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Original Article

# Analgesic Effect of Bupivacaine-Dexmedetomidine versus Bupivacaine-Midazolam in Caudal Anesthesia for Pediatric Hypospadias Surgeries

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## ABSTRACT

**Background:** Dexmedetomidine and Midazolam were utilized as adjuvants for extending the duration of analgesia; the most common local anesthetic used globally for Caudal anesthesia (CA) is a single dose of plain bupivacaine. To achieve adequate post-operative analgesia, we aimed to compare bupivacaine-dexmedetomidine and bupivacaine-midazolam in caudal anesthesia in pediatric hypospadias surgeries. **Methods:** We conducted a prospective randomized double-blind controlled clinical study on 51 patients who were scheduled for hypospadias surgery aged from 3 to 8 years; they were allocated randomly into three equal groups (17 patients in each group): Group C (Control): received bupivacaine 0.25% total volume 1ml/kg only, Group D: who received bupivacaine 0.25% in addition to dexmedetomidine 1µg/kg total volume 1ml/kg, Group M: received bupivacaine 0.25% in addition to midazolam 50µg/kg total volume 1ml/kg. The postoperative vital signs, adverse events and duration of the caudal analgesia were assessed utilizing the pediatrics observational Face, Legs, Activity, Cry, Consolability scale (FLACC) pain scale. **Results:** Group D had the lowest significant FLACC pain score, followed by Group M, then Group C (P=0.00), Duration of Caudal block was the highest in Group D [14 hours, 95% CI(13.26-14.7)] followed by Group M [10 hours, 95% CI(9.6-10.36)] then Group C [4 hours, 95% CI(3.5-4.49)]. Time to first request analgesics was the highest in Group D [14 hours, 95% CI(12.2-14.7)] followed by Group M [10 hours, 95% CI(9.22-10.7)] then Group C [4 hours, 95% CI(5.23 – 6.77)], with statistically significant differences between the 3 groups (P<0.001).
**Conclusion:** Combining bupivacaine with dexmedetomidine or midazolam dramatically extends the time of postoperative analgesia, which in turn increases the time until the patient requires another analgesic. Compared to a mixture of midazolam and bupivacaine, the analgesic profile of the dexmedetomidine plus bupivacaine combination was superior, and there were no significant side effects or disturbances in hemodynamic parameters.
**Keywords:** Bupivacaine, Dexmedetomidine, Midazolam, Caudal Anesthesia, Pediatric Hypospadias

## INTRODUCTION

Attention to patient-centered care has been linked to continuous progress in the medical industry and anesthesiology's unique role makes it crucial to guaranteeing patients' comfort [1]. Surgical correction of pediatric hypospadias is a challenging and often unpleasant procedure that can lead to a variety of complications, including but not limited to nausea, anxiety, postoperative agitation, bleeding, infection, urethral fistula and extended hospital stays [2].

Regional anesthetic techniques greatly reduce the need for systemic analgesics and the amount of pain felt after surgery. The caudal route is among the most straightforward, risk-free and effective techniques for pediatric surgery. In addition to reducing the need

for inhaled and intravenous (IV) anesthetics, caudal analgesia has several other potential benefits, including a diminished stress reaction to surgery, an easier and faster recovery and effective pain relief immediately following surgery [3].

Caudal anesthesia (CA) ranks high among the preferred regional techniques when dealing with children. Adult anorectal surgeries may also make use of it. The sacrococcygeal ligament, which covers the sacral hiatus formed by the unfused S4 and S5 laminae, is penetrated with a needle or catheter during caudal anesthesia. Common uses include urogenital, rectal, inguinal and lower limb surgeries below the umbilicus [4].

Numerous agents can be used as adjuvants for extending the duration of analgesia, including clonidine, pethidine ketamine, morphine, fentanyl, midazolam, diamorphine neostigmine, adrenaline, as well, and sodium bicarbonate. The most common local anesthetic used around the world for caudal anesthesia is a single shot of plain bupivacaine. [5].

The α2-adrenoreceptor agonist dexmedetomidine (DEX) is both powerful and very selective. Among its many uses are anesthetic, sedative-hypnotic, analgesic and sympatholytic properties [6]. By lowering the onset time, increasing the block time and decreasing the dosage of local anesthetics, dexmedetomidine is useful in neuraxial anesthesia. Caudal blocks in children can benefit from its analgesic and stress-reducing properties. It makes kids feel better and speeds up recovery [7].

Among midazolam's many useful effects are those of amnesic, muscle relaxant, anxiolytic, anticonvulsant, hypnotic and sedative. The substance has a short half-life. Belongs to the family of medicines known as benzodiazepines. Because of its short half-life and quick start-up, this medicine stands out among other medications in its class [8].

