Section: Anaesthesiology

Original Research Article

ANALYSING THE STRESS RESPONSE DURING PEDIATRIC CARDIAC SURGERY: A COMPARISON OF CAUDAL FENTANYL AND CAUDAL DEXMEDETOMIDINE

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Abstract

Background: Paediatric patients who undergo open-heart procedures on cardiopulmonary bypass experience a sharp increase in inflammatory response. In our study, we hypothesised that dexmedetomidine, as an adjuvant in the caudal direction, modulates the stress response after open heart surgery. **Materials and Methods:** In a prospective, randomised, double-blind study, 25 of 50 patients were administered either a single dose of caudal dexmedetomidine (1mcg/kg dexmedetomidine + 0.25% bupivacaine) or a single dose of caudal fentanyl (1mcg/kg fentanyl + 0.25% bupivacaine) with a total volume of 1.5 ml/ kg. To assess the inflammatory response, serum cortisol and blood glucose levels were measured before sternotomy (baseline), during sternotomy, and after the procedure. The haemodynamic variables, HR and BP, were periodically recorded, and the FACES pain score and extubation time were monitored in the PACU. **Result:** A comparison of demographic variables such as age, weight, aortic cross-clamp time, CPB (Cardiopulmonary bypass) time, and duration of surgery were statistically insignificant. The dexmedetomidine group showed significantly reduced serum cortisol and blood glucose levels than the caudal fentanyl group. The haemodynamic response, postoperative analgesia, and extubation time were significantly better in the caudal dexmedetomidine group. Extubation time was shorter in the BD group than in the BF group. Early extubation decreases ventilator-associated complications during the postoperative period and the length of ICU stay. **Conclusion:** Using caudal dexmedetomidine could decrease the stress response to surgical stimuli and give superior postoperative analgesia and expedited extubation, shortening ICU (Intensive care unit) stays.

INTRODUCTION

Cardiopulmonary bypass frequently results in a stress hormonal response, increased cortisol and leptin release and decreased insulin production. During open heart surgery, a systemic inflammatory response may lead to organ malfunction and hyperdynamic circulatory instability.[1] Compared to adults, children exhibit a more pronounced stress response, which increases postoperative morbidity and lengthens hospital stays. It has been demonstrated that caudal epidural anaesthesia with additives inhibits the surgical stress response and influences the postoperative prognosis.[2] It is also an excellent strategy for the postoperative pain management of children after open heart surgery.[3] Including various adjuvants such as dexmedetomidine and fentanyl, the duration of action of the single-shot caudal anaesthesia can be prolonged.[4]

Adjuvants in regional anaesthesia have been successfully used with alpha 2-adrenoreceptor agonists. Dexmedetomidine has a high ratio of α 2/α 1 activity (1620:1 compared to 220:1 for clonidine), making it a highly specific and selective alpha-2 adrenoreceptor agonist.[5] Dexmedetomidine acts specifically on the CNS without causing undesirable cardiovascular side effects via activating receptors.[6] In this study, the effectiveness of fentanyl or single-shot caudal dexmedetomidine added to 0.25% bupivacaine to reduce postoperative pain and the stress response in pediatric patients after open heart surgery is compared. The primary objective was to assess stress hormone levels, and the secondary objective was to assess postoperative pain scores and early extubation.

Aim

This study aimed to evaluate the effects of caudal dexmedetomidine on stress response and

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postoperative analgesia in paediatric heart surgery patients.

MATERIALS AND METHODS

This was a prospective randomised controlled study with observer blinding conducted in the paediatric cardiothoracic surgery unit of the Institute of Child Health and Hospital for Children, Madras Medical College, between April and July 2019. This study was conducted after receiving written approval from the ethics committee of my institution and parental (or guardian) consent.

Inclusion Criteria

This study included 50 RACHS (risk adjustment for congenital heart surgery) category I paediatric patients aged 2–10 years who underwent elective surgical correction for atrial septal defect (ASD).

