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Dexmedetomidine versus propofol in reducing atrial fibrillation after cardiac surgery

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ABSTRACT

Objectives: Atrial fibrillation is a common complication associated with cardiac surgery after cardiopulmonary bypass with a deleterious effect on morbidity and mortality. The current study aimed to compare between dexmedetomidine and propofol in reducing atrial fibrillation after cardiac surgery.
Design: A randomized prospective cohort study.
Setting: Conducted in Alexandria main university hospital.
Participants: 98 patients of either sex ASA II physical status aged 40–60 years.
Interventions: All patients were subjected to either propofol or dexmedetomidine infusion after cardiac surgery according to the assigned group.
Measurements and Main Results: The patients were divided into two groups where first group received dexmedetomidine infusion as postoperative sedation and the second group received propofol infusion. Both groups were assessed for incidence of atrial fibrillation, hypotension and length of intensive care stay. Incidence with atrial fibrillation was 0.9% in dexmedetomidine group vs. 13% in propofol group (P = 0.001) and intensive care stay was prolonged in propofol group 4.6 ± 1.2 day vs. 2.7 ± 1 for dexmedetomidine group (P = 0.002). There was no statistically significant difference between both groups regarding blood pressure or heart rate.
Conclusion: The use of dexmedetomidine for sedation after cardiac surgery was associated with a lower incidence of atrial fibrillation and hence decreased the duration of intensive care stay.

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1. Introduction

Open heart surgery using cardiopulmonary bypass (CPB) is considered the main treatment for heart diseases like coronary artery disease, congenital and valvular heart disease. [1] The combination of CPB, ischemia reperfusion and surgical trauma elicit a strong systemic inflammatory response which is characterized by the release of inflammatory cytokines and activation of immune cells resulting in many postoperative organ injuries. [2] Recovery after surgery is frequently associated with atrial fibrillation and delirium. [3]

The primary goal of sedation in postoperative cardiac patients is to relieve anxiety, and minimize the pain from sternotomy, intercostal tubes, retrosternal tubes and leg wound [3], as well as to minimize the cardiac instability from sympathetic overdischarge [4].

Proper sedation and analgesia can decrease patient discomfort on mechanical ventilation, decrease the length of intensive care unit (ICU) [5] and hospital stay, and decrease the systemic inflammatory response and hence the overall susceptibility to the occurrence of atrial fibrillation [6].

Most patients need to experience a natural sleeping process to bear intubation and have a balanced physiological stress (tachycardia and hypertension). Inadequate sedation can increase morbidity and mortality, the risk of tachycardia and hypertension, pulmonary vascular resistance, and oxygen consumption. [7,8]

Atrial fibrillation is considered to be the most common cardiovascular problem after cardiac surgery with an incidence of 10–50% especially in patients undergoing valve surgery who are considered to be at a greater risk. [9,10]

Atrial fibrillation may result in hemodynamic instability [9,10], cognitive impairment [10], thromboembolic events, and congestive heart failure. [11] Also, it prolongs hospitalization leading to an increased cost on the patients, so prevention of postoperative atrial fibrillation would markedly decrease morbidity and mortality. [11,12]

Factors that contribute to increase risk of occurrence of arrhythmias include preexisting myocardial dysfunction, a complex operation associated with myocardial damage, [13] myocardial ischemia, postoperative electrolyte disturbance [14], and cardiopulmonary bypass related inflammatory response and catecholamine surge. [15]

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Dexmedetomidine a highly selective α adrenoceptor agonist has been recently introduced in anesthesia practice [16]. It is currently being used for continuous intravenous sedation in intensive care setting and procedural sedation in non-intubated patients [17]. It has analgesic, sympatholytic, anesthetic-sparing, and hemodynamic stabilizing properties, which have been used as an adjunct to local anesthetics for prolongation of their effect. [18]

Dexmedetomidine has several complex physiological effects on the heart. It has a direct dose dependent cardio-protective effect against reperfusion injury. [19] Also at high doses it has a subendocardial to subepicardial flow that would provide a good recovery from myocardial injury. [20] In addition, it has a sympatholytic effect that allows reduction in heart rate and consequently the myocardial oxygen demand. [21] Also, it has anti-inflammatory properties and decreases the use of opioids and benzodiazepines that contribute to the occurrence of postoperative delirium and hence provides sedation very similar to natural sleep. [22]