There are several benefits to using ultrasound to guide caudal anesthesia rather than approaches that rely on landmarks. Despite the high success rate (over 96%) of the landmark strategy, it seems that the utilization of ultrasound improves the first puncture success rate compared to the standard approach [9].

We aimed at this study to compare bupivacaine-dexmedetomidine and bupivacaine-midazolam in caudal anesthesia in pediatric hypospadias surgeries to achieve adequate post-operative analgesia.

## METHODS

We conducted this prospective randomized controlled clinical trial on 51 patients scheduled for hypospadias surgery aged 3 to 8 years at Zagazig University Hospitals from June 2023 to December 2023.

After the Zagazig University Faculty of Medicine Research Ethics Committee (IRB#10767/7-5-2023), All parents or caregivers of participants were asked to sign an informed consent. Human subjects research adhered to the guidelines set in the Declaration of Helsinki, which is part of the World Medical Association's Code of Ethics. Inclusion criteria: The study included 51 patients of both sexes aged 3–8 years, with body mass index (BMI) equal to 5%: 85% of BMI (kg/ m2) of the same age and sex, American Society of Anesthesiologists (ASA) classes I and II, who were scheduled for elective hypospadias surgeries. Exclusion criteria: Patients who were excluded from the study were those who had known allergies, sensitivity to dexmedetomidine or bupivacaine, chest infection within two weeks, patients who had contradictions to caudal block as infection at the site of injection, coagulopathy or patients individuals who have a history of mental retardation or developmental delay, which may make it challenging to assess their pain levels.

Complete medical history from the parents or caregivers, physical examinations, and laboratory investigations were performed on all study participants, including complete blood count (CBC), random blood glucose, kidney function test, liver function test and coagulation profile. The anesthesiologist who performed the preoperative block on the patient and the anesthesiologist who followed the perioperative block were different to ensure the blinding of the study. A thorough preoperative evaluation of each patient was done during the preoperative visit, including history by the parents, general and systemic physical examinations and laboratory investigations.

The patient kept fasting for 6 hours (hrs) for solid meals and 2 hrs for water or clear fluid. When the patient was connected to the monitors, baseline vital parameters were recorded: heart rate, blood pressure and oxygen saturation. Inhalational sevoflurane anesthesia was done to facilitate IV cannula insertion. After insertion of the i.v cannula, general anesthesia was induced using intravenous anesthetic medication in the form of a standard dose of propofol 1% (2.5mg/kg) and an analgesic dose of ketamine (0.5mg/kg) endotracheal intubation facilitated with neuromuscular blocker using non-depolarizing muscle relaxant in the form of atracurium 0.5mg/kg. Anesthesia was maintained with atracurium (0.1mg/kg) and inhalational isoflurane 1-1.5%. Caudal anesthesia was performed after general

anesthetic induction. If the physician was right-handed, the patient was placed in the left lateral position with their hips and knees flexed. If the provider was left-handed, the patient should be placed in the right lateral position.

The ultrasound probe was covered in a sterile cover. To provide a longitudinal visualization, the probe was subsequently turned 90 degrees. Visualization of the needle's tip and length allowed for its advancement at a 20-degree angle. After ensuring the needle was in the caudal space on the screen, aspirate carefully to ensure there was no cerebrospinal fluid (CSF) or blood. The volume was injected in the caudal block (1 ml/kg) in the form of used drugs according to each group: Group C: (Control group) Patients received caudal anesthesia total volume 1ml/kg 1st half of this volume bupivacaine 0.5% and 2nd half saline 0.9% to obtain bupivacaine concentrate 0.25%. Group D:( Dexmedetomidine): Patients received caudal anesthesia total volume 1ml/kg 1st half of this volume bupivacaine 0.5% and 2nd half saline 0.9% to obtain bupivacaine concentrate 0.25%. And dexmedetomidine 1µg/kg by: 1ml of dexmedetomidine (100µg) was diluted in 10ml saline 0.9%. Hence, each ml contained 10µg, from which 1ml of dexmedetomidine was diluted again in 10ml saine 0.9%. Hence, each ml contains 1µg, so we had 2 syringes 10ml,1st contains 10µg/ml and 2nd contains 1µg/ml to adjust doses for different weights of the studied patients.

Group M(Midazolam): Patients received caudal anesthesia total volume of 1ml/kg 1st half of this volume was bupivacaine 0.5% and 2nd half saline 0.9%, and midazolam (50µg/kg) by:1ml of midazolam(5000µg) was diluted in 10ml saline 0.9%. Hence, each ml contained 500µg from which 1ml of midazolam was diluted again in 10ml saline 0.9%, so each ml contained 50µg so had 2 syringes 10ml,1st contained 500µg/ml and 2nd contained 50µg/ml to adjust doses for different weights of the studied patients.

