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Research Article

Dexmedetomidine as an Anaesthetic Adjunct in Patients Undergoing Elective Off-Pump Coronary Artery Bypass Graft Surgery

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ABSTRACT

Background: The aim of the present study was to study the hemodynamic profile of dexmedetomidine during induction and distal anastomosis of coronary arteries in patients undergoing OPCAB in comparison to the institutional practice of using midazolam.

Methods: In Group I, (n=25) patients were anaesthetised using fentanyl, pancuronium bromide, Isoflurane and midazolam. Group II (n=25) patients received a loading dose of dexmedetomidine infusion (1µg/Kg) over 10 minutes followed by an infusion of dexmedetomidine at the rate of 0.6 µg/Kg/hour, along with fentanyl, Pancuronium bromide and isoflurane. Heart rate (HR) mean arterial pressure (MAP), pulmonary artery (PA) catheter derived data and BIS were recorded at baseline, at 1 and 3 minutes after induction, at 1, 3 and 5 minutes after intubation, and at 5 and 30 minutes after protamine administration. MAP and HR were recorded every 10 min during the operation, except during distal anastomosis of the coronary arteries when it was recorded every 5 minutes after application of the Octopus tissue stabilising system.

Results: The intubation response by way of increase in HR was much less in group II and stabilized by 5 min after intubation. The accompanying hypotension at 1 minute after induction was more in group II, but it was clinically acceptable (81.68±21.74 mm Hg). During distal graft anastomoses HR was in the range of 68 beats/min to 85 beats/min in group II vs. 85 beats/min to 100 beats/min in Group I. The MAP was lower in this group during the distal anastomosis, but it was within clinically acceptable range (> 65 mm Hg).

Conclusion: Dexmedetomidine is a viable option as an anaesthetic adjunct in a loading dose of 1µg/Kg followed by an infusion of 0.6 µg/Kg. Future studies will be necessary to show if this provides any outcome benefits.

Introduction

Surgery and postoperative stress cause sympathetic stimulation leading to an increase in blood pressure (BP) and heart rate (HR). These are associated with an increase in myocardial oxygen demand predisposing the myocardium to ischaemia, especially in patients with coronary artery disease (CAD). In patients undergoing off-pump coronary artery bypass (OPCAB) surgery, maintaining stable hemodynamics (HR and BP) is of paramount importance, especially while the coronary stabilizer is in place. The sedative, hypnotic and amnestic properties of benzodiazepines such as midazolam are a useful adjunct to opioids

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during cardiac surgery and they are a part of anaesthetic protocol at our institute. Dexmedetomidine, an α_2 -adrenoreceptor agonist is an analgesic with additional beneficial effects such as a decrease in sympathetic tone with attenuation of hemodynamic and neuroendocrine response to stress [1, 2]. It has been shown to reduce the anaesthetic and opioid requirement in patients undergoing CABG [3, 4]. It has also proven to provide hemodynamic stability (in a dose of 2.64 µg/Kg), owing to its effect in controlling the adrenocortical as well as cardiac function in patients undergoing vascular surgery, a patient population, who have a high incidence of CAD [1]. In addition, it leads to a decrease in plasma levels of cortisol, epinephrine, norepinephrine and serotonin and provides cardioprotective effects [5, 6]. It, thus, appears to be a useful agent during cardiac surgery.

The major drawbacks of dexmedetomidine are its propensity to cause bradycardia and hypotension [4]. There are a few reports of dexmedetomidine and its hemodynamic effects in patients undergoing OPCAB. The aim of the present study was to compare the hemodynamic profile of dexmedetomidine versus midazolam in patients undergoing OPCAB using Bi-spectral index (BIS) guided anaesthetic technique. As secondary efficacy variables, we also looked for untoward incidences such as bradycardia, hypotension and heart blocks.