Propofol is a hypnotic and sedative drug, which is used for short- and long-term sedation therapy in mechanically ventilated patients. [23]It also has more superiority over benzodiazepines regarding ease of weaning, easier and faster recovery from sedative effect and hence helps rapid neurological assessment. [24]Nevertheless its prolonged use or large dose sedation affects the hemodynamics of the patient and limits its use. [25]

Recently, a number of prophylactic strategies have been used for prevention of postoperative atrial fibrillation but not very commonly used [26], may be because of lack of community evidence potential risk of some regimens or complexity of some regimens. [27]

The aim of the present study was to identify the incidence of postoperative atrial fibrillation while the secondary outcomes were the duration of mechanical ventilation, ICU stay and the hospital stay.

2. Methodology

All preoperative cardiac medications were continued till the day of surgery. Premedication was provided by midazolam 0.02 mg/kg and fentanyl 0.5 µg/kg to all patients 20 minutes before surgery.

A five lead ECG, non-invasive arterial blood pressure and pulse oximetry were applied to all patients in the operating room. After subcutaneous injection of 2 ml lidocaine 2%, a radial artery catheter was inserted for continuous blood pressure monitoring.

Anesthesia was induced by fentanyl 2–3 µg/kg and rocuronium bromide (0.6 mg/kg) to facilitate endotracheal intubation for all patients. It was maintained with sevoflurane and incremental doses of rocuronium bromide (0.1 mg /kg) during the whole duration of surgery.

A central venous catheter was inserted in the Rt internal jugular and esophageal temperature probe was inserted after tracheal intubation.

The same surgery team operated all the patients. The surgery took place under cardiac arrest with CPB. The surgical steps were standardized with medium sternotomy and pericardiotomy.

Unfractionated heparin was given 500 IU/kg to achieve activated clotting time (ACT) of more than 480 sec during CPB. CPB was started after aortic and venous cannulas were inserted.

Myocardial protection was established by intermitted blood cardioplegia repeated at interval of 30–45 min. Hematocrit value was maintained at 20–25% during CBP period and 27– 30% in the post bypass period.

The sevoflurane concentration, vasoactive drugs rates, e.g., noradrenaline and fluid replacement were adjusted to maintain optimal blood pressure (MAP 50–65 mmHg) during CBP. Mean arterial blood pressure (MAP) and arterial blood gas analysis were observed and recorded during surgery. At the end of CPB, protamine sulphate at a dose of 1 mg/kg for every 100 IU heparin was given to reverse the anticoagulation effect.

The aortic cross-clamping time, CPB duration, extubation and length of stay in ICU and hospital were recorded.

On arrival to the ICU, the patients were on mechanical ventilation, and were classified randomly into two groups:-

2.1. DEX group

Patients were subjected to dexmedetomidine infusion at a rate of 0.5 µg/kg.

2.2. Propofol group

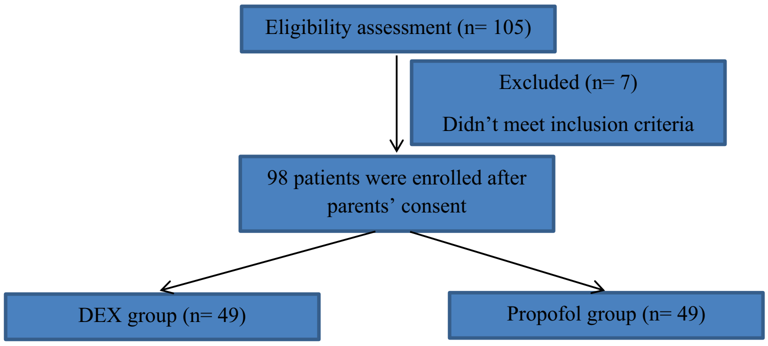
Patients were subjected to propofol infusion at a rate of 25 µg /kg/min.

