in pediatric patients.

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