The prepared volume was injected slowly at a < 10 ml/30 rate. The inhalational anesthetic was withdrawn, and the muscle relaxant was replaced with a combination of 0.05 mg/kg of neostigmine and 0.01 mg/kg of atropine as the surgical process came to a close. After the patient regained consciousness, extubation was done, and they were moved to the postoperative anesthetic care unit (PACU). The time to remove the endotracheal tube (extubation time was the duration from the discontinuation of inhalational anesthesia to the removal of the endotracheal tube) was recorded.

During postoperative period, the following parameters were monitored: Patient and operative characteristics, including age (years), Sex (M), ASA (I or II), BMI (kg/m2) and Operative time (min). Vital parameters, including HR, MAP and SPo2, were recorded on arrival to the operating room as a baseline value after induction of general anesthesia, after caudal anesthesia, and after skin incision. Every 10 minutes throughout the operation, and will be monitored post-operative at PACU at time intervals 10 minutes till discharge and at ward every 2 hours for 24h. Extubation time: The duration from the discontinuation of inhalational anesthesia to the removal of endotracheal tube.

Duration of caudal block analgesia: The duration of the caudal analgesia was recorded at 2-hour intervals for 24 hours using the pediatric observational FLACC pain scale [10]. This was defined as the time it took from the caudal injection to the first request for analgesics; in cases where the pain was severe, a rescue dose of 15 mg/kg of paracetamol was administered by drip. 0 indicates no pain or discomfort, 1–3 mild, 4–6 moderate, and 7–10 severe pain or discomfort. Incidences of side effects were recorded and managed, including respiratory depression, hypoxia, hypotension and bradycardia.

Duration of PACU stay: The adverse events were recorded and managed. The patient was discharged from PACU when the modified Aldrete score became more than 9 [11].

Sample size: According to 95% Ci power 80% ratio of sample size 2:1 mean of time needed for first analgesic request in bupivacaine and Dexmedetomidine 14.4 hours ± 2.36 hours mean of time- needed for first analgesic request in bupivacaine and midazolam was 12 hours ± 3.69 hours [12].so sample size was 51 patients,17 in each group using Open EPI version 13.

**Statistical analysis**: The data was processed using SPSS, version 27.0, IBM's statistical analysis software. The Kolmogorov-Smirnov and the Shapiro-Wilk tests were used to ensure the data was normal. An independent sample t-test was employed to compare the two sets of continuous data. Events and percentages were used to represent categorical data. The Chi-square (x2) test or Fisher Exact test was used to compare the two groups categorical data. We used either a mixed linear model with Bonferonni adjustments when missing values were present or a General linear model with Bonferonni adjustments when continuous data was measured repeatedly. When the p-value was less than 0.05, the significance level was considered.

## RESULTS

Table 1 : show that the mean age of included children in Group D, Group M, and Group C was 4.47, 4.65 and 4.88 years old, respectively. Operation time was 50.59±8.27 minutes in Group D, 54.71±6.24 minutes in Group M, and 52.35±7.52 minutes in Group C. Extubation time was 7.35±1.90 in group D, 7.88±1.69 in group M and 8.35±1.41 in group C. The mean PACU stay of included children in Group D, Group M and Group C was 14.47, 14.24 and 14.41 minutes, respectively.

**Figure 1**: show that there was non-statistically significant differences between groups regarding intra-operative heart rate, mean arterial pressure, peripheral oxygen, heart rate at PACU, mean arterial pressure at PACU, SPO2 at PACU, heart rate at the ward, MAP at the ward and SPO2 at the ward.

**Figure 2:** show that regarding FLACC pain score, there was a significant increase in FLACC pain score, recorded during repeated measurement, in Group C compared with Group D and Group M. Group D had the lowest pain score, followed by Group M then Group C (P=0.00) .

**Table 2:** show that duration of Caudal block was the highest in Group D [14 hours, 95% CI(13.26-14.7)] followed by Group M [10 hours, 95% CI(9.6-10.36)] then Group C [4 hours, 95% CI(3.5-4.49)], Time to first request analgesics was the highest in Group D [14 hours, 95% CI(12.2-14.7)] followed by Group M [10 hours, 95% CI(9.22-10.7)] then Group C [4 hours, 95% CI(5.23 – 6.77)] with statistically significant differences between the 3 groups (p=0.00).

**Table 4:** show that the rescue dose of paracetamol differed significantly between group C and groups D and M (p=<0.001) (Table 3). Non-statistically significant differences were revealed between both groups as regards the adverse events: Respiratory depression, Hypoxia, Hypotension and Bradycardia (p>0.05).

