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Effect of Dexmedetomidine Infusion on Surgical Pleth Index in Pediatrics Undergoing Hypospadias Repair; A Prospective Observational Study

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ABSTRACT

Background: *Postoperative pain management plays a crucial role in patient recovery, with concerns persisting about early postoperative pain, especially in pediatric populations.*

Objectives: *This study explores the impact of dexmedetomidine infusion, without a bolus dose, on the Surgical Pleth Index (SPI) in children undergoing hypospadias repair.*

Methods: *Ninety pediatric patients (1-7 years, ASA I-II) scheduled for hypospadias surgery were assigned to receive either dexmedetomidine infusion (0.5 µg/kg/hr) or a control solution. SPI, hemodynamic parameters, analgesic requirements, sedation depth, and various perioperative variables were meticulously assessed.*

Results: *The dexmedetomidine group exhibited lower SPI, heart rate, and blood pressure, indicating improved nociception control and reduced stress response during surgery. Despite a higher incidence of hypotension and bradycardia, the dexmedetomidine group required less rescue analgesia, had lower FLACC scores, and demonstrated prolonged PACU analgesic duration. Comparable surgical and anesthesia times were noted between the groups.*

Conclusions: *Dexmedetomidine infusion without a bolus dose significantly impacted SPI, reflecting improved nociception control in pediatric hypospadias surgery. Despite associated side effects, the benefits include reduced rescue analgesia requirements and improved postoperative pain management. These findings contribute to optimizing pain management strategies in pediatric urologic surgery.*

Keywords

Dexmedetomidine, Hypospadias repair, Surgical Pleth Index, Pediatric anesthesia.

List of Abbreviations

SPI: Surgical Pleth Index, HR: Heart Rate, SBP: Systolic Blood Pressure, MABP: Mean Arterial Blood Pressure, DBP: Diastolic Blood Pressure, PACU: Post Anesthesia Care Unit, NRS: Numeric Rating Scale, FLACC: Face, Legs, Activity, Cry, Consolability (pain assessment tool), NCT: ClinicalTrials.gov registration number prefix, NCT05727969: ClinicalTrials.gov registration number for the study, SF Figures: Supplementary File Figures, Precedex: Trade name for dexmedetomedine, ABP: Arterial Blood Pressure, ECG: Electrocardiography.

Background

The Surgical Pleth Index (SPI) is a non-invasive measure reflecting the patient's sympathetic reaction to surgical stimulation [1,2]. Developed recently, SPI serves to gauge postoperative pain and monitor nociception [3]. Demonstrating efficacy in balancing nociceptor activation and analgesia, SPI surpasses traditional indicators like blood pressure and heart rate [4,5]. SPI values

range from 0 to 100, correlating with pain; higher values suggest a more intense surgical stimulus [6], derived from pulse oximetry measures, including heart rate (HR) and photo-plethysmo-graphic amplitude (PPGA) [3,7].

Hypospadias surgery in children is known for its significant pain and various perioperative side effects, including anxiety, stress response, pain, agitation, nausea, and prolonged hospital stays [8,9]. Dexmedetomidine, a short-acting α2-adrenoceptor agonist, has been administered in varying dosages for anesthetic objectives in children, showing benefits in urethroplasty procedures as an adjuvant to caudal block anesthesia [10-12]. Research suggests that dexmedetomidine, known for relieving pain and inducing drowsiness [13,14], reduces surgical stress reactions in patients [15,16], serving safely and efficiently as an adjuvant analgesic during surgery. Despite its known benefits, no pediatric study has explored how dexmedetomidine affects postoperative pain via its impact on SPI. In adults, dexmedetomidine was found to reduce intraoperative SPI, alleviating unpleasant sensations [17].

Our hypothesis is that precedex infusion in absence of a potion dosage may affect Surgical Pleth index in young patients experiencing hypospadias correction. Understanding the impact of dexmedetomidine on SPI in pediatric patients undergoing hypospadias treatment is crucial for optimizing pain management techniques. This study aims to shed light on the link between SPI and dexmedetomidine infusion, potentially improving outcomes and standards of care in pediatric urologic surgery.

