

Hemodynamic Effects of Dexmedetomidine in Patients undergoing Off Pump Coronary Artery Bypass Grafting Surgery (OPCAB): A Placebo Controlled Prospective Randomized Double Blind Study

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Abstract

Aims & Objectives: To study the effect of Dexmedetomidine on hemodynamic parameters in cases of OPCAB during

- Intubation,
- Intraoperatively during grafting and
- Postoperatively till extubation.

Methods: A prospective randomized double blind study involving 60 patients of either sex undergoing elective OPCAB was conducted; patients were randomly divided into two groups of 30 each. Patients received either Dexmedetomidine as loading dose of 1µg/kg over 10 min followed by a maintenance dose of 0.5µg/kg/hr (group A) or a placebo infusion of normal saline (Group B). The hemodynamic response during intubation, intraoperative hemodynamic variations, the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded before extubation, during extubation, at 1, 3 minutes and every 5 minutes thereafter. Extubation quality was assessed on a 5 point scale and sedation by Richmond Agitation-Sedation Scale. *Results:* In Dexmedetomidine group (group A) heart rate, BIS value was on the lower side compared to the placebo group (group B). The increase in heart rate in group A was significant only at 1 min after intubation whereas in group B it extended during 3rd & 5th min after intubation. The intraoperative variations in heart rate, mean arterial pressure (MAP), mean pulmonary arterial pressure (MPAP) were minimal in group A as compared to group B. There was significant increase in heart rate and mean arterial pressure ($p < 0.001$) during extubation in group B. Ninety percent of patients in group A and 16.7% in group B could be extubated smoothly. The average time to extubate was 292.50±45.3 min and 255±56min minutes in groups A, and B respectively (P value 0.13). *Conclusion:* Dexmedetomidine is a good adjuvant to general anaesthesia, reduces the stress response to intubation and provides minimal variations in hemodynamic intraoperatively. Dexmedetomidine continued postoperatively provides adequate sedation and reduces the stress response to extubation without prolonging the time to extubation.

Keywords: Coronary Artery Bypass Grafting; Dexmedetomidine; Extubation; Hemodynamic; Intubation.

Introduction

Stress response induced by laryngoscopy [1], intubation, tracheal suctioning and extubation causes an increase in heart rate and blood pressure due to sympathoadrenal activity, which increases the myocardial work load, oxygen consumption and incidence of ischemia especially in patients with

coronary artery disease undergoing coronary bypass grafting surgery [2,3]. Dexmedetomidine with the central α_2 agonist effect decreases the central sympathetic drive and hence decreases the stress response to intubation [4,5]. By minimizing the variability in the heart rate it provides suitable condition for grafting in off pump coronary artery bypass grafting surgeries. Dexmedetomidine with its sedation and analgesic property when continued

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post operatively provides adequate sedation also reduces the hemodynamic stress response during extubation [6]. Lack of respiratory depression, arousal sedation and hemodynamic stability makes Dexmedetomidine a better choice to attenuate the pressor response to extubation with an added advantage of preventing emergence delirium.

Patients and Methods

After the approval of the institutional ethical committee and written consent from the patients this prospective randomized placebo controlled double blind study was conducted involving 60 patients undergoing elective off pump coronary artery bypass grafting surgery (OPCAB). Inclusion criteria were patients aged between 35-70 yrs., ejection fraction >40%. The exclusion criteria were heart block (LBBB), left main coronary artery occlusion, valvular dysfunction, kidney or liver dysfunction, intubation time lasting longer than 20 seconds, anticipated difficult intubation, intra operative cardiac arrest, on pump conversion and post-operative re-exploration cases were excluded. All patients received 10 mg diazepam and 40 mg pantoprazole as premedication on the previous night and early morning on the day of surgery along with their routine cardiac medications. Surgery was done by same cardiac team.