**Table (1):** Baseline characters, extubation time and PACU stay of included patients.

| | Group D | Group M | Group C | P value |
|---|---|---|---|---|
| Age | 4.47±1.46 | 4.65±1.50 | 4.88±1.50 | .721 |
| BMI | 17.03±3.45 | 17.63±2.67 | 17.45±2.63 | .828 |
| Operation time (min) | 50.59±8.27 | 54.71±6.24 | 52.35±7.52 | .275 |
| | Group D | Group M | Group C | P value |
| Extubation time | 7.35±1.90 | 7.88±1.69 | 8.35±1.41 | .232 |
| PACU stay (minutes) | 14.47±1.01 | 14.24±1.20 | 14.41±0.94 | .796 |

**Table (2):** Duration of Caudal block, and Time to first request analgesics in the studied patients

| Duration of Caudal block | median | 95% CI | P value |
|---|---|---|---|
| Group D | 14 | 13.264- 14.736 | P1, P2, P3= 0.00 |
| Group M | 10 | 9.632- 10.368 | |
| Group C | 4 | 3.503- 4.497 | |
| Time to first request analgesics | | | |
| | median | 95% CI | P value |
| Group D | 14 | 12.2- 14.7 | P1, P2, P3= 0.00 |
| Group M | 10 | 9.22- 10.7 | |
| Group C | 6 | 5.23- 6.77 | |

Data were represented as median and 95% confidence interval, Kruskal - Wallis Test followed by Mann-whiteny test; ; P1: indicate the difference between Group D and Group M; P2: indicate the difference between Group D and Group C; P3: indicate the difference between Group M and Group C.

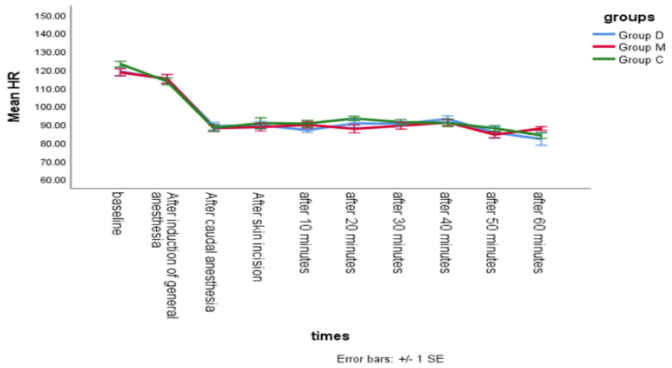
**Table (3):** repeated measurements for rescue dose of paracetamol

| Rescue dose of paracetamol | Group D | | Group M | | Group C | | P value |
|---|---|---|---|---|---|---|---|
| | N | mean±SD | N | mean±SD | N | mean±SD | |
| 2 hr | 0 | ---- | 0 | ---- | 0 | ---- | --- |
| 4hr | 0 | ---- | 0 | ---- | 8 | 218.1±30 | --- |
| 6hr | 0 | ---- | 0 | ---- | 9 | 264.4±37.9 | --- |
| 8hr | 0 | ---- | 3 | 281.4±36.3 | 7 | 240±50 | 0.23 |
| 10hr | 0 | ---- | 6 | 221.7±42.6 | 3 | 233.3±28.9 | 0.64 |
| 12hr | 7 | 224.28±28.2 | 4 | 267.5±55.6 | 8 | 260±14.1 | P1, P2, P3 >0.05 |
| 14hr | 6 | 225±36.40 | 7 | 290±84.85 | 3 | 255±47.7 | P1, P2, P3 >0.05 |
| 16hr | 4 | 237.5±35 | 2 | 240±14.14 | 7 | 262.9±21.4 | P1, P2, P3 >0.05 |
| 18hr | 3 | 225±36.4 | 7 | 250±34 | 3 | 235±13.2 | P1, P2, P3 >0.05 |
| 20hr | 2 | 237.5±35 | 4 | 200±45 | 7 | 267.14± 21.38 | P2, P3 <0.05, P1 >0.05 |
| 22hr | 0 | ---- | 0 | ---- | ١ | 280 | --- |
| 24 hr | 1 | 200 | 0 | --- | 3 | 223.3±46.18 | >0.05 |
| Overall | 17 | ١٢.56±٣٧2 .91١ | 17 | 389.4±142 .63 | 17 | 882.65± 379.44 | P1= 0.07, p2, p3=0.00 |