Materials and Methods

I Sample Size and Patient Selection

We were planning a study of continuous response variables from matched pairs of study subjects. Prior data indicated that the difference in the response of matched pairs is normally distributed with a standard deviation of 14. If the true difference in the mean response of matched pairs is 10, we will need to study 23 pairs of subjects to be able to reject the null hypothesis that this response difference is zero with probability (power) 0.9. The Type I error probability associated with this test of null hypothesis was 0.05. Therefore, in this prospective, randomized study 50 patients, undergoing elective OPCAB were divided into two groups. Exclusion criteria were age ≥ 70 years, left ventricular ejection fraction (EF) of < 40%, redo surgery, combined procedures, New York Heart Association (NYHA) class III and IV, any systemic diseases like chronic obstructive pulmonary disease and renal, hepatic or neurological disease. The patients were randomly allocated to two groups: Group I (Control, n=25) and Group II (dexmedetomidine, n=25) by computer generated randomization table. All the patients received premedication as per the institutional protocol with intramuscular morphine 0.2 mg/Kg and promethazine 0.5 mg/Kg, 30 minutes before surgery. In the operating room, taking aseptic precautions, a 23 G Y-cannula, intra-arterial cannula and pulmonary artery (PA) catheter were placed under local anaesthesia. Routine monitoring consisted of HR, invasive BP, BIS and peripheral oxygen saturation monitoring (SpO_2).

In Group I, patients were anaesthetized by the standard institutional protocol using opioid (fentanyl 8-10 µg/Kg), muscle relaxant (pancuronium bromide 0.1mg/Kg) and midazolam (0.02mg/Kg). Anaesthesia was maintained with intermittent doses of fentanyl, pancuronium bromide, midazolam and isoflurane. Group II patients received a loading dose of dexmedetomidine (1µg/Kg) as an infusion over 10 minutes, fentanyl (8-10µg/Kg) and pancuronium bromide (0.1mg/Kg). Anaesthesia was maintained with intermittent fentanyl, pancuronium bromide and an infusion of dexmedetomidine at the rate of 0.6 µg/Kg/hour and isoflurane. The infusion of dexmedetomidine was discontinued at the end of surgery. A target BIS value of 40-60 was maintained in both the groups (by titrating Isoflurane) at all times during induction of anaesthesia and surgery. In both the groups, hemodynamics [HR, mean arterial pressure (MAP)], PA catheter derived data and BIS were recorded at baseline (soon after insertion of the PA catheter under local anaesthesia), at 1 and 3 minutes after induction of anaesthesia and again at 1, 3 and 5 minutes after endotracheal intubation. Thereafter, MAP and HR were recorded every 10 min during the operation, except during distal anastomosis of the native coronary artery [left anterior descending (LAD), obtuse marginal (OM) and right coronary (RCA)] when it was recorded every 5 minutes after application of the Octopus tissue stabilising system (OTSS). PA catheter derived data were also obtained at 5 and 30 minutes after protamine administration.

Patient outcome as regards, time to extubation, stay in intensive care unit (ICU), discharged/ expired, inotropic support and the use of intra-aortic balloon pump (IABP) were also noted. In both the groups, nitroglycerin was infused routinely at a rate of 0.3 µg/Kg/min continuously from the start of the procedure. Ringer's solution or succinylated gelatine was infused to maintain a sufficient preload and a CVP of 8-10 cm of H_2O at the discretion of the attending anaesthesiologist. Body position was changed appropriately to aid the visualization during distal anastomosis, vasoactive drugs (Dopamine/Dobutamine/Adrenaline/Vasopressin/ or a combination/ IABP) were administered, if necessary, to maintain a MAP > 70 mm Hg. Nasopharyngeal temperature was maintained at 35-36ºC. All OPCAB procedures were performed by any one of the two surgical teams. After surgery, dexmedetomidine infusion was discontinued and patients were transferred to the cardiac ICU where they were managed according to the institutional protocol.

II Statistical Methods

Data are presented as mean ± SD. Categorical data are presented as number of patients per category (n). Student's t-test was used to compare independent means. A chi-square test was used to compare categorical variables. P-values <0.05 were considered statistically significant.

