The Egyptian Journal of Hospital Medicine (July 2024) Vol. 96, Page 3305-3313

Evaluation of The Safety and Efficacy of Dexmedetomidine as an Anesthetic Adjuvant in Coronary Artery Bypass Grafting Surgeries

Omar Mohamed El-Safty, Abeer Mohamed El-Deek, Dalia Ahmed Ibrahim, Hany Magdy Fahim, Mohammed Khaled Shaker *

Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, Egypt.

* **Corresponding author:** Mohammed Khaled Abdelhameed Ahmed Shaker,
Email: dr.moh.khalid.shaker@hotmail.com, Phone: +20 114 111 1124

ABSTRACT:

Background: Coronary artery bypass grafting (CABG) is a key treatment for coronary artery disease, yet it carries a significant risk of complications due to surgical stress. Dexmedetomidine, an alpha-2 agonist, has been shown to modulate the surgical stress response and provide intraoperative hemodynamic stability, though its intraoperative use in cardiac surgeries is less explored.

Objective: This study aimed to evaluate the safety and efficacy of dexmedetomidine as an anesthetic adjuvant in CABG surgeries.

Patients and Methods: A prospective randomized controlled trial was conducted on 50 patients undergoing CABG, divided into two groups: Group D (dexmedetomidine) and Group P (placebo). Patients in Group D received dexmedetomidine throughout surgery, while Group P received saline. Hemodynamic parameters including heart rate, systolic (SBP), and diastolic blood pressure (DBP) were measured at multiple time points. Secondary outcomes included cortisol levels, opioid requirements, and incidence of postoperative cardiac complications.

Results: Dexmedetomidine significantly reduced heart rate and blood pressure at critical surgical milestones ($P < 0.001$). Mean SBP and DBP were lower in Group D compared to Group P, as was the need for vasodilators (12% vs. 64%, $P < 0.001$). Opioid requirements were reduced by 30% in Group D (mean fentanyl dose: 7.64 ± 1.58 µg/kg vs. 10.4 ± 1.44 µg/kg in Group P, $P < 0.001$). Postoperative cortisol levels were also significantly lower in Group D ($P < 0.001$).

Conclusion: Dexmedetomidine provides enhanced hemodynamic stability, reduces opioid requirements, and attenuates the stress response during CABG surgery, demonstrating its potential as an effective anesthetic adjuvant.

Keywords: Systolic blood pressure, Diastolic blood pressure, Mean blood pressure, Coronary artery bypass grafting, Cardio-pulmonary bypass, Coronary artery disease.

INTRODUCTION

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide. Despite recent epidemiological data indicating a decline in deaths related to ischemic heart disease, it continues to be associated with high morbidity and mortality rates [1]. Coronary artery bypass grafting (CABG) surgery is one of the primary therapeutic approaches for CAD, though it is not without complications. The 30-day mortality rate for on-pump CABG is approximately 1.2%, and for older patients (aged >65 years), the mortality rate climbs to 8.1% within one year [2].

Globally, more than 7 million invasive cardiovascular procedures are performed annually. According to the Society of Thoracic Surgeons (STS), the overall complication rate for CABG surgeries can reach as high as 30.1%. Significant postoperative complications include delirium, infections, acute renal failure (ARF), and major adverse cardio-cerebral events (MACE), which encompass permanent or temporary stroke, coma, myocardial infarction (MI), heart block, and cardiac arrest [3]. Cardiovascular events make up more than half of all perioperative complications, leading to prolonged hospital stays and elevated mortality rates. These complications are estimated to result in annual healthcare costs exceeding $20 billion. While the surgical stress response plays a significant role, the underlying causes of these complications are multifactorial. Alpha-2 receptors, a subtype of noradrenergic receptors, are essential in modulating the sympathetic nervous system. The activation of alpha-2 receptors inhibits norepinephrine release, which can be leveraged to reduce the surgical stress response and induce sympatholysis [4].

Dexmedetomidine, an alpha-2 agonist, was approved by the FDA in 1999 for sedation in adult intensive care patients. Its potential benefits in the ICU include aiding in ventilator weaning, enhancing pain management, and improving postoperative anesthesia after cardiac surgery, as several studies have demonstrated. Research has shown that dexmedetomidine reduces the need for intravenous and inhaled anesthetics during non-cardiac surgeries, decreases the requirement for postoperative opioid analgesics, and ensures intraoperative hemodynamic stability. However, there is limited evidence on the use of dexmedetomidine as an intraoperative adjunct in cardiac surgeries [4].

This study aimed to assess the potential advantages and limitations of using dexmedetomidine as an intraoperative adjunct during CABG.