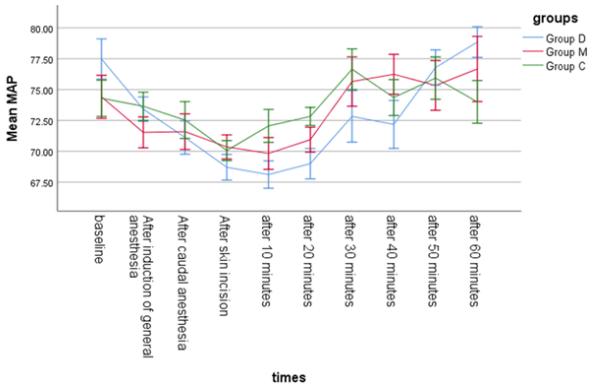
P1: indicate the difference between Group D and Group M; P2: indicate the difference between Group D and Group C; P3: indicate the difference between Group M and Group C.

**Table (4):** Post-operative complications

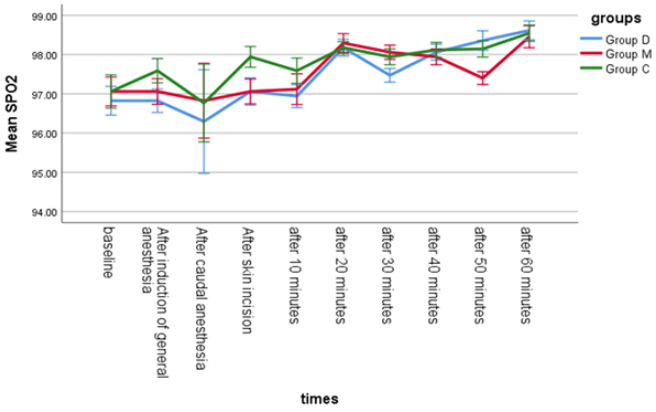
| | Group D | Group M | Group C | Exact fisher test | P value |
|---|---|---|---|---|---|
| Respiratory depression | 0(0.0%) | 0(0.0%) | 0(0.0%) | ---- | --- |
| Hypoxia | 0(0.0%) | 0(0.0%) | 0(0.0%) | ---- | ---- |
| Hypotension | 0(0.0%) | 1(5.9%) | 0(0.0%) | 1.857 | 0.99 |
| Bradycardia | 2(11.8%) | 0(0.0%) | 1(5.9%) | 1.940 | .764 |


groups
Group D
Group M
Group C
Mean HR
150.00
140.00
130.00
120.00
110.00
100.00
90.00
80.00
70.00
60.00
baseline
After induction of general anesthesia
After caudal anesthesia
After skin incision
after 10 minutes
after 20 minutes
after 30 minutes
after 40 minutes
after 50 minutes
after 60 minutes
times
Error bars: +/- 1 SE

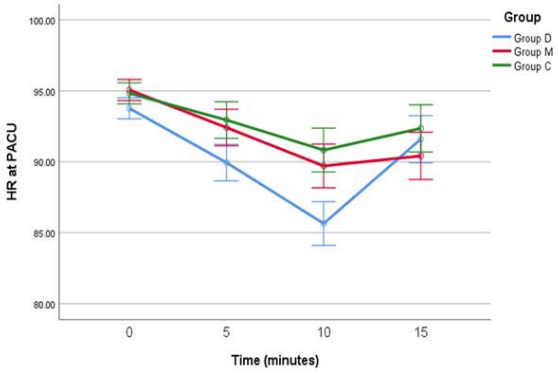
A


groups
Group D
Group M
Group C
Mean MAP
80.00
77.50
75.00
72.50
70.00
67.50
baseline
After induction of general anesthesia
After caudal anesthesia
After skin incision
after 10 minutes
after 20 minutes
after 30 minutes
after 40 minutes
after 50 minutes
after 60 minutes
times

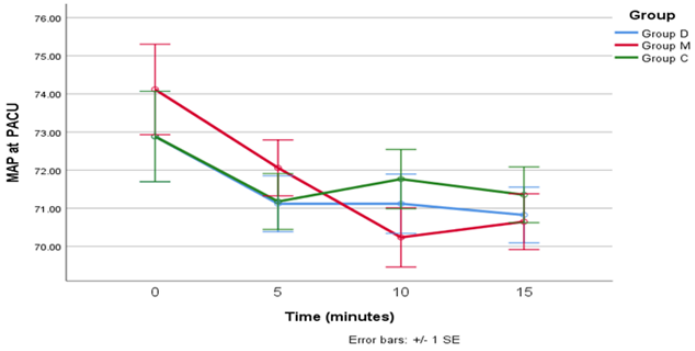
B


groups
Group D
Group M
Group C
Mean SPO2
99.00
98.00
97.00
96.00
95.00
94.00
baseline
After induction of general anesthesia
After caudal anesthesia
After skin incision
after 10 minutes
after 20 minutes
after 30 minutes
after 40 minutes
after 50 minutes
after 60 minutes
times