Results

The two groups were similar with respect to age, weight, height, gender, body surface area (BSA) (Table 1). Table 2 shows the PA catheter derived parameters in the two groups at various stages. The two groups were similar with respect to baseline PA catheter derived data. In Group I, the HR increased significantly at 1 min post-intubation and remained so throughout the study period. In Group II the HR increased significantly at 3 min after intubation but stabilised at 5 min post intubation. It again increased significantly at 5 min and 30 min after protamine administration. Comparison of HR between the two groups showed that although the HR was more in Group I at all points in time, it did not assume statistical significance. The MAP in Group I decreased significantly from baseline at 3 min post-induction and at 3 min post-intubation and remained so throughout the study period. In Group II, the MAP decreased at 1 min post-induction and remained so throughout the study period. Between the groups comparison showed that the MAP was

less in Group II at all times and became significantly less, 1 min post-induction. The stroke index (SI) decreased significantly in both the groups, 1 min post-induction and remained so throughout the study period, but it was not significantly different between the two groups. Likewise, the CI (cardiac index) decreased significantly from baseline in both the groups at 1 min post-induction and remained so throughout the study period. However, in Group II the CI recovered at 5 and 30 min after protamine administration. Although the CI was less in Group I at all-time points, it did not assume statistical significance.

Table 1: The demographic variables in the two groups.

Variable	Group I (control) N=25	Group II (dexmedetomidine) N=25
Age (years) (Mean ±SD)	56.76±10.83	54.60±9.84
Sex (M/F) (n)	21/4	20/5
Weight (Kg) (Mean ±SD)	63.48±8.85	60.16±13.04
Height (cm) (Mean ±SD)	165.48±5.84	163.96±8.85
BSA (m^2) (Mean ±SD)	1.69±0.12	164±0.19

BSA: Body Surface Area; SD: Standard Deviation.

Table 2: Comparison of PAC derived hemodynamic parameters between Group I (n=25) and Group II (n=25).

Variable	Group	Baseline	1 minute post induction	3 minutes post induction	1 minutes post intubation	3 minutes post intubation	5 minutes post intubation	5 minutes after protamine	30 minutes after protamine
HR (beats/min	Group I	71.40±18.23	72.88±20.71	74.8±18.44	80.00±19.73*	82.16±20.38*	76.60±18.14*	87.92±18.88*	84.60±19.46*
	Group II	68.76±13.59	68.72±13.62	71.28±15.93	74.04±10.79	76.72±11.53*	73.16±15.41	83.64±17.18*	82.68±17.33*
MAP (mm Hg)	Group I	102.08±16.35	99.96±19.22#	84.08±16.47*	96.44±30.71	92.56±17.07*	86.36±13.34*	79.96±12.08*	83.16±12.97*
	Group II	98.04±14.96	81.68±21.74*#	84.88±29.82*	90.12±18.65	89.44±17.08*	83.40±18.99*	72.80±13.07*	77.64±9.64*
SI (mL/beat/m^2)	Group I	42.72±12.36	37.68±13.45*	31.76±9.05*	30.60±10.37*	29.64±9.79*	30.68±8.98*	27.72±9.28*	29.68±14.19*
	Group II	44.92±16.61	36.68±12.03*	33.28±11.67*	34.56±12.21*	31.84±10.14*	32.88±10.44*	32.16±15.31*	33.84±14.48*
CI (L/min/m^2)	Group I	2.90±0.86	2.60±0.85*	2.28±0.64*	2.38±0.76*	2,27±0.61*	2.30±0.75*	2.33±0.74*	2.35±0.90*
	Group II	3.07±1.36	2.50±0.95*	2.43±0.99*	2.50±0.81*	2.41±0.71*	2.33±0.69*	2.61±1.12	2.92±1.47
PCWP (mm Hg)	Group I	12.48±6.49	12.40±6.84	11.80±5.61	12.20±6.03	11.80±5.87	10.60±5.26	9.28±3.22*	9.36±3.86*
	Group II	9.56±4.65	11.16±4,46	11.76±5.62	11.60±5.22	10.28±3.43	9.64±3.07	9.84±3.41	8.92±3.94
CVP	Group I	6.68±2.72	6.84±2.48	6.76±2.40	6.44±2.43	6.64±2.54	6.56±2.16	5.24±2.68*	5.56±2.84
	Group II	5.84±2.79	5.80±2.97	5.88±2.71	5.84±2.73	5.92±2.83	6.00±2.72	5.56±3.21	5.72±2.94
SVRI	Group I	2779.44±796.34	3102.24±1210.41	2827.12±1024.41	3118.64±1299.76	3145.40±912.60	3028.92±1257.65	3027.04±1672.12	3007.28±1537.56
	Group II	2632.64±756.44	2587.60±915.95	2702.56±860.24	2817.44±838.13	2951.64±901.88	2766.96±912.90	2394.20±1161.61	2829.00±2057.14
PVRI	Group I	269.92±126.47	290.16±164.00#	292.80±217.24	339.12±287.26#	283.16±199.62	281.62±167.49	163.32±83.68*	202.96±135.37*
	Group II	208.48±100.60	181.44±102.59#	238.44±173.88	191.56±115.81#	255.20±156.12	205.32±95.43	134.72±77.33*	150.68±84.33*
SvO_2 (%)	Group I	75.84±6.69							75.73±7.12
	Group II	75.96±6.50							79.27±8.79
BIS	Group I	91.00±5.77	62.44±11.52*	53.76±7.42*	52.16±9.02*	51.52±7.77*	52.64±7.91*	49.08±6.59*#	49.56±8.41*#
	Group II	92.92±6.05	58.88±13.49*	54.28±11.91*	51.56±11.54*	49.84±10.36*	48.80±7.42*	54.28±8.80*#	56.32±6.57*#