Patients were randomly divided into two groups Dexmedetomidine (group A) and control (group B) of 30 each by closed envelope method. After the patient was received in the operating room the monitors were attached including BIS monitor. A peripheral intravenous line and arterial line were inserted under local anaesthesia. Basal readings of heart rate, blood pressure and BIS were recorded. Premedication with 0.03mg/kg of Inj.Midazolam i.v was given to all patients. Syringes containing aqueous solution of either Dexmedetomidine or saline as placebo was prepared in a double blind fashion by an anaesthesiologist who was not involved in the study. The infusion was started at the rate of 1 μ /kg over 10 min followed by maintenance dose of 0.5 μ /kg/hr. After 5 min of the loading dose the heart rate, blood pressure and BIS values was recorded. Anaesthesia was induced with inj. Midazolam 0.03mg/kg I.V, inj.Fentanyl 5 μ /kg I.V along with inj.Propofol 1mg/kg I.V. Endotracheal intubation was facilitated by 0.15mg/kg of inj.Vecuronium I.V. Intubation was performed by same Anaesthesiologist. Heart rate and blood pressure were recorded at 1 min, 3 min and 5 min

post intubation. Anaesthesia was maintained with Isoflurane 0.6%-1% in O₂ & air mixture along with inj.Fentanyl 1 μ /kg/hr & inj.Vecuronium 1 μ /kg/hr I.V infusion.

Pulmonary artery catheter was inserted through right internal jugular vein. Hemodynamic parameter HR, BP, pulmonary artery pressure and BIS were monitored. If BIS >60, rescue dose of inj.Propofol 0.5mg/kg I.V along with inj.Fentanyl 1 μ /kg I.V was given. With adequate depth BP and HR were stabilized with inj.NTG/inj.Esmolol/inotropes and inotrope score was recorded.

At the time of subcutaneous closure of skin the infusion of Fentanyl and Vecuronium was stopped while Dexmedetomidine/placebo infusion was continued postoperatively till the time of extubation. Post-operative pain was managed in both groups with Tab.

Paracetamol 500mg Qid through Ryle's tube/PO and inj.Tramadol 1mg/kg I.V BD. Hemodynamic parameters were recorded hourly, at the time of extubation 1,3,5 & 10 min post extubation. Quality of extubation was evaluated based on cough immediately after extubation; using a 5 point scale.

1= No coughing

2= Smooth extubation, minimal coughing (1-2 times)

3= Moderate coughing (3-4 times)

4= Severe coughing (5-10 times)

5= Poor extubation (laryngospasm / coughing >10 times)

Time to extubation was also noted.

Sedation was assessed by Richmond Agitation-Sedation Scale (Table 1).

Data was analysed using SPSS V19 software, all data were presented as mean \pm SD, paired t test was used to compare variable within the group and unpaired t test was used to compare variables between the two groups, chi-square test was used to analyse the categorical data. A p value of less than 0.05 was considered statistically significant.

Results

Demographic and surgical data between the two groups were comparable (Table 2). The two groups were comparable with respect to the age, weight, gender, ejection fraction, baseline heart rate, mean arterial pressure (MAP), BIS value and the average number of grafts.

Table 1: The Richmond Agitation–Sedation Scale

Score	Term	Description
4	Combative	Overtly combative or violent; immediate danger to staff
3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
2	Agitated	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

Table 2: Demographic data and surgical details

	Group A	Group B	P value
Age (years)	57.35+/-8.190	56.95+/-8.962	0.869
Weight(kg)	64.15+/-11.403	66.25+/-9.233	0.525
Gender(male/female)	23/7	26/4	0.633
Ejection fraction (%)	54.25+/-7.025	51.01+/-6.25	0.747
Preoperative medications			
• ACEIs,	5	4	
• Beta blockers ,	4	5	
• Calcium channel blockers	4	6	0.812
• ACEIS +CCB	7	5	
Number of Grafts	3.05+/-0.604	2.8+/-0.52	0.170
Duration of surgery	286+/-37.57	265+/-32.43	0.415
Inotrope score (24hrs)	4.85+/-1.81	4.25+/-1.37	0.097

Heart rate significantly decreased from the baseline to the pre-induction value in the group A. The heart rate was low in the group A throughout surgery and postoperatively compared to group B (Figure 1). Increase in the heart rate in group A from intubation to 1min, 3min, and 5min post intubation were 5%, 5%, and 0.5% respectively whereas in group B following intubation there was statistically significant increase in the HR at 1min, 3min and 5 min. it was 12%, 19% and 10% respectively. Though there was increase in the heart rate in the group A at 1min but it was not significant. The hemodynamic variations in group A was minimal during grafting

in group A as compared to the group B. There was fall in the MAP after the start of infusion in group A (Figure 2). After induction there was a fall in MAP in both the groups. Following intubation in group A, there was rise in MAP at 1min which decreased by 3rd min, whereas in group B MAP significantly increased at 1min and 3min post-intubation. Intraoperative fluctuations in MAP was minimal in group A as compared to group B (Figure 2). During extubation there was a significant increase in MAP at 1, 3, 5 min and settled by 10th min in group B whereas it increased during extubation and settled by 3rd min in group A.