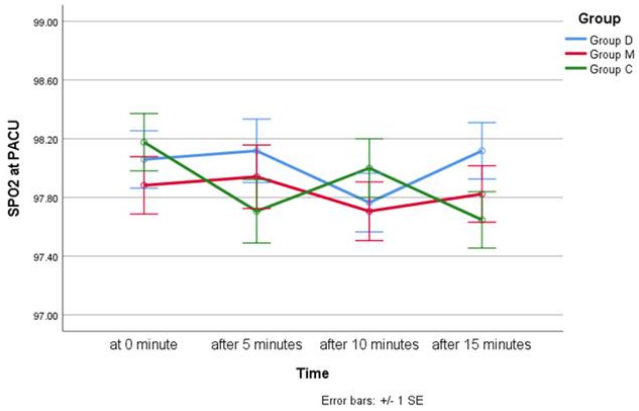
C


Group
Group D
Group M
Group C
HR at PACU
100.00
95.00
90.00
85.00
80.00
0
5
10
15
Time (minutes)

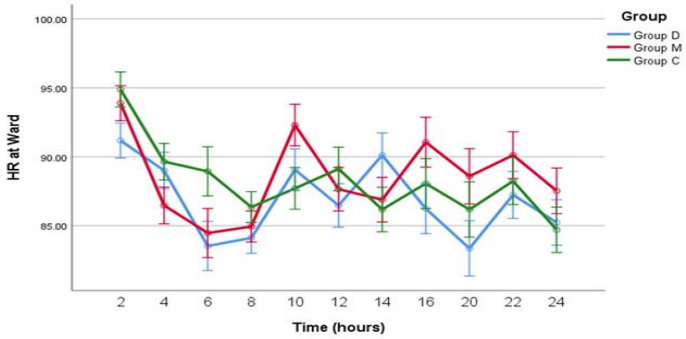
D


Group
Group D
Group M
Group C
MAP at PACU
76.00
75.00
74.00
73.00
72.00
71.00
70.00
0
5
10
15
Time (minutes)
Error bars: +/- 1 SE

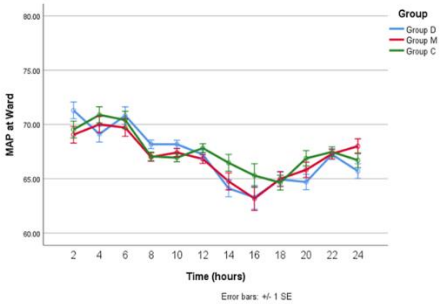
E


Group
Group D
Group M
Group C
SPO2 at PACU
99.00
98.60
98.20
97.80
97.40
97.00
at 0 minute
after 5 minutes
after 10 minutes
after 15 minutes
Time
Error bars: +/- 1 SE

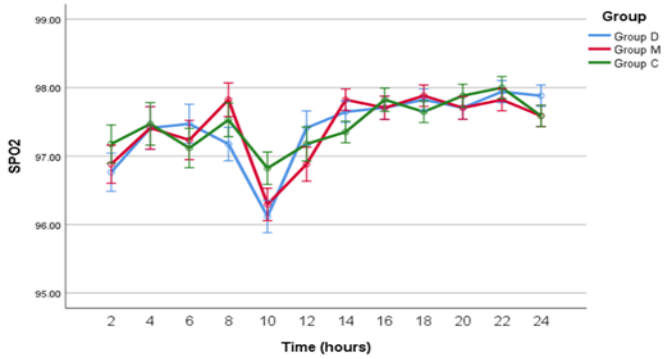
F


Group
Group D
Group M
Group C
HR at Ward
100.00
95.00
90.00
85.00
2
4
6
8
10
12
14
16
20
22
24
Time (hours)

G


Group
Group D
Group M
Group C
MAP at Ward
80.00
75.00
70.00
65.00
60.00
2
4
6
8
10
12
14
16
18
20
22
24
Time (hours)
Error bars: +/- 1 SE

H




I

**Figure 1:** Line Charts for A: repeated measurements of intra-operative heart rate, B: repeated measurements of intra-operative mean arterial pressure, C: repeated measurements for intra-operative saturation of peripheral oxygen, D: repeated measurement of heart rate at PACU, E: repeated measurements of mean arterial pressure at PACU, F: repeated measurements of SPO2 at PACU, G: repeated measurements of heart rate at ward, H: repeated measurements of MAP at ward, I: repeated measurements of SPO2 at ward