*P<0.05, compared to baseline, #P<0.05, Group I vs. Group II.

MAP: Mean Arterial Pressure; CVP: Central Venous Pressure; MPAP: Mean Pulmonary Artery Pressure; PCWP: Pulmonary Capillary Wedge Pressure; HR: Heart Rate; SI: Stroke Index; CI: Cardiac Index; SVRI: Systemic Vascular Resistance Index; PVRI: Pulmonary Vascular Resistance Index; LVSWI: Left Ventricular Stroke Work Index; RVSWI: Right Ventricular Stroke Work Index; SvO_2: Mixed Venous Saturation; BIS: Bispectral Index.

The PCWP (pulmonary capillary wedge pressure) was significantly less in Group I at 5 and 30 min after protamine administration. There was no change in SVRI (systemic vascular resistance index) in the two groups. The PVRI (pulmonary vascular resistance index) decreased significantly in both the groups at 5 and 30 min after protamine administration. Comparison between the two groups showed that PVRI was significantly more in Group I at 1 min post-induction and at 1 min post-intubation. The mixed venous oxygen saturation (SvO_2) did not change significantly in both the groups when compared to baseline. The BIS value was maintained between 40 and 60 in both the groups at all times during the operative procedure. Tables 3-5 show the comparison of HR and MAP in the two groups during distal graft anastomosis of LAD, OM and RCA at 5 min intervals. The baseline was considered as the reading before induction of anaesthesia. In both the groups the HR increased and the

MAP decreased significantly from the baseline at 5 min and remained so during the anastomosis. Comparison of the HR and MAP between the two groups showed that the HR was more in Group I becoming significant at 20 and 25 min and the MAP was less in Group II becoming significantly less 5 min after application of OTSS. Table 6 shows the comparison of intraoperative HR and MAP in the two groups after completion of the distal graft anastomoses till the patient was transferred to the cardiac ICU.

Table 3: Comparison of hemodynamic parameters between the two groups during distal anastomosis of LAD.

VARIABLES	**Baseline**		**5 min**		**10 min**		**15 min**		20 min		**25 min**		**30 min**	
	Group I (n=25)	Group II (n=25)	Group I (n=25)	Group II (n=25)	Group I (n=25)	Group II (n=25)	Group I (n=24)	Group II (n=25)	Group I (n=21)	Group II (n=18)	Group I (n=12)	Group II (n=11)	Group I n=(10)	Group II (n=4)
HR	71.40±18.23	68.76±13.59	92.00±18.77*	77.94±9.00*	91.87±17.58*	75.35±10.43*	91.81±20.78*	76.35±12.89*	90.13±14.79*	75.21±9.13*#	96.66±24.85*	71.55±9.83#	86.50±14.84*	76.25±9.74
MAP	102.08±16.35	98.04±14.96	88.43±15.11*	73.11±15.97*#	83.31±8.48*	72.88±12.50*#	80.50±12.03*	72.47±10.67*#	83.86±12.72*	73.50±8.78*#	93.11±10.60*	75.66±9.48*#	89.25±9.76	66.00±5.58*#

*P<0.05, compared to baseline, #P<0.05, Group I vs. Group II, (n=number of patients).

