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Research Article

Dexmedetomidine; an adjuvant drug for fast track technique in pediatric cardiac surgery

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KEYWORDS

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Abstract *Background:* Simple surgical procedures in pediatric open cardiac surgery can be planned for early extubation by using dexmedetomidine alpha2 agonist. Early extubation is associated with shortening of postoperative ventilation and intensive care unit length of stay. The aim of this study was to examine the effects of dexmedetomidine on recovery profile, ICU length of stay, analgesic needs, and hospital stay in pediatric patients undergoing elective correction of congenital heart diseases using CPB.

Methods: Forty patients with age ranging from 2–10 years of either sex submitted for elective correction of simple congenital heart diseases undergoing CPB. All patients were premedicated in preoperative area with intramuscular 0.1 mg/kg midazolam and 0.015 mg/kg atropine sulfate. Patients were randomly classified into one of two equal groups ($n = 20$). In the Dex group, patients received an initial bolus dose of dexmedetomidine (0.4 μg/kg) over 10 min, followed by continuous infusion of 0.5 μg/kg/hr. In the control group, patients received an initial bolus dose of saline over 10 min, followed by continuous infusion of 0.5 μg/kg/hr.

Results: MAP, HR, the total dose of intra-operative fentanyl, vasodilator needs, time of extubation, pain score, ICU length of stay and hospital stay were significantly higher in the control group when compared with DEX group. Also in control group these were significant decrease in HR and MAP relative to baseline. There was significant increase in duration of inotropic support in control group than DEX group.

Conclusion: Dexmedetomidine is a short-acting alpha2-adrenoceptor agonist with many desirable clinical benefits that encourage its use in the perioperative period. Dexmedetomidine has anesthesia-sparing effects, it decreases MAP, HR and with reasonable analgesic effect.

1. Introduction

Fast tracking in cardiac surgery refers to the concept of early extubation, mobilization and hospital discharge in an effort to reduce costs and perioperative morbidity [1].

Early extubation after pediatric open cardiac surgery is still not common practice. Several more recent studies describing

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early extubation in children have included only simple repairs such as atrial septal defects procedures not requiring CPB, and relatively low risk patients, very early extubation refers to planned extubation either in the operating room or immediately upon arrival in the intensive care unit [2].

Shortening of both postoperative ventilation and intensive care unit (ICU) length of stay are important goals to avoid complications related to mechanical ventilation, to improve patient outcome, and to reduce costs of ICU treatment [3].

Dexmedetomidine is a highly specific, selective alpha2 adrenoceptor agonist [4]. It has activity at the imidazoline receptors involved in central blood pressure control also causes reduction in sympathetic nervous system activity [5]. With dexmedetomidine, there are a number of reasons for the growing and renewed interest in the use of alpha2-adrenoceptors agonists as sedatives: dexmedetomidine compared to clonidine is a much more selective alpha2-adrenoceptor agonist. In addition, dexmedetomidine is shorter-acting drug than clonidine and has a reversal drug for its sedative effect, Atipamezole. These properties render dexmedetomidine suitable for sedation and analgesia during the whole perioperative period [6].

To our knowledge it is the first study to examine the effects of dexmedetomidine on recovery profile, ICU length of stay and hospital stay in pediatric patients undergoing corrective surgery for congenital heart diseases using CPB.

2. Patients and methods

After approval of the local ethics committee of Anesthesia and Surgical Intensive Care Department, Faculty of Medicine, Mansoura University Children Hospital and obtained written informed consent from the parents of all patients, 40 patients with age ranging from 2 to 10 years of either sex submitted for elective correction of simple congenital heart diseases undergoing CPB at Mansoura University children hospital. From January 2012 to August 2012 patients of redo open heart surgery, endocarditis, neurological diseases, renal diseases, hepatic diseases, pulmonary diseases, heart failure and moderate to severe pulmonary hypertension and previous adverse reaction to any of the study medication were excluded from the study. All patients were premedicated in preoperative area with intramuscular 0.1 mg/kg midazolam and 0.015 mg/kg atropine sulfate before induction of general anesthesia. ECG, peripheral oxygen saturation and noninvasive blood pressure were monitored. Supplemental O_2 was provided via a face mask.