Exclusion Criteria

This study excluded patients with RACHS category II and above and those scheduled for emergency surgery. Children with altered sacral and caudal anatomy and those with local infection at the block site.

Patients were divided into two distinct groups. 1) Patients who were administered with bupivacaine 0.25% & dexmedetomidine 1mcg/kg (group BD) and 2) with bupivacaine 0.25% &fentanyl 1mcg/kg (group BF).

Six hours of fasting was advised before surgery. Age, weight, heart rate, non-invasive blood pressure (NIBP), and arterial oxygen saturation (SPO2) at baseline were recorded. The required sizes of the oropharyngeal airway, bougie, and endotracheal (ET) tubes were accessible. Under strict aseptic conditions, syringes containing the volume to be administered in the caudal block were prepared. After 20G or 22G cannula insertion, general anaesthesia was induced with midazolam 0.1 mg/kg, fentanyl (10 µg/kg), and thiopentone (5 mg/kg). Followed (0.1 mg/kg of vecuronium was administered to aid endotracheal intubation with an appropriate-sized ET tube.

Patients were positioned laterally in both groups, and the caudal block was accomplished using a 23 G bevelled short needle under sterile conditions. After the caudal block, a central venous catheter and an arterial catheter were inserted. All patients underwent a median sternotomy. Heparin 3 – 4 mg/kg was administered at least 60 min after caudal block. On cardiopulmonary bypass, to maintain perfusion pressure in the 50 – 60 mmHg range at 26 – 34 °C, the estimated flow rate was BSA x [2.4-3.2] L/min after bicaval venous cannulation. During rewarming, haemofiltration (CUFF and MUFF) is performed as a protocol, along with starting milrinone at 0.375 µg/kg/min as an early postoperative therapy while weaning from bypass.

Serum cortisol and blood glucose levels were measured immediately after induction (baseline), sternotomy, and surgery. Serum cortisol levels were measured using the eCLIA (electrochemiluminescence immunoassay Technique) method. The Hexokinase technique determines the glucose concentration in the serum. Before induction [baseline], 10 minutes after caudal injection, 10 minutes after sternotomy, after cardiopulmonary bypass, and upon PACU (post-anaesthesia care unit) entry and extubation, heart rate, systolic, diastolic, and mean blood pressure were measured.

Standard monitoring (heart rate, invasive blood pressure (IBP), central venous pressure (CVP), SPO2, end-tidal CO2 (ETCO2), and temperature) was used to monitor patients. A failed caudal block was defined as an increase in heart rate and mean arterial pressure after skin incision and sternotomy compared with baseline readings. A patient with a suspected unsuccessful block was administered 10 µg of intravenous fentanyl and excluded from the study. After the procedure, the patients were sent to the PACU. Haemodynamics were monitored, and the weaning process began. Patients who met the criteria for extubation were extubated, and the heart rate, mean arterial pressure (MAP), and SPO2 were measured in both groups. Using the paediatric FACES pain scale score ranging from 0 to 5, the postoperative pain score was measured upon arrival and every half-hour for 6 hours. Suppose that the pain score exceeds two at any time. Rescue analgesia with IV paracetamol (15 mg/kg) or IV fentanyl 0.5mcg/kg was administered, and the time necessary for rescue analgesia was recorded in both groups.

Statistical Analysis

The unpaired t-test was used to compare the dexmedetomidine and fentanyl groups. ANOVA was used to compare the intervention groups' mean serum cortisol and glucose values.