Objectives

The study aims to show the effect of precedex infusion in absence of giving a potion dosage on surgical pleth index in pediatrics experiencing hypospadias repair intraoperative and at PACU discharge.

Methods

Aim, Design, and Setting

This prospective observational study aims to investigate the impact of dexmedetomidine infusion, without a bolus dose, on the Surgical Pleth Index (SPI) in pediatric patients undergoing hypospadias repair. The research is set to be conducted at Fayoum University Hospital, following approvals from the local Institutional Ethics Committee and the institutional review board.

Study Participants

Ninety patients were inclusively enrolled in the study. Group D (Dexmedetomidine group) and Group C (Control group), With 45 patients per group.

Ethical Considerations

Grant number M637 was used for the research and this approval number was taken by the local ethical committee of Fayoum University, Faculty of Medicine. Before being included in the trial, every eligible patient had to sign a detailed informed consent form, ensuring strict adherence to ethical norms.

Clinical Trials.govRegistration

The trial's information is transparent and easily accessible due to its registration with ClinicalTrials.gov, where it is identified by the number NCT05727969 and 1st posted on 14/02/2023.

Primary Outcome Measures

- The SPI number at termination of surgery (skin closing down).

Secondary Outcome Measures

- The SPI number (pre-induction (starting point of measurement), at time of endotracheal tubal insertion, at the start of the surgery (skin surgical cut), at PACU discharge.
- MABP (mean arterial blood pressure) and HR (pre-induction (starting point of measurement), at time of endotracheal tube insertion, at the start of the surgery (skin surgical cut), finish of the surgery (skin closing down), at post anesthetic care unit lay out and 24 hours post-surgical intervention.
- Need of vaso active drugs (ephedrine or atropine).
- FlACC score for analgesia (at PACU discharge and 2, 4, 6, 12, and 24 hours postoperatively).
- Ramsy sedation score for depth of sedation. (at PACU discharge and 2 hours postoperative).
- Surgical time. (Is the time from when the surgical physician of record begins the intervention till the child leaves the procedure)?.
- Anesthesia time. (Is a continuous period from the beginning of anesthesia to the finish of an anesthesia facility)?
- Extubation time. (Time from the end of surgery to airway extubation of at least 15 min).
- Total opioid consumption.
- Time of 1st analgesia dose required postoperative.
- Total non-steroidal consumption during the 1st 24 hr.

Inclusion Criteria

- (1-7)-year-old.
- The American Society of Anesthesiologists physical status classification I-II.
- Hypospadias operation.

Exclusion Criteria

- Children having a history of intellectual disability.
- Developmental slawness.
- Hypersensitivity to precedex.
- Regional anesthesia.
- Heart and vascular disease.

Procedure

Clinical assessments and investigations excluded contra-indications. A comprehensive preoperative examination included measurements, vital signs, and various laboratory tests. In the operating theater, cases were observed by the SPI, ABP, heartbeat oximeter, and ECG. General anesthesia induction involved the inhalation of sevoflurane and oxygen, followed by intravenous cannula insertion. Patients were randomly assigned to either the dexmedetomidine group (0.5 μg/kg/hr infusion) or the control group (lactated Ringer solution). Anesthesia maintenance included

isoflurane, oxygen, and atracurium infusion. Intraoperatively, interventions addressed bradycardia, hypotension, tachycardia, and hypertension. Post-surgery, paracetamol (15 mg/kg IV) was administered, and patients were assessed for the quality of analgesia using the FLACC scale at specific intervals. Rescue analgesia with diclofenac sodium (1 mg/kg rectally) was provided if the FLACC scale exceeded 4. Nurses were instructed to administer oral paracetamol (30 mg/kg) based on pain evaluation, and data collectors recorded information. Sedation depth was evaluated using the Ramsy sedation score. PACU discharge utilized The Modified Aldrete Score, with adverse events, such as decreased heartbeat below 80 beat/minute for infant and below 70 beat/minute for older children, decreased blood pressure, imprudent sedation, breathing depression, postsurgical anxiety, nausea and vomiting observed for 24 hours. Data on SPI, heart rate (HR), and mean arterial blood pressure (MABP) were recorded at key points, including pre-induction, intubation, the beginning and end of the operation, PACU discharge, and 24 hours postoperative, and compared between the dexmedetomidine and control groups.