LAD: Left Anterior Descending Artery.

Table 4: Comparison of hemodynamic parameters between the two groups during distal anastomosis of OM.

VARIABLES	**Baseline**		**5 min**		**10 min**		**15 min**		20 min		**25 min**		**30 min**	
	Group I (n=25)	Group II (n=25)	Group I (n=20)	Group II (n=20)	Group I (n=20)	Group II (n=20)	Group I (n=20)	Group II (n=17)	Group I (n=14)	Group II (n=11)	Group I (n=7)	Group II (n=10)	Group I (n=5)	Group II (n=4)
HR	71.40±18.23	68.76±13.59	92.55±22.82*	80.60±16.26*	95.55±22.49*	80.95±15.34*#	90.65±21.17*	77.70±13.57*#	88.21±21.26*	75.73±11.49*	92.14±20.30*	75.80±12.09 *	79.40±35.70	68.75±12.04
MAP	102.08±16.35	98.04±14.96	82.45±13.44*	69.35±14.98*#	77.80±10.45*	71.05±12.20*	81.30±11.36*	69.00±13.49*	82.00±11.27*	67.00±12.83*#	83.57±15.96*	72.00±13.08*	90.25±17.54	67.25±9.91*

*P<0.05, compared to baseline, #P<0.05, Group I vs. Group II, (n=number of patients).

OM: Obtuse Marginal Artery.

Table 5: Comparison of hemodynamic parameters between the two groups during distal anastomosis of RCA.

VARIABLES	**Baseline**		**5 min**		**10 min**		**15 min**		20 min		**25 min**		**30 min**	
	Group I (n=25)	Group II (n=25)	Group I (n=14)	Group II (n=17)	Group I (n=14)	Group II (n=17)	Group I (n=14)	Group II (n=16)	Group I (n=8)	Group II (n=12)	Group I (n=5)	Group II (n=7)	Group I (n=2)	Group II (n=2)
HR	71.40±18.23	68.76±13.59	92.86±15.69*	79.94±13.34*#	92.40±16.36*	82.82±20.82*	94.64±19.02*	81.50±22.49*	97.87±20.47*	81.08±25.16*	93.00±16.43	87.57±29.98	102.50±3.53	66.50±4.95 #
MAP	102.08±16.35	98.04±14.96	84.14±11.26*	69.65±15.56*#	79.57±10.77*	71.00±12.48*	75.57±9.88*	70.25±12.13*	73.78±4.71*	71.75±11.23*	74.60±10.06*	72.86±12.51*	89.50±4.95	79.00±1.41

*P<0.05, compared to baseline, #P<0.05, Group I vs. Group II, (n=number of patients).

RCA: Right Coronary Artery.

Table 6: HR and MAP after distal graft anastomosis till the end of surgery in the two groups.