RESULTS

A comparison of demographic variables such as age, weight, aortic cross-clamp time, CPB (Cardiopulmonary bypass) time, and duration of surgery was given in [Table 1], and those were not statistically significant. After sternotomy and after surgery, the mean serum cortisol [Table 2] and blood glucose [Table 2] values of the dexmedetomidine group patients were measured, and they were found to be lower than those of the fentanyl group and considered to be statistically significant because the p-value was < 0.05. The baseline values did not show statistically significant differences between the two groups. Similarly, the heart rate and arterial pressure recorded in periodic intervals in the caudal dexmedetomidine group were lower than those in the caudal fentanyl group. They were found to be statistically significant ($p < 0.05$), except for the baseline variables [Table 3]. FACES pain scores for analgesia [Table 4] were also analysed and compared between the two groups, and pain scores were found to be lower in the dexmedetomidine group than in the

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fentanyl group. The graphs represent variances in the groups' serum cortisol, blood glucose, and FACES pain scores [Figure 1].

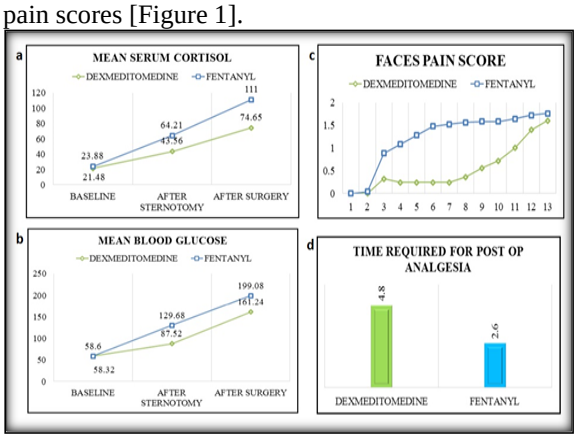

Figure 1: Comparison of serum cortisol, blood glucose, face pain score, and time to postoperative rescue analgesia between the two groups.

In the dexmedetomidine group, the mean time required for postoperative rescue analgesia was approximately 4.8 hours, with a standard deviation of 1.12 hours. In the fentanyl group of patients, the mean time duration required for the postoperative rescue analgesia is around 2.6 hours, with a standard deviation of 0.91 hours. The time duration required for postoperative rescue analgesia was compared between the dexmedetomidine and fentanyl groups, which was higher than the dexmedetomidine group and considered to be statistically significant because the p-value was <0.05 [Table 5]. Extubation time was shorter in the BD group than in the BF group. Early extubation decreases ventilator-associated complications during the postoperative period and the length of ICU stay.

Table 1: Comparison of demographic variables between two groups

Variable	Group BD (n=25)	Group BF (n=25)
Weight (kg)	11.5 ± 3.3	12.5 ± 2.1
Age (months)	23.6 ± 11.4	26.2 ± 7.8
Duration of aortic cross-clamp (min)	26 ± 4.1	25.2 ± 5.6
Duration of CPB (min)	46.2 ± 5.8	4.7 ± 5.2
Duration of surgery (min)	168.5 ± 14	170.2 ± 17

Table 2: Comparison of serum cortisol levels (µg /dl) between the two groups.

Bupivacaine with Serum cortisol (µg /dl)	Dexmedetomidine	Fentanyl	P value
Baseline	21.48 ± 2.73	23.88 ± 3.19	0.124
After Sternotomy	43.56 ± 4.7	64.21 ± 9.6	0.001
After Surgery	74.65 ± 5.7	111 ± 14.46	0.002
Blood Glucose (mg/dl)			
Baseline	58.32 ± 5.06	58.6 ± 5.13	0.847
After Sternotomy	87.52 ± 6.93	129.68 ± 11.6	0.001
After Surgery	161.24 ± 8.65	199.08 ± 18.51	0.002

Table 3: Comparison of haemodynamic variables between the two groups.