Sample Size

Computation was finished using IBM SPSS category 29 for Windows. A whole of 45 children per group are required to be capable of catching an anticipated change in the surgical pleth index depending on previous study [18]. This sample size was calculated using a power of 80% and alpha of 0.05.

Statistical Analysis

Descriptive statistics for the changeable were introduced in the form of mean with standard deviation or median with interquartile range for numerical chargeables, while frequencies and percentages were used for categorical chargeables. Differentiation between the two categories was done after put to the test for ordinariness of the distribution using Shapiro-wilk test. The statistical analysis was finished using the independent samples t test or using the non-parametric Mann Whitney test for numerical changeable. Categorical changeable were compared using Chi Square test or Fisher's exact test. IBM SPSS version 28 for Windows software was used for the analysis. A p-value of < 0.05 was reflected to be statistically remarkable.

Results

There was no statistically significant difference between both groups regarding characteristics (Table 1). SPI in all timepoints was significantly lower in dexmedetomidine group compared to control group, (P<0.001) (Table 1).

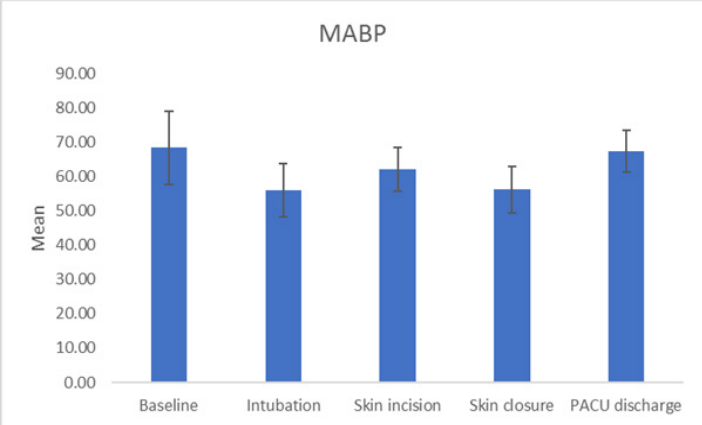
HR at baseline, after intubation, skin incision and at PACU discharge was significantly lower in dexmedetomidine group compared to control group, (P<0.05) (Table 2).

MABP: Initial mean arterial blood pressure, PACU: post-anesthesia care unit MABP in all time points was not significantly different in both groups (SF Figure 1). Anesthesia time and extubation time were significantly higher in dexmedetomidine group compared to control group, (P<0.001) (Table 2).

Table 1: Comparison of SPI and Characteristics between the two groups.

SPI		Mean ± SD	P value
Baseline	Control Dexmedetomidine	151.93 ± 28.42 80.38 ± 43.71	**<0.001***
Intubation	Control Dexmedetomidine	88.6 ± 32.67 50.09 ± 38.91	**<0.001***
Skin incision	Control Dexmedetomidine	81 ± 32.61 57.6 ± 32.38	**<0.001***
Skin closure	Control Dexmedetomidine	83.73 ± 21.05 60.87 ± 25.2	**<0.001***
PACU discharge	Control Dexmedetomidine	140.33 ± 26.01 70.67 ± 24.88	**<0.001***
Age	Control Dexmedetomidine	5.31 ± 1.61 5.31 ± 1.61	>0.999
Weight	Dexmedetomedine Control	18.22 ± 4.29 18.22 ± 4.29	>0.999
Height	Dexmedetomedine Control	90.27 ± 10.76 90.27 ± 10.76	>0.999

SPI: Surgical Pleth Index, PACU: post-anesthesia care unit



SF Figure 1: MABP of the studied patients in both groups.

Table 2: Comparison of HR, surgical time, anesthesia time and extubation time across both groups between the two groups.

