RESEARCH ARTICLE

The Effect of Dexmedetomidine on the Incidence of Atrial Fibrillation after Coronary Artery Bypass Graft Surgery

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Background: Atrial fibrillation (AF) may occur in patients after coronary artery bypass surgery (CABG). Dexmedetomidine is a selective agonist of the alpha-2 adrenergic receptor with sedation, anti-anxiety and analgesic effects.
Therefore, the aim of the present study was to investigate the effect of sedation with dexmedetomidine on the incidence of AF in patients admitted to the intensive care unit after CABG surgery.
Methods: In this study, 100 patients underwent CABG surgery and randomly divided into two groups of dexmedetomidine and control. In the dexmedetomidine group, the drug was initiated at the time of closing the sternum at a dose of 0.7 µg/ kg /h and continued in the ICU at a dose of 0.5 µg/ kg /hr as an adjuvant and primary analgesic. Then, the effect of dexmedetomidine on atrial fibrillation and the effects of medication on the duration of hospitalization, the cost of hospitalization and stay in ICU, as well as heart rate, blood pressure and pain in patients were investigated first.
Results: The results showed that there was no significant difference in the incidence of AF after CABG surgery between the two experimental and control groups. On the other hand, patients in the dexmedetomidine group were hospitalized less frequently in the hospital than the control group, which led to a reduction in hospital costs. In addition, pulse, systolic blood pressure, and pain and sedation were significantly lower in control group ($P<0.05$).
Conclusion: Although the use of dexmedetomidine did not result in a difference in the incidence of AF after CABG surgery, the use of this drug reduced hospital stays, pulse rate, blood pressure and pain in patients.
Keywords: dexmedetomidine; atrial fibrillation; Coronary artery bypass graft surgery

Cardiovascular disease is responsible for 50% of deaths in developed countries and 25% of deaths in developing countries [1-2].

Many patients with coronary artery disease may require coronary artery bypass graft (CABG) surgery to reduce or eliminate angina pectoris symptoms [3].

Atrial fibrillation (AF) is common in the first 4-5 days after CABG surgery and is reported to occur in 25-40% of the patients [4]. Sex, left ventricular dysfunction, left atrium enlargement, chronic pulmonary disease, diabetes and obesity are facors that may affect the incidence of AF in the postoperative period [5].

AF after CABG surgery is associated with higher complications such as thromboembolism, renal failure, heart failure, and an increase in the length of stay in the hospital leading to higher costs and higher mortality rates [6-7].

Despite the many advances in surgical techniques, the incidence of AF after CABG has not decreased [8].

Various studies have been done to reduce the incidence of AF after CABG surgery. Antiarrhythmic drugs that have been proven to reduce the risk of AF after surgery include beta-blockers (sotalol) and amiodarone [9].

Dexmedetomidine is a selective agonist of the α-2 adrenergic receptor with sedation, anti-anxiety and analgesic effects which is used as a sedative drug in the intensive care unit [10-12].

Dexmedetomidine was first approved by the FDA in 1999 for short-term (less than 24 hours) surgeries for adolescents admitted to ICU and under mechanical respiration with the tracheal tube [13-15]. Previous studies have shown a positive effect of medication in cardiovascular function of patients undergoing various surgeries [16-17].

In this study, the effect of dexmedetomidine on reducing the incidence of AF in patients admitted to the intensive care unit after CABG surgery was studied.

Methods

After approval of ethics committee of Tehran University of Medical Sciences this study was conducted at Shariati hospital.

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Patients undergoing CABG surgery were enrolled in the study.

Inclusion criteria: patients aged 40-70 years, American Association of Anesthesiology class II and III, creatinine levels below 2mg/dl, ejection fraction higher than 40%, and absence of a permanent pacemaker and absence of significant underlying neurological disorders that prevent the titration of a sedative or analgesic drug, pulmonary disease, arrhythmia prior to surgery and history of hypertension.

Exclusion Criteria: The need for multiple rescue doses for sedation

On arrival to the operating room, ECG monitoring and pulse oximetry, and invasive control of blood pressure (IBP monitoring) was initiated for all the patients.

At the time of closing the sternum, patients were randomly assigned into two groups of dexmedetomidine (DEX) and control group based on a previously prepared list.

In the DEX group, dexmedetomidine infusion was started at the closing of sternum at a dose of 0.7 µg / kg / h and was continued in the postoperative period in the ICU at a dose of 0.5 µg / kg / hr as an adjuvant drug and as an analgesic.