In both groups anesthesia was induced by inhalation of sevoflurane carried by oxygen, with loss of consciousness a peripheral intravenous indwelling cannula was inserted, then fentanyl (3–5 μg/kg) was given, tracheal intubation and neuromuscular blockade were facilitated by rocuronium 0.9 mg/kg, positive pressure ventilation was applied via face mask at a rate of 20–28 breath per minute. Patients were mechanically ventilated with 50% O_2 in air and the end tidal CO_2 was monitored by side-stream capnogragh and maintained between 30 and 35 mmHg, then central venous and an arterial catheter were inserted and entropy module was attached to the patient's forehead. Anesthesia was maintained with sevoflurane titrated to keep the entropy value around 50, increment doses of fentanyl were given to maintain heart rate and blood pressure within 20% of the basal value with maximum total dose of 10 μ/kg and constant infusion of esmeron (0.3 mg/kg/hr) to maintain muscle relaxation. Neuromuscular blockade was reversed at the end of surgery if the patient was valuable for extubation. All patients received ringer's acetate solution 4 ml/kg/hr for first 10 kg, 2 ml/kg/hr for next 10 kg, 1 ml/kg/hr for each kg. Patients were randomly classified into one of two equal groups ($n = 20$). In the Dex group, patients received an initial bolus dose of dexmedetomidine (0.4 μg/kg) over 10 min immediately after induction, followed by continuous infusion of 0.5 μg/kg/hr. All over the operation and was discontinued at the end of CPB. A similar volume of normal saline was given in the control group.

Hemodynamic variables HR and MAP were recorded at baseline, after induction, after skin incision, post sternotomy, 20 min post CPB and after closure of sternum.

Operative parameters as total dose of fentanyl, aortic cross clamping time (min), CPB time, duration of surgery (min), needs of DC shocks, duration of inotropic support and total dose of vasodilator needs were recorded in all patients.

ICU parameters as time of extubation, pain score by objective pain discomfort score (blood pressure, crying, moving, agitation, verbal), ICU length of stay, and hospital length of stay.

In all patients, the heart was approached through a standard median sternotomy. The ascending aorta, SVC and IVC were cannulated for cardiopulmonary bypass (Stockert instrument, Germany) using a membrane oxygenator and a nonpulsatile roller pump flow with average rate around 100–150 ml/kg/min. with an arterial filter after elevation of the ACT above 480 s using heparin (300–400 i.u/kg). Moderate hypothermia (32 °c) was allowed, after aortic cross clamping, all patients received custodial cardioplegia (50 ml/kg). Hematocrit was maintained between 20% and 25% during CPB, with addition of blood as necessary and anesthesia was maintained by propofol infusion 100–150 μg/kg/min after adding of 3 mg/kg to CPB prime. Nitroglycerin infusion was initiated during the rewarming period, to keep MAP around 50 mmHg.

2.1. Sample size calculation

Sample size was done, based on extubation time. We expect to have a difference of 1.5 between the two groups. Using the t test for comparison and setting alpha to 0.05, we need minimally 21 cases in each arm to detect a similar difference with 80% power. We increase the sample to 30 cases in each arm. Calculations were done using medcalc software Windows.

Data were first tested for normality by Klomogorov–Smirnov test. Normally distributed continuous data were analyzed by using student *t*-test. Non-normally distributed continuous and ordinal data were analyzed using Mann-Whitey U test. Categorical data were analyzed by Chi-square or Fisher's exact test as appropriate. The results are presented as mean (SD), median (interquartile range), or number of patients as appropriate. A P value < 0.05 was considered statistically significant. Statistical analyses were performed using the SPSS for Windows, version 18.

3. Results

Table 1 shows the patients characteristics of the studied groups, control group ($n = 20$), and DEX group ($n = 20$),

Table 1 Demographic data of the studied groups: control group (n = 30); DEX group (n = 30); data are in number, mean ± SD.

	Control group	DEX group	P value
Age (years)	4.75 ± 3.18	4.42 ± 3.09	0.49
Weight (kilogram)	18.6 ± 8.8	17.7 ± 8.2	0.63
Sex M/F	11/19	12/18	0.99
Surgical procedures			0.79
ASD repair	12	16	
VSD repair	18	14	

there were no significant difference between the two groups as regards, age, weight, height, M/F ratio and the type of surgical procedure.

In the present study, MAP and HR were significantly high in the control group when compared with DEX group post induction and throughout the surgery. Also HR and MAP were significantly high in control group relative to its baseline values (Figs. 1 and 2 respectively).

There was significant increase in total dose of intra-operative fentanyl, pain score, duration of inotropic support, vasodilator needs, time of extubation, ICU length of stay and hospital stay together with high readings of entropy values in control group than DEX group (Tables 2–4 and Fig. 3 respectively).

There was no significant difference between the two groups as regard aortic cross clamp time, CPB time, duration of surgery, need of DC shocks for defibrillation (Table 2).

4. Discussion

Dexmedetomidine is a selective α2-adrenoceptor agonist. Its action is different according to the site of receptors. Alpha2-adrenoceptors are found in peripheral and central nervous systems, in effector organs such as the liver, kidney, pancreas, eye vascular smooth muscles and platelets [7].