HR		Mean ± SD	P value
Baseline	Control Dexmedetomidine	172.2 ± 13.96 152.22 ± 43.03	**0.005**
Intubation	Control Dexmedetomidine	151.31 ± 25.65 117.67 ± 31.94	**<0.001***
Skin incision	Control Dexmedetomidine	154.02 ± 13.18 146.24 ± 13.65	**0.007**
Skin closure	Control Dexmedetomidine	139.73 ± 20.68 138.91 ± 21.12	0.852
PACU discharge	Control Dexmedetomidine	156.31 ± 21.31 138.38 ± 20.18	**<0.001***
Surgical time	Control Dexmedetomidine	131.69 ± 5.46 131.69 ± 5.46	>0.999
Anesthesia time	Control Dexmedetomidine	131.69 ± 5.46 151.78 ± 10.01	**<0.001***
Extubation time	Control Dexmedetomidine	12.98 ± 4.25 34.56 ± 5.42	**<0.001***

HR: Heart rate, PACU: post-anesthesia care unit.

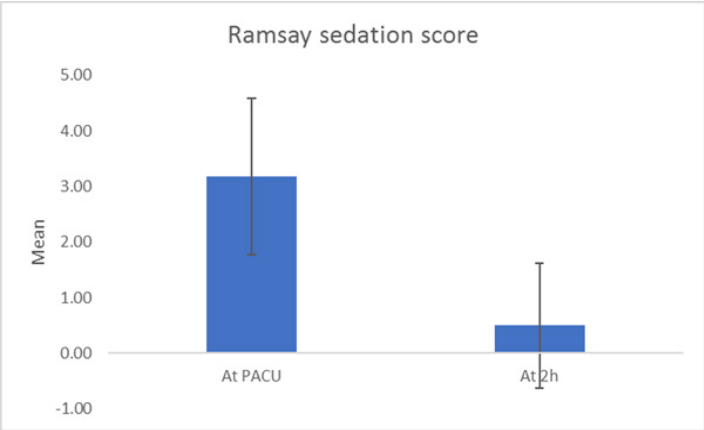
FLACC score in all timepoints was significantly lower in dexmedetomidine group compared to control group, (P<0.001) (Table 3).

Table 3: Comparison of FLACC score and drug consumption across both groups.

FLACC score		Mean ± SD	P value
At PACU	Control Dexmedetomidine	5.71 ± 1.38 3.04 ± 0.98	**<0.001***
At 2h	Control Dexmedetomidine	6.91 ± 1.28 4.42 ± 0.72	**<0.001***
At 4h	Control Dexmedetomidine	8.04 ± 1.26 5.07 ± 1.23	**<0.001***
At 6h	Control Dexmedetomidine	9.31 ± 0.73 7.42 ± 1.63	**<0.001***
At 24h postoperatively	Control Dexmedetomidine	10 ± 0 8.87 ± 1.12	**<0.001***
Fentanyl	Control Dexmedetomedine	24.78 ± 4.64 24.78 ± 4.64	>0.999
Paracetamol	Control Dexmedetomedine	38.44 ± 7.96 0 ± 0	**<0.001***

FLACC: Face, Legs, Activity, Cry and Consolability, PACU: post-anesthesia care unit.

RAMSAY sedation score at PACU and 24 hours of the operation was significantly higher in dexmedetomidine group compared to control group, (P<0.001) (SF Figure 2). Consumption of paracetamol was significantly lower in dexmedetomidine group compared to control group, (P<0.001) (Table 3). Incidence of decreased blood pressure and incidence of decreased heart rate were significantly higher in precedex group compared to control group, (P<0.001). (Table 4).



SF Figure 2: RAMSAY sedation score of the studied patients in both groups.

Comparison of Groups at Different Time Points

In all time intervals, mean SPI in Dexmedetomidine was lower than mean SPI in control group, (P<0.001).

Comparison of Time Points in Each Group

In control group, mean SPI after intubation, skin incision and skin closure was lower than mean SPI at baseline (P<0.001) and mean SPI at PACU discharge was higher than mean SPI after intubation, skin incision and skin closure (P<0.001).

Table 4: Comparison of need of vasoactive drugs, incidence of hypotension and bradycardia across both groups.