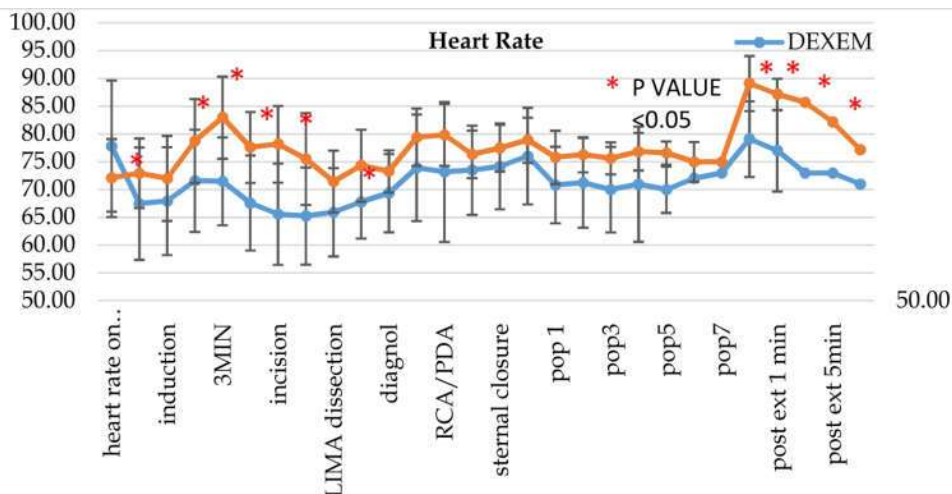


Fig. 1: Comparison of perioperative heart rate between two groups

Pulmonary artery catheter was inserted post induction. The mean pulmonary artery pressure (MPAP) increased post skin incision but to lesser extent in group A and it was lower throughout surgery in group A compared to group B. During extubation there was a significant increase in MPAP at 1, 3, 5 min in group B settled by 10th min in group B whereas it increased during extubation and settled early in group A.

After start of inj. Dexmedetomidine infusion, there was a significant fall in BIS value in group A and BIS value was persistently lower in the group A throughout the surgery. After extubation the heart

rate, MAP and MPAP were significantly increased in group B comparatively. 55% of patients in group A were mildly sedated with Richmond Agitation Sedation Scale (RASS) score of -1 whereas 65% of patients in group B were anxious with RASS score of 1. Extubation time in both the groups were comparable (group A 292.50±45.3 min and group B 255±56min).

Based on 5 point score extubation quality was compared (Table 3). Around 86% patient in group A had score less than 3, only 13% had 3 score indicating smooth extubation, whereas in group B 46% had score 3 and 30% had score 4 indicating severe cough during extubation.

Table 3: Comparison of extubation quality in study groups

Extubation quality	Group A		Group B		P value 0.0003
	No	%	No	%	
1	3	10	0	0	
2	23	76.7	7	23.3	
3	4	13.3	14	46.7	
4	0	0	9	30	
5	0	0	0	0	
Total	30	100	30	100	

Discussion

Myocardial protection is one of the major concerns of anaesthesiologist in a patient with coronary artery disease (CAD) undergoing CABG. Myocardial insult can occur during the time of induction of anesthesia due to hypotension caused by anesthetic drugs and due to pressor response of laryngoscopy and endotracheal intubation and also postoperatively during extubation. Various drugs and methods like Fentanyl, Esmolol, Nicardipine, Lignocaine spray have been used to reduce this stress response [6,7].

Dexmedetomidine, a potent α_2 agonist decreases the sympathoadrenal activity leading to stability in heart rate and blood pressure [8]. Its central CNS stimulation of parasympathetic outflow and inhibition of sympathetic outflow from locus cereleus in the brain stem plays a prominent role in sedation and anxiolysis [9].