In the present study, we noted that patients who received dexmedetomidine showed significant decrease in HR, MAP, pain score, fentanyl requirements, entropy values, ICU length of stay and hospital stay when compared to control group.

A biphasic cardiovascular response has been described after the administration of dexmedetomidine. A bolus of 1 μg/kg results in a transient increase in blood pressure and a reflex decrease in heart rate. This initial response is attributed to the direct effects of alpha2 B-adrenoceptor stimulation of vascular smooth muscle. This response can be attenuated by a slow infusion over 10 min, but even at slower infusion rates, the transient increase in mean BP and the decrease in HR over the first 10 min are shown. This initial response is followed by a decrease in BP. Both these effects are presumably caused by an inhibition of central sympathetic outflow that overrides the direct effects of dexmedetomidine on the vasculature [8].

In our study there is a significant decrease in HR and MAP in dexmedetomidine group when compared to control group. The reduction in MAP may be attributed to decreasing sympathetic outflow and circulating catecholamines by dexmedetomidine [9]. Also dexmedetomidine has been associated with decrease in HR, in part because of sympatholytic effects of this drug, but also because of a vagal mimetic effect [10].

These effects match with monophasic effect of dexmedetomidine (low dose of 0.25–0.5 μg/kg resulted in a monophasic decrease in MAP) as we used a dose less than 1 μg/kg, which also explain the lower needs of vasodilators in DEX group than control group [11]. Our findings are supported by previous studies done by Talk, and Ebert who proved that the use of dexmedetomidine associate with biphasic effect of dexmedetomidine in large dose and monophasic effect in small dose [12,13].

Another important finding in this study is the significant reduction in the total dose of intraoperative fentanyl and pain score in DEX group relatively to control group, this is in accordance with Venn et al. that showed a reduction in opioids requirements of 50% in twenty adult ICU patients [14]. Also this was confirmed by Martin's study of 401 post-surgical patients [15].

It is known that dexmedetomidine decreases noradrenergic output from the locus cereleus allowing for increased firing of inhibitory neurons including GABA. Primary analgesic effects and potentiation of opioid-induced analgesia result from the

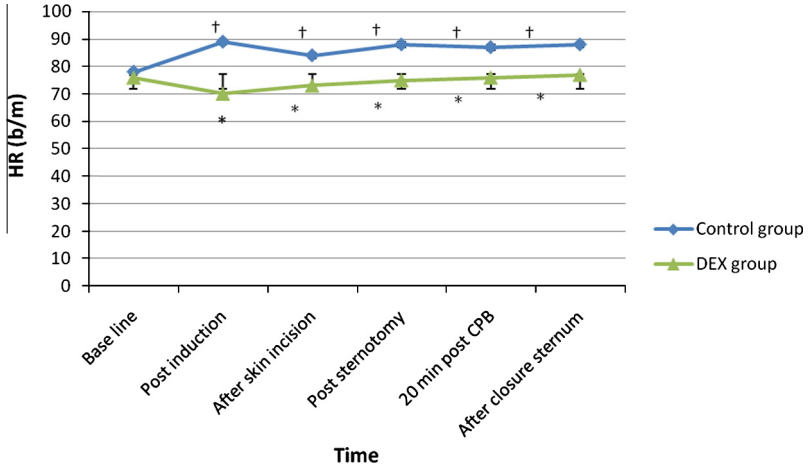

Figure 1 Heart rate (HR) changes, (beat/minute) in the studied groups. * $P < 0.001$significant when compared with the control group. † $P < 0.001$ significant when compared with the basal value.

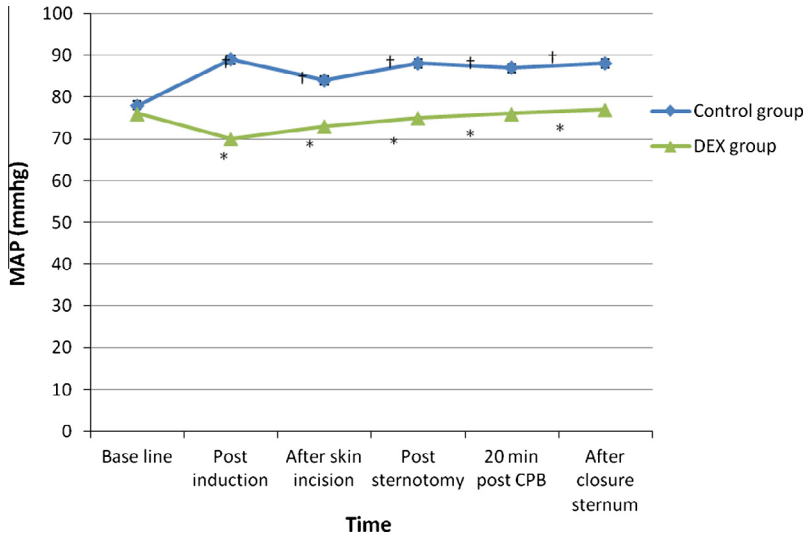

Figure 2 Mean arterial pressure changes (MAP), (mm Hg) in the studied groups. *** $P < 0.001$ significant when compared with the control group.