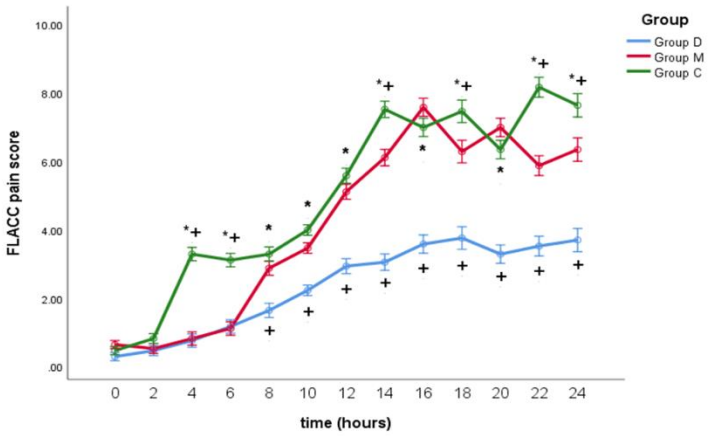



**Figure (2):** line chart for repeated measurements of FLACC pain score

*indicates a statistically significant difference with group D; + indicate a statistically significant difference with group M.

## DISCUSSION

In the current study, Groups A and M, which consisted of bupivacaine and dexmedetomidine and Group C, which consisted of bupivacaine and midazolam, had much longer times to first analgesic request (TTFAR) than Group C, which consisted of bupivacaine alone. Additionally, patients in group C utilized more analgesics after surgery compared to groups M and D. In addition, group D had a considerably greater TTFAR compared to group M. All three groups, however, had comparatively low rates of side events.

The duration of action and dose-dependent side effects are the limitations of using local anesthetics without adjuvants [13]. Compared to groups D and M, group C had the shortest duration of analgesia and reached a pain level of 4 or higher, the earliest in this study.

The fact that group D's TTFAR was the longest of the four groups corroborates the results of El-Hennawy et al. [6], who found that combining dexmedetomidine and bupivacaine during caudal anesthesia greatly increases postoperative TTFAR, suggesting the presence of analgesic synergism between the two drugs. Evidence shows that dexmedetomidine causes local vasoconstriction and intensifies neurons' local anesthetic conduction block [14].

This study used the same protocol as Goyal et al. [15] in administering 1 ml/kg of bupivacaine 0.25% with 1µg/kg dexmedetomidine for postoperative analgesia. According to research by Sharpe et al. [16], inadequate anesthesia would be achieved even with a volume of 0.5 ml/kg of ordinary bupivacaine. This suggests that to obtain surgical analgesia in pediatric caudal blocks,

an ideal dosage and sufficient amount of bupivacaine are necessary.In pediatric caudal blocks, the effectiveness of a small volume (0.5 ml/kg) of bupivacaine was lower than that of an average volume (1 ml/kg) of the same concentration (0.25%), as shown by Akpoduado et al. [17].

In the present study, the combination of 1µg/kg of caudal adjuvant dexmedetomidine and 0.25% of bupivacaine did not cause any negative effects. Greater unfavorable effects were observed without an increase in analgesic benefits at 2 µg/kg dexmedetomidine, according to Al-Zaben et al. [18].El-Hennawy et al. [6] also discovered that adding 2 µg/kg of dexmedetomidine to 0.25% caudal bupivacaine during the perioperative phase did not significantly change the HR in pediatric patients having lower abdominal procedures, which is consistent with the current study's results.

This is in line with the findings of Rashid et al. [19], who also observed no variation in the size of MAP alterations in patients undergoing sub umbilical surgery and given 1ml/kg of 0.25% bupivacaine with 2µg/kg of dexmedetomidine for caudal block.

Also, the present study findings agree with the results of El-Hennawy et al. [6], who found that Dexmedetomidine, when added to bupivacaine, provides longer-lasting caudal analgesia to children without causing any adverse effects or dramatically slowing down their recovery time after the general anesthetic. Also, Saadawy et al. [20] found that no significant respiratory depression, bradycardia or hypotension were recorded in children aged 1-6 years who underwent unilateral inguinal hernia surgery, orchidopexy or hypospadias when dexmedetomidine was added to bupivacaine in a caudal block.

Also, the present study findings agree with the results of Anand et al. [3], who examined the effects of dexmedetomidine in combination with caudal ropivacaine on lower abdominal surgeries in children and discovered that there were no instances of clinically significant postoperative complications like postoperative nausea and vomiting (PONV), respiratory depression, urinary retention, pruritus, hypotension and bradycardia. Also, in agreement with these results, Rashid et al. [19] found that no patients in any group experienced bradycardia or hypotension and no one reported substantial respiratory depression in their study.