			Group		P value
			Control	Dexmedetomidine	
Need of vasoactive drugs	No	N	21	28	0.138
		%	46.7%	62.2%	
	Yes	N	24	17	
		%	53.3%	37.8%	
Incidence of hypotension	No	N	45	31	**<0.001***
		%	100.0%	68.9%	
	Yes	N	0	14	
		%	0.0%	31.1%	
Incidence of bradycardia	No	N	45	31	**<0.001***
		%	100.0%	68.9%	
	Yes	N	0	14	
		%	0.0%	31.1%	

In Dexmedetomidine group, mean SPI after intubation, skin incision and skin closure was lower than mean SPI at baseline (P<0.05) and mean SPI at skin closure and PACU discharge was higher than mean SPI after intubation (P= 0.036, P<0.001 respectively) (Figure 1).

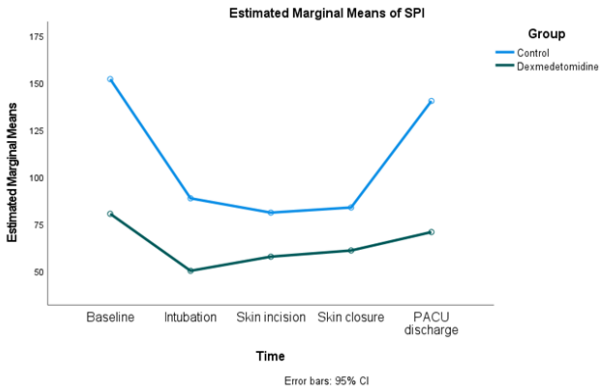


Figure 1: SPI of the studied patients at different time points in both groups.

Comparison of Groups at Different Time Points

At baseline, after intubation, skin incision and at PACU discharge, mean HR in Dexmedetomidine was lower than mean HR in control group, (P<0.05).

Comparison of Time Points in Each Group

In control group, mean HR after intubation, skin incision, skin closure and at PACU discharge was lower than mean HR at baseline (P<0.05), and mean HR after skin incision and at PACU discharge was higher than mean HR after skin closure (P= 0.001, 0.002 respectively). In Dexmedetomidine group, mean HR after intubation was lower than mean HR at baseline and after skin incision, skin closure and at PACU discharge (P<0.001) (Figure 2).

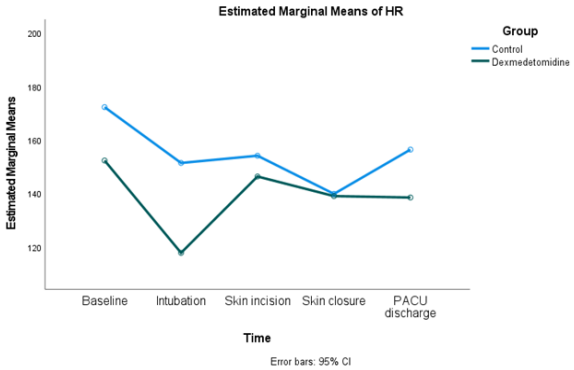


Figure 2: Heart rate of the studied patients in different time points in both groups.

Comparison of Groups at Different Time Points

After skin incision mean MABP in Dexmedetomidine was higher than mean MABP in control group, (P= 0.041).

Comparison of Time Points in Each Group

In control group, mean MABP after intubation, skin incision, and skin closure was lower than mean MABP at baseline (P<0.001), mean MABP after skin incision was higher than mean MABP after intubation (P= 0.009), and mean MABP at PACU discharge was higher than mean MABP after intubation, skin incision and skin closure (P<0.001). In Dexmedetomidine group, mean MABP after intubation and skin closure was lower than mean MABP at baseline (P<0.001), mean MABP skin incision was higher than mean MABP after intubation and skin closure (P<0.001), and mean MABP at PACU discharge was higher than mean MABP after intubation, skin incision and skin closure (P<0.001) (Figure 3).