All patients were connected to 5 lead ECG for continuous monitoring of heart rate and rhythm. Also invasive arterial blood pressure monitoring was carried out as well as urine output.

Sedation rates and infusion rates continued till extubation. Detection of ECG changes continued for the next 72 h after surgery and extubation till discharge from ICU.

Follow up in the ward by daily ECG continued in the next 48 h after discharge from ICU. The quality of the patient sedation was examined by the Richmond Criteria. [28] Patient pain was measured every 2 h using behavioral pain scale (BPS) [29]; If BPS >3, 3–5 mg morphine was administered to obtain BPS<3.

During the patient stay in the ICU, MAP and HR were measured in both groups every 30 minutes in the first 2 h till extubation then hourly for 48 h after extubation.



2.3. Statistics

To analyze data, SPSC (Version 19) was used. Mean and standard deviation were used for analysis of quantitative data and independent T test was used to compare bet the 2 groups. P <0.05 is considered significant. [30]

This sample was estimated statistically by the medical statistical department, all analysis was conducted by using SPS software. Statistics for nominal data (occurrence of AF, ICU and hospital duration) were conducted using Pearson's Chi-square procedure.

Statistics for continuous data hemodynamic parameters (systolic, diastolic and mean blood pressure and heart rate) were conducted through the student's t-test. All tests were conducted at an alpha level (0.05).

2.4. Patients

After approval of the local ethical committee and with an informed written consent from each patient, the study was carried out on 98 patients of either sex, ASA II physical status aged 40–60 years, admitted to Alexandria Main University Hospital and scheduled for major cardiac surgery whether CABG or valve replacement from March 2017 till December 2018.

The inclusion criteria were ASA II, elective cardiac surgery with cardiopulmonary bypass, lack of prior atrial fibrillation or flutter.

Patients were excluded when they have at least one of the following criteria on arrival to the ICU: HR < 50 bpm, atrioventricular conduction block grade II or III, MAP <55 mm Hg (despite appropriate volume resuscitation and vasopressors), and duration of surgery exceeded 8h (because these patients probably had complications that would not be representative to the typical cardiac study).

2.5. Flow diagram

2.6. Search Method

Publications describing the relevant information are searched in PubMed and Google Scholar, Scopus and Web of Science and database. Search terms included dexmedetomidine, cardiac surgery, arrhythmias, cardiac protection, tachycardia, bradycardia, hypotension and hypertension. Papers published in English language in the last 20 years were searched.

3. Results

Data were collected from 105 patients who were operated in Alexandria Main University Hospital between March 2017 and December 2019. Seven patients who were excluded from the study as they did not met the inclusion criteria.

The patients were divided into two groups where first group (DEX group) received dexmedetomidine infusion and the second group (propofol group) received propofol infusion.

Patients in DEX group consumed more morphine compared with propofol group but with less duration of intubation (P = 0.01, 004 respectively) (Table 1).

There were no statistically significant differences between both groups regarding MAP and heart rate except on day 3 postoperative where patients in propofol group experienced more increase in heart rate (P = 0.236, 0.312, 0.411, respectively, for MAP & 0.732, 0.421, 0.001, respectively for HR) (Tables 2 & 3).

There was a significant change between the two groups as regards the occurrence of atrial fibrillation. Only two patients developed atrial fibrillation in the DEX group; one gradually resorted to sinus rhythm without any intervention, whereas the second case needed amiodarone infusion to regain sinus rhythm, whereas in the propofol group 20 patients developed AF and treated by amiodarone and 5 of them were resistant to treatment and needed electric cardioversion whereas three cases developed slow AF and continued on antiarrhythmic treatment. And so these patients in the propofol group needed to stay in ICU 2 days more than the DEX group (Table 4 & 5).

Table 1. Duration of intubation and morphine consumption between both groups.

	DEX group	Propofol group	P value
Morphine consumption (mg)	14.44	9.67	0.01
Duration of intubation (hour)	2.93	3.42	0.04

Table 2. Mean arterial blood pressure between both groups.

	DEX group	Propofol group	P value
1st day	77.6	78.5	0.236
2nd day	78.5	77.4	0.312
3rd day	76.9	78.4	0.411

Table 3. Heart rate between both groups.