If Richmond score was higher than 2 or critical care pain observation tool(CPOT≥3), to control agitation and pain, 0.1 µg / kg / h of dexmedetomidine was added. If this action was not effective after 20 minutes, a rescue agent was used.

If, despite this, the patient still needed rescue doses (more than one dose per hour), fentanyl infusion was started at 0.5-2 µg/ kg /hr and the patient was excluded from the study. Rescue agents included fentanyl, morphine and midazolam.

The following parameters were recorded at 1, 2, 3, 5, 7 and 9 hours after surgery: vital signs, Richmond score, CPOT Pain Score mechanical ventilation, sodium levels, analgesics, inotropes and vasodilators and antiarrhythmic drugs.

Also, episodes of sinus tachycardia and hypertension, bradycardia, and hypotension were recorded.

Patients in the control group underwent routine sedation with midazolam (1-2 mg/hr) and fentanyl (0.5-2 µg/kg/hr) after transfer to the ICU. Like the dexmedetomidine group, the above parameters were recorded at 1, 2, 3, 5, 7, 9 hrs after surgery and in the ICU.

In the case of Richmond score≥2 or CPOT≥3, for the control of agitation and pain, titration of midazolam and fentanyl was done.

In case of tachyarrhythmias, such as SVT and Rapid AF, standard treatment was done in the ICU.

Statistical Analysis

With the estimate of the incidence of 10% postoperative AF after dexmedetomidine administration, compared with the incidence of 17.5% in the control group with $\alpha = 0.05$ and 80%, the sample size was estimated to be 50 in each group.

Comparison of quantitative variables between two groups was done by independent T-test or Mannwhitney test and comparing qualitative variables by Chi Square Test. The significance level in all tests was considered to be $\alpha = 0.05$.

Results

In this study, 100 patients were enrolled in the study. Thirty-eight patients were male (76%) and 12 (24%) were female, in the dexmedetomidine group. In the control group, 39 cases (78%) were male and 11 (22%) were female (Figure1).

Also, the mean age of the patients receiving dexmedetomidine was 55.32 ± 8.99 years and the mean age of the control group was 59.10 ± 6.27 years, which was not significantly different between the two groups (P> 0.05).

The patients in this study suffered from at least one underlying illness, the most common underlying diseases were IHD (86 cases) and diabetes (59 cases). Details of the distribution of underlying illness in both groups in the (Table 1) has been shown. The prevalence of hypothyroidism, COPD and asthma was 13%, 10%, and 3% respectively.

Figure 1- Distribution of patients in the studied groups

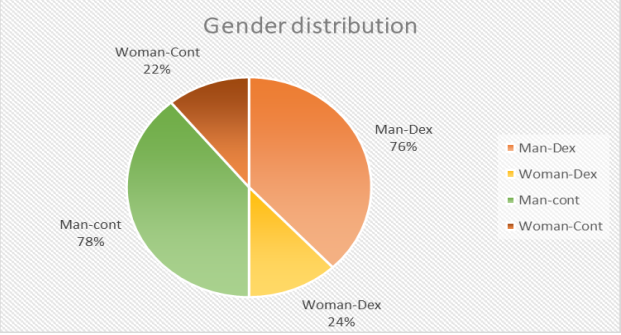

Table 1- Prevalence of diseases between the groups

Total	Control	Dexmedetomidine	group
10 (10%)	4 (8%)	6 (12%)	IHD only
25 (25%)	11 (22%)	14 (28%)	DM + IHD
11 (11%)	7 (14%)	4 (8%)	HTN + IHD
11 (11%)	5 (10%)	6 (12%)	DM + HTN
17 (17%)	9 (18%)	8 (16%)	DM + HTN+ IHD
13 (13%)	7 (14%)	6 (12%)	Hypothyroidism + IHD
10 (10%)	6 (12%)	4 (8%)	IHD + COPD
3 (3%)	1 (2%)	2 (4%)	Asthma + DM + HTN

Ischemic Heart Disease (IHD) ،Diabetes Mellitus (MD), Hypertension (HTN), Chronic Obstructive Pulmonary Disease (COPD)

Table 2- Distribution of clinical parameters in both control and dexmedetomidine group