Variable	Group	Baseline	10 min	20 min	30 min	40 min	50 min	60 min	70 min	80 min	90 min	100min	110 min	120 min
HR	Group I	(n=25) 71.40±18.23	(n=25) 87.48±18.08*	(n=25) 86.64±19.88	(n=25) 88.12±19.19	(n=25) 84.80±16.03	(n=24) 88.17±17.99*#	(n=21) 87.14±20.84*	(n=20) 85.80±22.52*	(n=18) 89.67±15.74*	(n=17) 90.94±16.57*	(n=14) 89.86±18.64*	(n=9) 94.11±22.21*	(n=6) 97.17±21.23*
	Group II	(n=25) 68.76±13.59	(n=25) 82.44±19.91	(n=25) 80.84±14.84	(n=25) 82.36±16.04	(n=25) 82.08±17.44	(n=24) 74.50±21.14#	(n=21) 79.38±13.10	(n=21) 82.95±16.13	(n=21) 82.95±16.12	(n=11) 84.48±17.38*	(n=16) 82.94±18.54	(n=11) 83.91±21.02	(n=10) 84.90±17.92
MAP	Group I	(n=25) 102.08±16.35	(n=25) 73.60±15.70*	(n=25) 68.96±14.20*	(n=25) 76.20±12.69*	(n=25) 79.68±14.92*#	(n=24) 80.96±11.79*	(n=21) 80.14±10.49*	(n=20) 77.30±12.70*	(n=18) 81.89±11.64*#	(n=17) 81.65±12.66*	(n=14) 82.57±12.83*#	(n=9) 83.22±11.65*	(n=6) 78.83±9.58*
	Group II	(n=25) 98.04±14.96	(n=25) 73.44±12.76*	(n=25) 69.64±13.07*	(n=25) 70.32±10.00*	(n=25) 71.60±10.53*#	(n=24) 76.83±11.66*	(n=21) 75.33±11.10*	(n=21) 76.81±16.10*	(n=21) 68.81±15.06*#	(n=21) 77.28±17.64*	(n=16) 83.19±14.95*#	(n=11) 68.00±7.91*	(n=10) 70.60±11.37*

*P<0.05, compared to baseline, #P<0.05, Group I vs. Group II, (n= number of patients).

In Group I the HR was more than the baseline becoming significant at 10, 50, 60, 70, 80, 90, 110 and 120 min. in Group II the HR was more as compared to baseline but did not assume statistical significance except at 90 min. Between the Groups analysis showed that the HR was more in Group I at all times assuming statistical significance at 50 min only. The MAP was statistically less from 10 min throughout the study period in Group I as well as in Group II. Between group comparisons revealed that the MAP was significantly less in Group II at 40, 80 and 100 min. Table 7 shows the inotropic support required by the patients in the two groups. No inotropic support was required in 11 patients and 12 patients in Group I and Group II respectively. Seven patients in Group I and 5 patients in Group II required either Dopamine or Dobutamine. One patient in Group I and two patients in Group II required Adrenaline while six patients in both the groups required both Adrenaline and Dopamine as inotropic support. The mean number of days spent in ICU was 3.08±0.64 days in Group I and 3.36±1.25 days in Group II (Table 7, p=NS). One patient in Group II expired due to multi-organ failure following low cardiac output and one patient needed IABP support in Group II (p=NS). The time to extubation was not significantly different in the two groups.

Table 7: Use of inotropic support and outcome in the two groups.

Variable	Group 1 (control) N=25	Group 2 (Dexmedetomidine) N=25
No inotropes (n)	11	12
Dopamine/dobutamine (n)	7	5
Adrenaline (n)	1	2
Adrenaline and dopamine (n)	6	6
Stay in ICU (days)	3.08±0.64	3.36 ±1.25
Patients expired (n)	0	1
IABP (n)	NIL	1

P=NS.

Discussion

The results of the present study show that the HR and MAP were generally on the lower side in the group II throughout the study period but assumed statistical significance only during distal and proximal graft anastomosis. In particular, the intubation response by way of increase in HR was much less in group II and stabilized by 5 min after intubation. The accompanying hypotension at 1 minute after induction was more in group II, but it was clinically acceptable (82 mm Hg). The patients undergoing OPCAB are especially susceptible to develop hemodynamic changes during distal anastomosis of the coronary arteries. In the present study hemodynamic parameters during distal anastomosis of individual vessels is being reported. Comparison of the HR between the two groups during various distal graft anastomoses showed that the HR was in the range of 68 beats/min to 85 beats/min in group II vs. 85 beats/min to 100 beats/min in Group I. Considering the desirable HR of 70-80 beats / min during distal graft anastomosis in OPCAB group II patients maintained a much better HR [7]. The MAP was lower in this group during the distal anastomosis, but it was within the acceptable range (> 65 mm Hg). Despite maintaining lower HR and MAP in group II, there was no significant difference in the inotropic requirements or outcome (the length of stay in ICU or mortality).