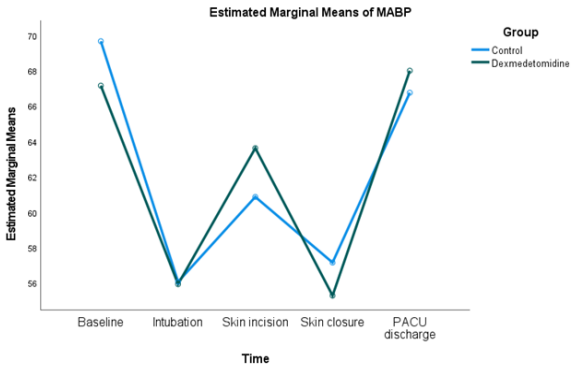


Figure 3: MABP of the studied patients at different time points in both groups.

Comparison of Groups at Different Time Points

In all time intervals mean FLACC score in Dexmedetomidine was lower than mean FLACC score in control group, (P<0.001).

Comparison of Time Points in Each Group

In control group, mean FLACC score after 2h, 4h, 6h and 24h of the operation was higher than mean FLACC score at PACU (P<0.001), mean FLACC score after 4h of the operation was higher than mean FLACC score after 2h of the operation (P<0.001), mean FLACC score after 6h of the operation was higher than mean FLACC score after 2h and 4h post operation (P<0.001), and mean FLACC score after 24h of the operation was higher than mean FLACC score after 2h, 4h, 6h and 24h of the operation (P<0.005). In Dexmedetomidine group, mean FLACC score after 2h, 4h, 6h and 24h of the operation was higher than mean FLACC score at PACU (P<0.001), mean FLACC score after 4h of the operation was higher than mean FLACC score after 2h of the operation (P= 0.008), mean FLACC score after 6h of the operation was higher than mean FLACC score after 2h and 4h post operation (P<0.001), and mean FLACC score after 24h of the operation was higher than mean FLACC score after 2h, 4h and 6h of the operation (P<0.001) (Figure 4).

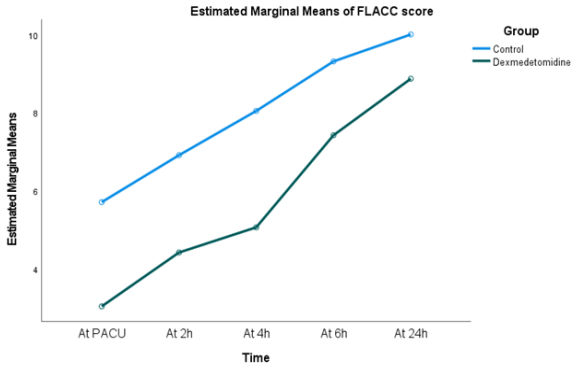


Figure 4: FLACC score of the studied patients at different time points in both groups.

Discussion

The study involved pediatric patients aged 2 to 7 years undergoing a surgical procedure, with key measurements including age, weight, height, and various physiological parameters. Parameters such as SPI, HR, SBP, and MABP were highest at baseline and lowest after intubation. Surgical and anesthesia times, as well as extubating time, were also recorded. Ramsay sedation scores, medication usage, and parental satisfaction were assessed. Dexmedetomidine group showed lower consumption of paracetamol, lower SPI, HR, SBP, DBP, and FLACC scores, but higher incidence of hypotension and bradycardia compared to the control group. Dexmedetomidine group had higher anesthesia and extubating times. The study found statistically significant differences between the groups for various parameters. DBP had the greatest value upon PACU discharge, while SPI, HR, SBP, and MABP had the highest values at baseline and the lowest values following intubation. SPI was much lower in the dexmedetomidine group at all time intervals than in the control group (P<0.001).

Many anesthesiologists continue to have concerns about postoperative pain management, especially with regard to early postoperative pain [19,20]. Dexmedetomidine is known to lower blood pressure and heart rate by stimulating α- 2 inhibitory neurons in the medullary vasomotor center and raising central vagal tone [21]. Opioids are necessary during surgery, but because of their negative side effects which include nausea from opioids,

respiratory depression, and a delayed recovery from general anesthesia it is now crucial to minimize opioid use [22,23]. Patients recover more quickly after surgery when fewer narcotics are used. The benefits of postoperative analgesia are enhanced by intraoperative dexmedetomidine [24,25]. Dexmedetomidine lowers the stress response and keeps the cardiovascular system stable [15]. Dexmedetomidine has been demonstrated in several trials to have opioid-sparing qualities [26,27], enhance pain relief, and reduce analgesic-related adverse effects [28,29].