In the present study, post-operative pain intensity was assessed by a pediatric observational FLACC pain scale**.** These results were in agreement with the study of Xiang et al. [14], who found that total consumption of postoperative analgesia was significantly lower in the group receiving 1µg/kg DEX plus bupivacaine when compared to the group receiving bupivacaine alone. The results of this study were also correlated with several studies that used other scales for pain assessment, such as Xiang et al. [14], who used the Children's and Infant's Postoperative Pain Scale (CHIPPS). Buttner and Finke [21] found that both the group that received bupivacaine alone and the one that received dexmedetomidine with bupivacaine reported satisfactory analgesia during the first four hours following surgery. The number of patients reporting adequate analgesia declined in both groups during the following 20 hours. However, the decline of the dexmedetomidine group was somewhat slower. Those who received dexmedetomidine reported much less pain.

In the studied groups, we observed the frequency of the need for postoperative rescue analgesia in the form of a paracetamol drip of 15mg/kg. We found that patients in Group C were more likely to require analgesia, while patients in group D were less likely to require analgesia. The present study findings were in correlation with the study of Xiang et al. [14], who found that total consumption of postoperative analgesia was significantly lower in the group receiving 1µg/kg DEX plus bupivacaine when compared to the group receiving bupivacaine alone.

Also, these results were in agreement with the study of Rashid et al. [19], who found that analgesic requirement in patients who received bupivacaine alone was statistically significantly higher as compared to patients who received dexmedetomidine with bupivacaine ($p < 0.05$). Also, in correlation with the study of El-Hennawy et al. [6], who observed that compared to the group that received bupivacaine alone, those who received caudal dexmedetomidine in conjunction with it used fewer analgesics during the postoperative period.

From the evidence provided by de Beer and Thomas [22], Kumar et al. [23] and Gulec et al. [24], it may be inferred that a caudal adjuvant dose of 50 µg/kg of midazolam is best. All three groups experienced relatively longer analgesic durations when using the same dose. Utilizing 70 percent nitrous oxide, 1 milliliter per kilogram of bupivacaine at a concentration of 0.25% and 50 micrograms per kilogram of midazolam is undeniably responsible for the finding reported by Kumar et al. [23].

Since sedation and analgesia are easily interchangeable in nonverbal children, the extended sedation observed in the bupivacaine plus midazolam group by Gulec et al. [24] may have been due to their observation of a significantly longer duration of

analgesia. Nevertheless, nitrous oxide was excluded from this investigation. According to Adetoye et al. [25], the duration of analgesia after caudal block surgery was only 7.97±0.90 hours when using 50 µg/kg of caudal midazolam and 1 ml/kg of 0.125% bupivacaine. This finding lends credence to Joshi et al. [26], who also found that adding adjuvants with a subanaesthetic bupivacaine concentration of 0.125% might not be enough to affect postoperatively. A shorter TTFAR (5.20 hours) was reported by Abodesira et al. [27] when caudal 0.5 ml/kg ropivacaine mixed with 50 µg/kg midazolam was administered, lending credence to the findings of Verghese et al. [28]. The sustained postoperative analgesia seen by Musa et al. [29] with 1 ml/kg of 0.25% caudal bupivacaine + 50 µg/kg of midazolam is consistent with our findings.

According to an intergroup evaluation, there was a statistically significant difference in the duration of postoperative analgesics between groups D and M, D and C, and M and C. Dexmedetomidine has a stronger intrinsic analgesic property than midazolam, which is why group D has a far better analgesic profile than group M. According to research by Bekker and Sturaitis [30], dexmedetomidine can decrease the transmission of substance-P-mediated nociceptive signals in the spinal cord. The different binding affinities of the two medicines toward their receptors could be another explanation for why group D's analgesic duration was longer than group M's. Dexmedetomidine has an 8-fold higher affinity for α2 adrenoceptors than clonidine Dundee. However, midazolam is just twice as effective at binding to GABA receptors [31]

**Limitations of this study:**

The current study had some limitations. Firstly, the sample size might be relatively small, with 51 subjects. The results may not apply to a broader population because of this. Secondly, since the study was conducted in a specific hospital, there was a potential for selection bias. The patient population might not fully represent the diversity and characteristics of all individuals with hypospadias Surgeries. This could affect the external validity of the study.

## CONCLUSIONS

Combining bupivacaine with dexmedetomidine or midazolam dramatically extends the time of postoperative analgesia, which in turn increases the time until the patient requires another analgesic. Compared to a mixture of midazolam and bupivacaine, the analgesic profile of the dexmedetomidine plus bupivacaine combination was superior and there were no significant side effects or disturbances in hemodynamic parameters.

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## Citation

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