Table 2 Intraoperative data: (total dose of fentanyl (μg/kg), cardiopulmonary bypass time (min), aortic cross clamp time (min), duration of surgery (min), total dose of nitroglycerin (μg/kg/min)). Control group ($n = 30$); DEX group ($n = 30$); data are in number, mean ± SD.

	Control group	DEX group	*P* value
Total dose of fentanyl (μg)	160 ± 12	145 ± 9*	<0.001***
Aortic cross clamp time (min)	29.9 ± 9.1	28.7 ± 11.5	0.65
Cardiopulmonary bypass time (min)	46.2 ± 10.4	45.1 ± 12	0.73
Duration of surgery (min)	136.2 ± 15	134.1 ± 19	0.64
Need for DC shock	2	1	0.92
Duration of intropic support (hr)	13.1 ± 2.3	9.6 ± 1.59*	<0.001***
Total dose of nitroglycerine dose (μg)	185 ± 9	153 ± 8*	<0.001***

* P < 0.05 significant when compared with the basal value.
*** *P* < 0.001 significant when compared with the control group.

Table 3 Postoperative data: Extubation time (hr), ICU length of stay (hr), hospital length of stay (days). Control group ($n = 30$); DEX group ($n = 30$); data are in mean ± SD.

	Control group	DEX group	*P* value
Extubation time (hr)	5 ± 1.22	2.1 ± 0.8	<0.001***
ICU length of stay (hr)	34.3 ± 12.1	26.7 ± 7.8	<0.001***
Hospital length of stay (days)	6.1 ± 1.0	4.2 ± 0.8*	0.002**

* *P* < 0.05 significant when compared with the control group.

Table 4 Postoperative pain score control group ($n = 30$); DEX group ($n = 30$); data are in median and interquartile range.

	Control group median (IQR)	DEX group median (IQR)	*P* value
1 h (ICU)	5(2–7)	2(0–3)*	<0.001***
4 h (ICU)	4(3–5)	2(0–5)*	<0.001***
8 h (ICU)	4(3–5)	2(0–3)*	<0.001***
12 h (ICU)	4(3–5)	2(0–3)*	<0.001***

* *P* < 0.05 significant when compared with the control group.

activation of α2-adrenergic receptors in the dorsal horn of the spinal cord and the inhibition of substance P release [16].

In our study we noted that low entropy values and early extubation time that run in accordance with Easley et al.

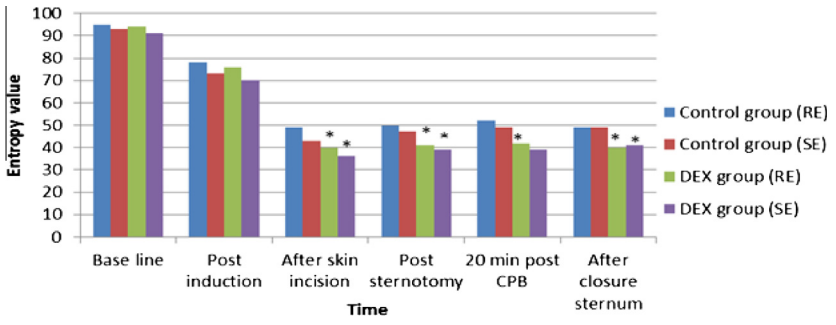

Figure 3 Entropy values of the studied groups. * $P < 0.05$ significant when compared with the control group.

who demonstrated earlier extubation in children following surgery for congenital heart diseases [17]. This Fact may be contributed to the anesthetic-sparing effect of dexmedetomidine. Aho, Khan and Fragen noted reduction in inhalational anesthetic requirements for maintenance of anesthesia. In addition, the use of dexmedetomidine produces intraoperative and postoperative opioid-sparing effect [18–20]. Early discharge from ICU and hospital is markedly increased in control group when compared to DEX group in our study. This may be attributed to low doses of anesthetic drugs that had been used, low total doses of fentanyl, more hemodynamic stability and early regain of consciousness.

5. Conclusions

In summary, dexmedetomidine is a short-acting alpha2-adrenoceptor agonist with many desirable clinical benefits that encourage its use in the perioperative period. Dexmedetomidine has anesthesia-sparing effects, it decreases MAP, HR and with reasonable analgesic effect.

Conflict of Interest

None.

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