Control	Dexmedetomidine	group / variables
20 (40%)	20 (40%)	On Pump
30 (60%)	30 (60%)	Off
615.8 ± 64.83*	571.5 ± 59.0	Intubation time(minute)
2.35 ± 0.67	2.15 ± 0.67	Number of grafts
6 (12%)	1 (2%)	Supraventricular tachyarrhythmia
1 (2%)	0 (0%)	Ventricular tachyarrhythmia
22 ± 3*	19 ± 2	Length of stay in ICU(hour)
5 ± 2*	4 ± 1	Length of stay in hospital(day)
0	0	Post surgery Mortality
3 (6%)	1 (2%)	AF incidence

*p<0.05

Distribution of clinical parameters studied in both control and dexmedetomidine group are presented in (Table 2). Average systolic blood pressure, pulse rate and pain score in the dexmedetomidine and control groups are also presented in (Table 3-4) and also in (Figure 2-5).

Table 3- Average systolic blood pressure, pulse rate and pain score in the dexmedetomidine and control groups

Post surgery pulse rate							Group
9hours	7hours	5hours	3hours	2hours	1hour	0	
83.2 ±10.64	79.6±9.19	81.4 ±13.80	87.95 ±15.98	90.6 ±12.65	98.5 ±17.48	102.8 ±15.79	Dexmedetomidine
98.3 ±10.37*	97.3 ±9.24*	95.3 ±10.14*	95.5 ±11.32	98.1 ±14.00	99.0 ± 14.85	98.3 ±14.07	control
Systolic blood pressure							**Group**
9hours	7hours	5hours	3hours	2hours	1hour	0	
117.4 ±11.46	113.5 ±12.45	105.9 ±10.89	103.7 ± 12.23	106.8 ± 15.45	107.3 ± 12.91	107.9 ± 14.74	Dexmedetomidine
130.8 ± 12.15*	121.7 ±13.05*	115.4 ±11.6*	111.3 ± 9.72*	111 ± 12.9	109.9 ± 10.87	104.7 ± 10.01	control
Diastolic blood pressure							**Group**
9hours	7hours	5hours	3hours	2hours	1hour	0	
72.94 ±9.76	68.15 ±7.36	64.8 ±9.45	61.6 ±12.92	65.1 ± 16.7	71 ±19.3	75.5 ±20.14	Dexmedetomidine
78.28 ±13.46	75.7 ±13.27*	70.95 ±13.62	65.8 ± 14.25	68.05 ±16.7	69.9 ±15.4	68.9 ± 15.84	control
Pain score(CPOT)							**Group**
9hours	7hours	5hours	3hours	2hours	1hour	0	
0.94±0.69*	0.58±0.64*	0.08±0.27*	0	0	0	0	Dexmedetomidine
1.9±0.73	1.3±0.86	0.54 ±0.50	0	0	0	0	control

Figure 2- Comparison chart of the pulse rate in both dexmedetomidine and control groups at different times

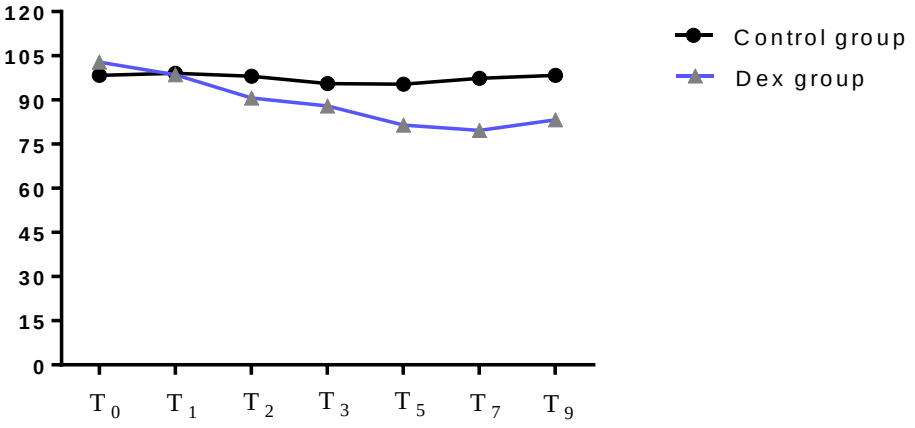

Figure 3- Comparison chart of systolic blood pressure in both dexmedetomidine and control groups at different times