In patients with CAD, mild myocardial depression (lower HR and MAP) is desirable and beneficial as it decreases the myocardial oxygen demand [8]. In this respect, the observed effects of dexmedetomidine in the present study can be considered as beneficial. However, extreme bradycardia and hypotension can be dangerous. This can be relevant in patients undergoing OPCAB, where the surgeon needs to manipulate the heart during distal anastomosis. Although with the improvements in the technology (suction-based stabilizers, apical positioners) and surgical expertise, the hemodynamic alterations are much less, they are not unknown [9, 10]. Similar results (obtundation in the increase in HR and BP in response to intubation and skin incision, decrease in the variability of systolic arterial pressure and decrease in the incidence of hypertension and tachycardia during operation, before and after bypass) have been reported with dexmedetomidine in patients undergoing on pump CABG [4, 11-13]. After all the distal anastomoses, MAP was significantly lower but in the clinically acceptable range (>70 mm Hg) in group II at 40 min, 80 min, 110 min and 120 min. This time period represented the performance of proximal anastomosis with side biting aortic clamp in place. During this time, a lower systolic BP and HR is desirable as it is convenient for the surgeon to perform the anastomosis as well as to provide protection against dissection of the aorta.

Opioid-based anaesthetic technique along with benzodiazepines and inhalational agents have been largely used during OPCAB. It is well known that volatile anaesthetics possess dose-dependent myocardial depressant properties. Therefore, as a part of balanced anaesthesia technique, the sedative, hypnotic and amnestic properties of benzodiazepines have been used as an adjunct to opioids during cardiac surgery [14, 15]. Dexmedetomidine is a more specific and selective alpha 2 agonist, producing dose-dependent sedation and analgesia. Although, dexmedetomidine-based anaesthesia has been found to produce relative bradycardia compared to midazolam-based anaesthesia, it has been shown to decrease isoflurane requirements to maintain hemodynamic parameters within predetermined limits and thus, dexmedetomidine is well appreciated as an anaesthetic adjunct with consistent results that it reduces anaesthetic requirements [11-13, 16, 17]. Use of dexmedetomidine has also shown a trend towards improved cardiac outcomes (decrease in the release of Troponin T in high-risk patients undergoing vascular surgery and decreased level of serum cardiac troponin I and creatine kinase MB in patients undergoing OPCAB relying primarily on tight control of heart rates [6, 18]. BIS is now considered to have a reliable predictive power of adequate anaesthetic depth, thus could guard against the occurrence of major hemodynamic events during the induction period [19, 20].

In the present study BIS values were maintained in a range of 48-58 in the patients who received dexmedetomidine infusion. This was comparable with the control group (BIS 49-62), in which patients received midazolam. The present study demonstrates that when used under-regulated doses using BIS monitoring, dexmedetomidine caused only mild (beneficial) effects on the HR and MAP and no extreme effects as reported in some of the earlier studies [21, 22]. Future studies will be necessary to show if this provides any outcome benefits.

Conclusion

Dexmedetomidine is a viable option as an anaesthetic adjunct in a loading dose of 1µg/Kg followed by an infusion of 0.6 µg/Kg. However, one should be watchful and be prepared to deal with extreme bradycardia and hypotension.