Bupivacaine with	Dexmedetomidine		Fentanyl		P Value	
	HR	MAP	HR	MAP	HR	MAP
Baseline	105	79	105	75	0.834	0.08
10 Min after caudal	89	65	99	70	0.001	0.001
10 Min after sternotomy	92	68	106	75	0.001	0.001
After the termination of CPB	98	72	105	77	0.016	0.001
On PACU admission	95	68	107	79	0.001	0.001
At extubation	106	72	115	82	0.001	0.001

HR-heart rate; MAP-mean arterial pressure; CPB- Cardiopulmonary bypass; PACU- post-anaesthesia care unit

Table 4: Analgesia – Faces Pain Score

Bupivacaine with	FACE Pain Score - Mean												
	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6
Dexmedetomidine	0	0	0.32	0.24	0.24	0.24	0.24	0.36	0.56	0.72	1	1.4	1.6
Fentanyl	0	0.04	0.88	1.08	1.28	1.48	1.52	1.56	1.58	1.58	1.64	1.72	1.76
P value	0	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.033	0.046	0.056

Table 5: Postoperative rescue analgesia in hours

Bupivacaine with	Mean	SD	P value
Dexmedetomidine	4.8	1.12	0.001
Fentanyl	2.6	0.91	

DISCUSSION

The term "stress response" refers to a variety of metabolic, endocrine, and immunological issues that result in extended hospitalisation following major surgery. Owing to this systemic response, several postoperative problems, including respiratory and coagulation issues, wound infection, cardiac and

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neurologic dysfunction, changes in liver and kidney function, and an increase in mortality, are possible.[1] Complex interconnected pathways produce inflammatory responses, including the production or activation of cytokines, complement, neutrophils, mast cells, thrombin, and other implicated inflammatory mediators.6 Dexmedetomidine could exert anti-inflammatory effects by stimulating the vagus nerve and cholinergic anti-inflammatory pathways. As a sympatholytic anaesthetic adjuvant, dexmedetomidine stabilises hemodynamic fluctuations throughout surgery and recovery, alters stress-induced sympatho-adrenal intubation reactions, and reveals a better outcome.[2]

As inferred from our study results, caudal dexmedetomidine (BD) in children with ASD undergoing open-heart surgery with CPB showed a statistically significant reduction in stress response and postoperative analgesia when compared to caudal fentanyl (BF). In our study, the serum cortisol level was lower in the caudal dexmedetomidine (BD) group than in the caudal fentanyl (BF) group. Many studies have supported these findings. Mukhtar et al,[7] showed lower cortisol levels in paediatric surgery patients receiving intravenous dexmedetomidine. Aho et al,[8] showed lower cortisol levels with intramuscular dexmedetomidine in laparoscopic GYN surgery. Caudal dexmedetomidine has a better α2 analgesic effect, but dexmedetomidine, an imidazole, inhibits cortisol synthesis when given via IM, IV (or) caudal route.[6] Blood glucose levels were lower in the caudal dexmedetomidine group (BD) than in the caudal fentanyl (BF). These findings are consistent with Mukhtar et al.[7] Generally, α2 adreno receptors inhibit insulin release and cause hyperglycemia; lower blood glucose levels observed were attributed to attenuation of sympathoadrenal response.[1]

The HR and MAP were lower in the BD group than in the BF group. These findings are consistent with Mukhtar et al. and Hosokawa et al., who reported that caudal dexmedetomidine did not produce profound bradycardia (or) hypotension compared to intravenous administration.[7-9]

Postoperative analgesia, assessed with FACES pain score, showed that the dexmedetomidine group was better when compared with caudal fentanyl, and these findings were supported by Saadawy et al.[10] Requirement of postoperative rescue analgesia was at 5 hours in dexmedetomidine group compared to 2.5 hours with fentanyl group. Extubation time was short in the dexmedetomidine group, as it gives adequate pain relief without respiratory depression.[5]

CONCLUSION

Children undergoing cardiac surgery experience a substantial postoperative oxidative stress response, which exacerbates postoperative morbidity. Caudal dexmedetomidine could decrease the stress response to surgical stimuli, provide superior postoperative analgesia, and expedite extubation, thereby shortening ICU stay.

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