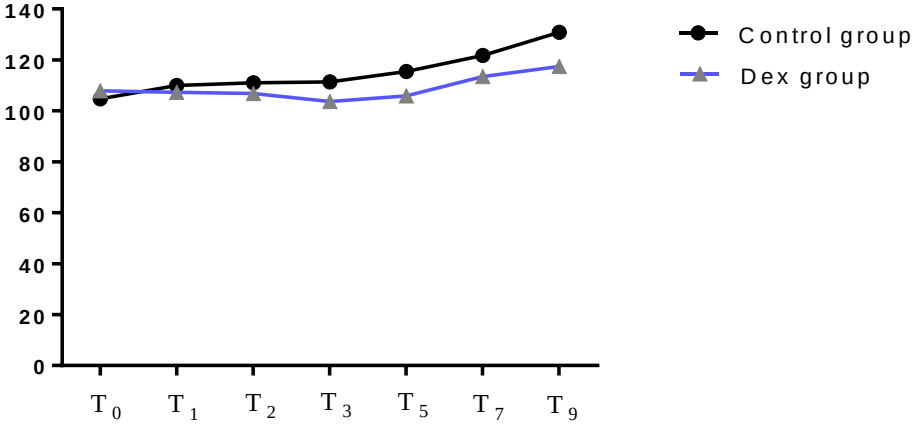

Figure 4- Comparison chart of diastolic blood pressure in both dexmedetomidine and control groups at different times

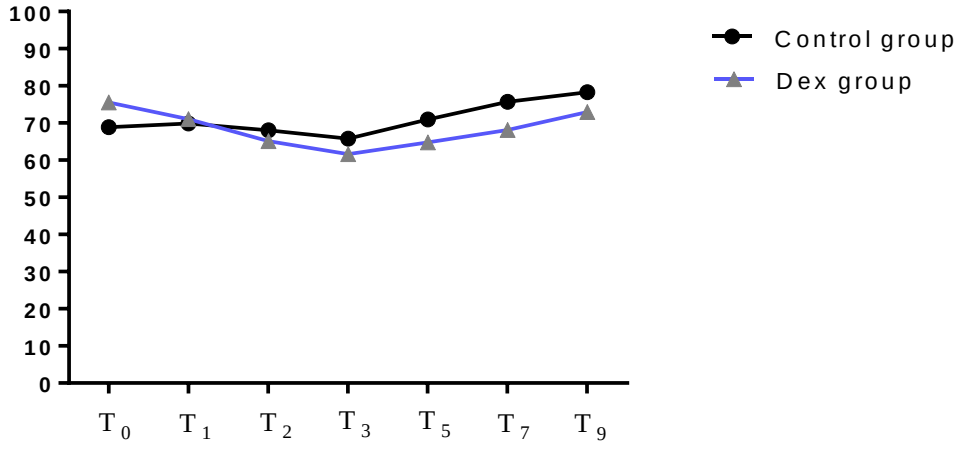

Figure 5- Comparison chart of pain score in both dexmedetomidine and control groups at different times