	DEX group	Prop	P value
1st day	83.4 ± 11	82.1 ± 10	0.732
2nd day	87.7 ± 12	86.9 ± 12	0.421
3rd day	83.2 ± 9	105.1 ± 12	0.001

Table 4. Comparison between both groups as regards the occurrence of atrial fibrillation, length of hospital stay and the use of inotropic support.

Variables	DEX group	Propofol group	P value
Arrhythmias	0.9%	13%	P = 0.001
ICU stay	2.7 ± 1	4.6 ± 1.2	P = 0.002
Anti-arrhythmic drugs	0.5%	11%	P = 0.001
Use of inotropes	4.5%	21.3%	P = 0.003

Table 5. Mean RASS score between the two groups.

Time	DEX group	Propofol group	P value
2h ICU admission	3.8	3.76	0.808
4 h ICU admission	3.2	2.91	0.092
6 h ICU admission	1.24	0.93	0.001

There was no difference between both groups regarding sedation score except 6 h after ICU admission (P = 0.808, 0.092, 0.001, respectively)

4. Discussion

To maintain a stable hemodynamic state is very important for ICU patients, but it is of utmost importance for patients undergoing open heart surgery. [31]

It was found in several studies that all sedatives are associated by different side effects. [31]In the current study, we found that the use of dexmedetomidine for sedation in the postoperative period was associated with a less incidence of atrial fibrillation in comparison with propofol. So we concluded that the use of dexmedetomidine for sedation helped to reduce the incidence of postoperative atrial fibrillation after open heart surgery.

However in different studies [32,33] comparing the use of dexmedetomidine and propofol for sedation, it was found that propofol was associated with decrease in blood pressure and cardiac output with its consequences on cerebral oxygenation unlike dexmedetomidine which was associated with more hemodynamic stability in postoperative cardiac patients.

In accordance with our study was a study carried out by Turan et al who used dexmedetomidine infusion after open heart surgery, they found that the incidence of atrial fibrillation was lower than that was previously reported in literature. However their registry was restricted to the initial 72 h postoperatively [34]. Another recent retrospective analysis of 16 patients reported significantly less AF in patients receiving dexmedetomidine [34].

In contrast to the present study was a study carried out by Tan et al, did nt support the use of dexmedetomidine as routine sedations because they found that it was associated with unstable hemodynamics that resulted in significant hypotension in hypovolemic and vasoconstrictor patients [35].

Other studies in which the authors studied the effect of dexmedetomidine on hemodynamics in cardiac patient postoperatively, they found that the use of dexmedetomidine was associated with hemodynamic instability and they did not support its use and other studies showed the need to use vasopressors, they also added that careful titration of dexmedetomidine didn't affect the stability of the hemodynamics of the patients. [36,37]

The negative chronotropic effect of dexmedetomidine has been explained by Herr and colleague in a prospective randomized study where they studied the sedative effect of dexmedetomidine in comparison to propofol infusion and concluded the beneficial effect of dexmedetomidine over propofol as a negative chronotropic effect, they concluded the incidence of AF was 55 in the dexmedetomidine group vs. 50% in the propofol group but the difference bet our study and theirs is that the infusion of dexmedetomidine and propofol was started with sternal closure but in our study the infusions were started on admission to ICU [5].

In accordance with the present study was a study carried out by Curtis et al, on the effect of dexmedetomidine in comparison to propofol on the hemodynamics of the patients in ICU and concluded that the use of dexmedetomidine helped to keep the hemodynamics of the patient stable and hence shortens the duration of ICU stay and shortens the duration of hospital stay. [38]

Another study that supports the current study was a met-analysis of 10 studies including a total of 15,816 patients conducted by Lin et al confirmed that the use of dexmedetomidine was associated with a shorter duration of mechanical ventilation after cardiac surgery. [39]

4.1. Summary

The use of dexmedetomidine in comparison to propofol infusion for sedation after open heart surgery was associated with a lower incidence of AF and was not associated with increased need of for vasopressors and hence decreased the duration of hospital stay.

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