Conflicts of Interest

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Declaration

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Permission

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Ethical Approval

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References

1. Talke P, Chen R, Thomas B, Aggarwall A, Gottlieb A et al. (2000) The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. *Anesth Analg* 90: 834-839. [Crossref]
2. Patel CR, Engineer SR, Shah BJ, Madhu S (2012) Effect of intravenous infusion of dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: A study with entropy analysis. *Indian J Anaesth* 56: 542-546. [Crossref]
3. Khalil MA, Azeem MSA (2013) The impact of dexmedetomidine infusion in sparing morphine consumption in off-pump coronary artery bypass grafting. *Semin Cardiothorac Vasc Anesth* 17: 66-71. [Crossref]
4. Menda F, Köner O, Sayin M, Türe H, Imer P et al. (2010) Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. *Ann Card Anaesth* 13: 16-21. [Crossref]
5. Wu H, Tang J, Pan J, Han M, Cai H et al. (2020) Effects of dexmedetomidine on stress hormones in patients undergoing cardiac valve replacement: a randomized controlled trial. *BMC Anesthesiol* 20: 142. [Crossref]
6. Chi X, Liao M, Chen X, Zhao Y, Yang L et al. (2016) Dexmedetomidine Attenuates Myocardial Injury in Off-Pump Coronary Artery Bypass Graft Surgery. *J Cardiothorac Vasc Anesth* 30: 44-50. [Crossref]
7. Virmani S, Tempe DK (2007) Anaesthesia for off-pump coronary artery surgery. *Ann Card Anaesth* 10: 65-71. [Crossref]
8. Kwak YL (2005) Reduction of ischemia during off-pump coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 19: 667-677. [Crossref]
9. Gründeman PF, Borst C, van Herwaarden JA, Verlaan CW, Jansen EW (1998) Vertical displacement of the beating heart by the octopus tissue stabilizer: influence on coronary flow. *Ann Thorac Surg* 65: 1348-1352. [Crossref]
10. Hemmerling TM, Romano G, Terrasini N, Noiseux N (2013) Anesthesia for off-pump coronary artery bypass surgery. *Ann Card Anaesth* 16: 28-39. [Crossref]
11. Ruesch S, Levy JH (2002) Treatment of persistent tachycardia with dexmedetomidine during off-pump cardiac surgery. *Anesth Analg* 95: 316-318. [Crossref]
12. Jalonen J, Hynynen M, Kuitunen A, Heikkilä H, Perttilä J et al. (1997) Dexmedetomidine as an anesthetic adjunct in coronary artery bypass grafting. *Anesthesiology* 86: 331-345. [Crossref]
13. Kabukçu HK, Sahin N, Temel Y, Titiz TA (2011) Hemodynamics in coronary artery bypass surgery: effects of intraoperative dexmedetomidine administration. *Anaesthesist* 60: 427-431. [Crossref]
14. Ruff R, Reves JG (1990) Hemodynamic effects of a lorazepam-fentanyl anesthetic induction for coronary artery bypass surgery. *J Cardiothorac Anesth* 4: 314-317. [Crossref]
15. But AK, Durmus M, Toprak HI, Ozturk E, Demirbilek S et al. (2005) Hemodynamic, hepatorenal, and postoperative effects of desflurane-fentanyl and midazolam-fentanyl anesthesia in coronary artery bypass surgery. *J Cardiothorac Vasc Anesth* 19: 597-602. [Crossref]

16. Cruickshank M, Henderson L, MacLennan G, Fraser C, Campbell M et al. (2016) Alpha -2 agonists for sedation of mechanically ventilated adults in intensive care units: a systematic review. *Health Technol Assess* 20: 1-117. [Crossref]
17. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T et al. (2008) Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. *Anesth Analg* 106: 1741-1748. [Crossref]
18. Feringa HHH, Bax JJ, Boersma E, Kertai MD, Meij SH et al. (2006) High dose beta blockers and tight heart rate control reduce myocardial ischemia and troponin T release in vascular surgery patients. *Circulation* 114: 1344-1349. [Crossref]
19. Heck M, Kumle B, Boldt J, Lang J, Lehmann A et al. (2000) Electroencephalogram bispectral index predicts hemodynamic and arousal reactions during induction of anesthesia in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 14: 693-697. [Crossref]
20. Kertai MD, Whitlock EL, Avidan MS (2012) Brain monitoring with electroencephalography and the electroencephalogram-derived bispectral index during cardiac surgery. *Anesth Analg* 114: 533-546. [Crossref]
21. Hui C, Cardinale M, Yegneswaran B (2017) Significant Bradycardia in Critically Ill Patients Receiving Dexmedetomidine and Fentanyl. *Case Rep Crit Care* 2017: 4504207. [Crossref]
22. Aikaterini A, Ioannis D, Dimitrios G, Konstantinos S, Vasilios G et al. (2018) Bradycardia Leading to Asystole Following Dexmedetomidine Infusion during Cataract Surgery: Dexmedetomidine-Induced Asystole for Cataract Surgery. *Case Rep Anesthesiol* 2018: 2896032. [Crossref]