Munise yildix et al. [3], conducted a prospective randomized trial involving 50 patients to study the effect of Dexmedetomidine on hemodynamic response during intubation and concluded that the blood pressure and heart rate increased more significantly in control group than in the Dexmedetomidine group.

In our study the increase in the heart rate in group A from intubation to 1min, 3min, and 5min post intubation were 5%, 5%, and 0.5% respectively whereas in group B it was 12%, 19% and 10% respectively. The increase in MAP at 1min, 3min and 5min post intubation compared to induction values were 5%, 2.6% and 0.5% in group A whereas it was 16%, 23% and 13% respectively in group B. (Figure 1,2).

Prabhat tewari et al. [10], conducted a prospective study using Dexmedetomidine as an adjunct to general anesthesia in hypertensive patients for OPCAB, they concluded that Dexmedetomidine provides stable hemodynamics in the intraoperative period. In our study heart rate in group A was persistently lower compared to group B, the MAP was comparable between the two groups except at induction and intubation. The MPAP was lower in group A at skin incision, sternotomy, during obtuse marginal artery and right coronary/posterior descending artery grafting but was not statistically significant (Figure 3).

BIS values in group A were significantly lower compared to group B (Figure 4) indicating the decreased requirement of anesthetic agents in group A which was comparable to previous studies [11].

Guler et al. [12], studied the effect of single dose of dexmedetomidine during extubation and