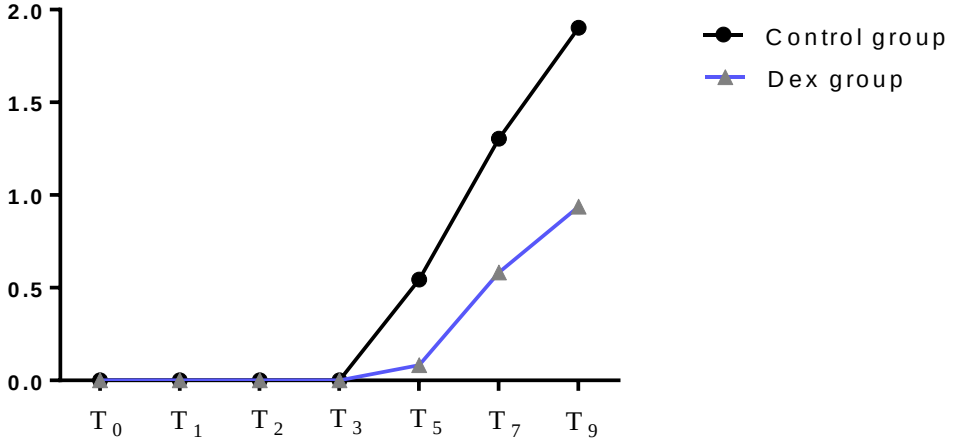

Table 4- Grading of sedation according to Richmond scale

	T0		T1		T2		T3		T5		T7		T9	
	Dex	con	Dex	con	Dex	Con	Dex	Con	Dex	Con	Dex	Con	Dex	con
Combative	0	0	0	0	0	0	0	0	0	0	0	2	0	2
Very agitated	0	0	0	0	0	0	0	0	0	0	0	0	0	7
Agitated	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Restless	0	0	0	0	0	0	0	0	0	0	0	12	0	8
Alert and calm	0	0	0	0	0	0	0	0	0	0	3	0	3	0
Drowsy	0	0	0	0	0	0	0	0	3	0	2	8	25	2
Light sedation	0	0	0	0	0	0	0	0	4	12	20	6	9	18
Moderate sedation	0	0	0	0	0	0	8	0	12	15	19	18	6	8
Deep sedation	0	0	2	0	5	2	9	37	16	19	6	4	0	0
Unarousable	50	50	48	50	45	48	33	13	15	4	0	0	0	0

Discussion

The present study showed that the use of dexmedetomidine did not lead to a difference between the two groups in terms of AF after CABG surgery, but the use of this drug decreased other parameters recorded including duration of stay in hospital, the duration of hospitalization in

ICU, pulse rate, blood pressure and pain.

In this study, the incidence of AF after CABG surgery in the two groups did not show any significant differences. In contrast to the findings of our study, Narisawa et al. (2015) evaluated 133 patients admitted to ICU after CABG. Their results showed that dexmedetomidine significantly reduced the incidence AF after CABG [18].

The reason for this difference in outcome may be related to the sample size, the type of surgery, the dose of the drug and the time and duration of the drug administration. Narisawa et al. (2015) used a 0.2-0.7 μg / kg / h dose of dexmedetomidine after extubation [18-20].

Ai et al. in a retrospective study on pulmonary surgery in cancer patients, showed that the use of dexmedetomidine decreased AF [21].

In this study, the incidence of extra ventricular arrhythmias after CABG did not differ significantly between the two groups; these results were different from the study by Chrysostomou et al., which showed that in their study the use of the post-operative dexmedetomidine during cardiac surgery significantly reduced the incidence of supraventricular arrhythmia and ventricular tachyarrhythmia in patients receiving dexmedetomidine compared to the control group [22].

They also showed that the use of dexmedetomidine reduces hospital stay and ICU residence time, in which the findings of Chrysostomou et al. (2011) were consistent with our study [22].

Rajput et al. (2014), showed in their study that dexmedetomidine reduced hospital stay [23].

In this study, pulse rate and blood pressure in both groups were evaluated at different hours after surgery. The results showed that pulse rate in patients receiving dexmedetomidine was lower than the control group.

In the case of hypertension, the same trend was observed; blood pressure decreased in patients receiving dexmedetomidine compared to the control group.

On the other hand, Rajput et al. (2014) showed that the use of dexmedetomidine significantly reduced the pulse rate and mean arterial pressure (MAP) of the recipient patients at 1, 2, 3 and 4 hours after surgery, compared to the control group. These findings were consistent with our study, which indicates that dexmedetomidine decreases pulse rate and MAP in patients [23].

In the present study, in addition to studying the effects of dexmedetomidine on cardiovascular parameters, the effect of this drug on pain and sedation in patients undergoing CABG surgery was studied. The results showed that according to the CPOT criteria, the patients in the two groups did not show any pain immediately after operation and 1, 2, and 3 hours after surgery.

Over time, at 5, 7, and 9 hours after surgery, pain was measured based on CPOT criteria in both groups, which was significantly lower in the group receiving dexmedetomidine than in the control group.

In addition to the amount of pain, the aim of this study was to investigate the effect of dexmedetomidine on the Richmond scoring method.

The results of our study showed that in the first hours of postoperative sedation in both groups was deep and over time, the sedation rate decreased in both groups, so that the difference in relaxation at 5, 7 and 9 hours after surgery in two groups, was significantly different.

One of the main limitations of the present study was that many cofounding factors may affect the incidence of AF which we tried to minimize them, but surely they still have their effect on the result, therefore a much larger study is needed to clarify the effect of dexmedetomidine on the incidence of postoperative AF.

Conclusion

Although the results of this study showed that the use of dexmedetomidine did not significantly decrease the incidence of AF, supraventricular tachyarrhythmia after CABG surgery, but the use of this drug decreased other parameters examined including hospital stay, pulse rate, blood pressure and pain in patients.

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