WANG et al. [17] findings align with our measures. The dexmedetomidine group showed lower SPI values at intubation and PACU discharge, indicating improved nociception control. Hemodynamic parameters, such as lower mean BP and HR at critical points, suggest reduced stress response. NRS pain scores were also lower in the dexmedetomidine group at PACU discharge, supporting our study's conclusion of improved pain control during hypospadias surgery in pediatric patients. Al-Zaben et al. [30] study strongly supports our results, demonstrating that dexmedetomidine significantly reduces intraoperative fentanyl needs, lowers sevoflurane concentrations, and prolongs extubating time. Similar to our findings, their study reveals decreased postoperative morphine requirements, extended PACU analgesic duration, and fewer patients requiring morphine. Al-Zaben et al. [30] also reports lower postoperative pain and behavior scores, along with reduced heart rate and mean blood pressure, aligning with our observed outcomes. This underscores the reliability of our findings, emphasizing the consistent positive impact of dexmedetomidine on postoperative analgesia and recovery in pediatric surgery.

Limitations

While our study provides valuable insights into the impact of precedex infusion on the SPI in pediatric cases undergoing hypospadias surgery, it is essential to acknowledge certain limitations. Firstly, the single-center nature of the study at Fayoum University Hospital may limit the generalizability of our findings to a broader population. Additionally, the incidence of decreased blood pressure and decreased heart rate in the precedex group, though effectively managed, raises concerns about the safety profile of this intervention. Furthermore, the study primarily focuses on short-term outcomes, and the long-term effects of dexmedetomidine infusion in this specific population remain an area for future exploration. Lastly, the observational design, while suitable for assessing immediate outcomes, may not establish causation conclusively.

Strengths

Notwithstanding these limitations, our study exhibits several strengths. The comprehensive assessment of multiple parameters, including SPI, hemodynamic variables, pain scores, and recovery metrics, contributes to a holistic understanding of the intervention's effects. The use of ClinicalTrials.gov registration (NCT05727969) ensures transparency and accessibility of our trial information. The large sample size, calculated based on a robust power analysis, strengthens the statistical power of our results, increasing the reliability of the observed differences between groups.

In considering the clinical implications of our study, it is essential to underscore the potential benefits of improved pain control and favorable hemodynamic outcomes associated with dexmedetomidine infusion in pediatric patients undergoing hypospadias repair. The observed reduction in reliance on opioids aligns with the current imperative to minimize opioid use due to its adverse effects, such as postoperative nausea, respiratory depression, and delayed recovery from general anesthesia. Furthermore, the enhanced recovery seen in our study, as reflected by shortened anesthesia and extubation times, holds promise for optimizing perioperative care and expediting the postoperative rehabilitation of these young patients. While the study acknowledges the incidence of hypotension and bradycardia in the dexmedetomidine group, it is crucial to highlight that these events were effectively managed, emphasizing the importance of vigilant monitoring and appropriate interventions. Despite the short-term focus of our investigation, the potential long-term benefits of dexmedetomidine infusion in terms of postoperative pain management and recovery warrant further exploration in future research. This study lays a foundation for future investigations to delve into the nuanced aspects of dexmedetomidine's role in pediatric surgery and contributes valuable insights to the ongoing discourse on optimizing anesthesia and analgesia in this vulnerable population.

Conclusion

In conclusion, our study sheds light on the intricate relationship between dexmedetomidine infusion and SPI in pediatric patients undergoing hypospadias repair. Despite the acknowledged limitations, our findings suggest that dexmedetomidine, without a bolus dose, is associated with improved pain control, as reflected by lower SPI values and favorable hemodynamic outcomes. The observed benefits in terms of reduced reliance on opioids and enhanced recovery align with existing literature, emphasizing the potential role of dexmedetomidine in optimizing perioperative care.

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