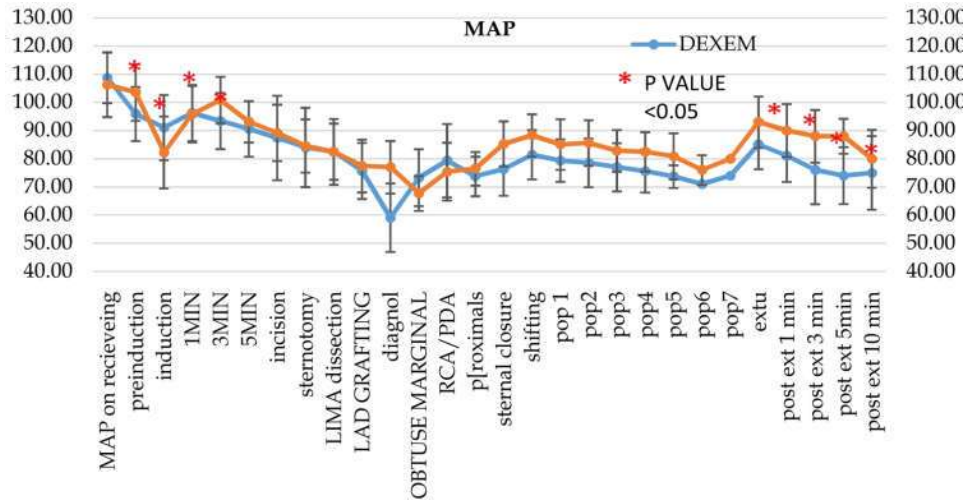


Fig. 2: Comparison of perioperative mean arterial pressure between two groups

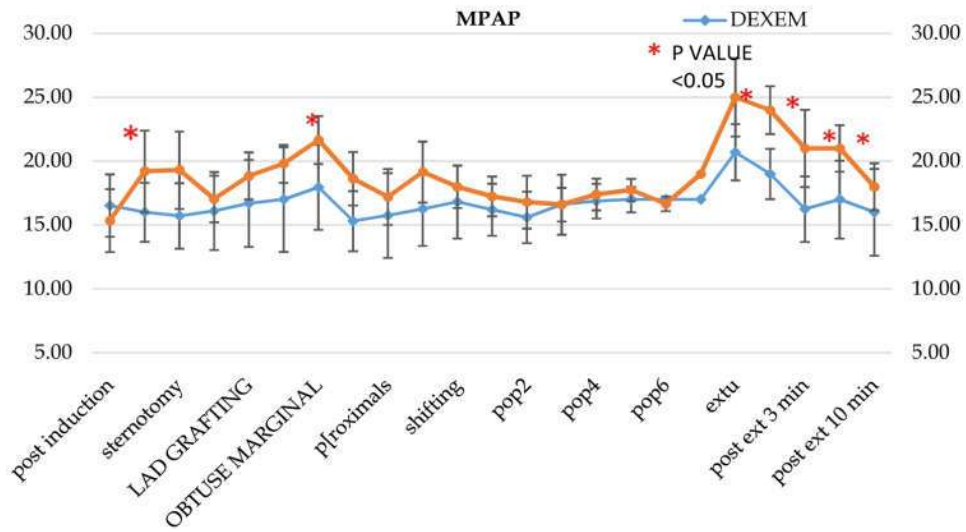


Fig. 3: Comparison of mean pulmonary arterial pressure perioperatively between two groups

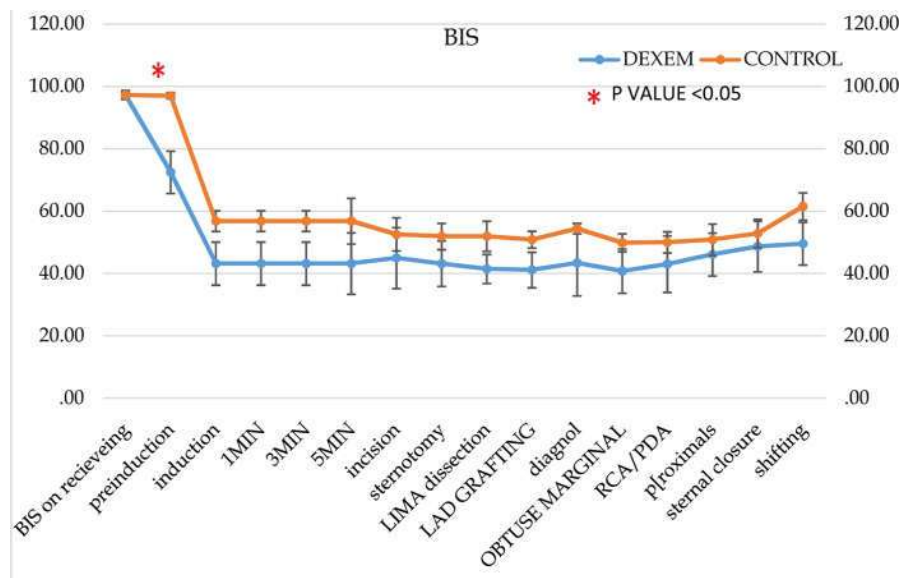


Fig. 4: Comparison of BIS values intraoperatively between two groups

concluded that heart rate, MAP increased at extubation in both the groups but increase was less significant in Dexmedetomidine group. In our study around 86% patient in group A had score less than 3 only 13% had 3 score indicating smooth extubation. Whereas in group B 46% had score 3 and 30% had score 4 indicating severe cough during extubation which was associated with increase in heart rate, MAP and MPAP. In group A the increase in heart rate at 2min post extubation was 15% which decreased to 7% by 10 min in relation to 1 hour preextubation values, whereas in group B it was 30% and 11% respectively. The MAP increased to 17% and 8% at 2 and 10 min postextubation in relation to 1 hour preextubation value whereas it was 23% and 5% in group B. The MPAP in group A increased by 23% at 2min postextubation in relation to 1 hour preextubation value and it returned to the baseline within 10 minutes, whereas in group B the increase was 32% and persisted till 10 minutes.

The observations in the present study are comparable with the results of the study done by Guler G et al suggesting a less significant increase in HR, SBP and DBP in response to extubation with 0.5µg/kg/hr they also suggested a better quality of extubation without causing any respiratory depression.

Limitations of the Study

Pulmonary artery pressures were not monitored during intubation, the plasma catecholamine levels were not measured for stress response and quantification of anaesthetic drugs requirement was not done.

Conclusions

Perioperative administration of Dexmedetomidine is an effective adjuvant to general anaesthesia, attenuates the stress response to intubation, provides minimal variations in hemodynamic parameters intraoperatively and enabling smooth extubation with significant reduction in cough, breath holding and laryngospasm. Dexmedetomidine provides adequate sedation in the post-operative period without causing respiratory depression.

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