PATIENTS and METHODS

The study was conducted on 50 patients assigned randomly according to a computer-generated list (Excel-Microsoft) into two groups; 25 patients in each group. Patients were of both sexes, 40-70 years old and eligible for inclusion if they had coronary artery

Received:10/4/2024
Accepted:10/6/2024

disease referred for CABG, which were done by experienced cardiovascular surgeons.

Timing of the study: 1 year (January 2017-December 2017).
Place of the study: Ain Shams University hospitals
Exclusion Criteria: were as follows

1. Patient's refusal to participate in the study.
2. Patients with known hypersensitivity to the study drug.
3. Acute myocardial infarction with elevated cardiac enzymes.
4. Severe impairment of cardiac contractility (ejection fraction ≤45 %) or any type of arrhythmia.
5. Significant valvular dysfunction.
6. Severe concurrent systemic disorder (e.g., kidney functions impairment, liver functions impairment or neurological disease).
7. Preoperative treatment with α2 agonist or α methyldopa.
8. If tracheal intubation was difficult, which takes more than 15 seconds.

- **Design of the Study*:*** prospective randomized control trial.
- **Setting of the Study:** Ain Shams University Hospitals.
- **Patient's Evaluation*:*** during the assessment, all enrolled patients were subjected to the following: assessment of baseline demographic characteristics and full history taking; including preexisting conditions (such as hypertension, dyslipidemia, diabetes mellitus, cerebrovascular stroke history and hypercoagulable state), organ functions.

Clinical examinations included: routine hematologic and laboratory measurements within 24 hours before the administration of the study drug, including complete blood count (CBC), liver function tests (LFT), random blood sugar (RBS), kidney function tests (KFT), partial thromboplastin time (PTT), prothrombin time (PT), and international normalized ratio (INR), electrocardiogram (ECG), echocardiography examination, cardiac enzymes, chest X-ray and coronary angiography.

Study Groups:

On admission to OR unit, the cases were randomized into two groups*:* **Group D (**25 patients**):** These patients received combined volatile and narcotic based anesthesia in addition to induction and maintenance infusion of dexmedetomidine according to the body weight throughout all steps of the surgery till start of skin closure. **Group P (**25 control patients**):** these patients received combined volatile and narcotic based anesthesia without addition of dexmedetomidine in any step of the surgery, instead placebo normal saline was given in the same way as study drug. Both groups in the preparation room underwent wide bore peripheral venous cannulation, arterial cannulation, central venous line was established, all were done under complete aseptic conditions. Then standard monitoring (non-invasive blood pressure, pulse oximetry, ECG) in addition to invasive blood pressure were settled. Then as regard **group D,** dexmedetomidine (Precedex®, dexmedetomidine hydrochloride, Pfizer company) loading dose (1 mic/kg) was diluted in 10 c.c. syringe with normal saline and was given over 20 minutes by a syringe pump in order to avoid the bradycardia, which was noted after rapid administration in multiple previous clinical trials, followed by maintenance infusion dose (0.5 mic/kg/min) all through the surgery including the cardiopulmonary bypass (CPB) time till start of skin closure when it was stopped, On the other hand **group P,** normal saline placebo was administered as a loading dose of normal saline in 10 cc syringe by a syringe pump over 20 minutes then start an infusion by 5 ml per hour till start of skin closure when was it stopped also.

Anesthesia Induction: All patients underwent preoxygenation for three minutes using a face mask with 100% oxygen. Anesthesia was initiated by administering thiopental as a 2.5% solution at a dose of 5 mg/kg until the loss of the eyelash reflex was observed, followed by fentanyl at 5 mcg/kg, rocuronium at 0.6 mg/kg, and midazolam at 0.02 mg/kg. If the anesthesiologist detected clinically significant chest wall rigidity induced by fentanyl during its administration, manual ventilation with 100% oxygen was provided. Rocuronium was either given immediately at a dose of 0.6 mg/kg or administered one minute after the fentanyl injection for muscle relaxation. Tracheal intubation was performed three to four minutes after full muscle relaxation was achieved.

Anesthesia maintenance

Anesthesia was maintained using sevoflurane at an inspiratory concentration of 1.7%. Rocuronium was infused at 0.2 mg/kg/min, along with incremental doses of fentanyl at 1 mcg/kg, to sustain anesthesia and keep blood pressure within 20-30% of baseline during periods of stress. Ringer's lactate was administered at a rate of 10 ml/kg/hour, along with either a dexmedetomidine infusion or a placebo. If needed, boluses of 5 ml/kg were given to maintain central venous pressure between 6-10 mmHg. End-tidal carbon dioxide levels were controlled within a range of 35-40 mmHg using mechanical ventilation with H_2O and a fractional inspired oxygen concentration of 1, along with an inspiration-to-expiration ratio of 1:2.

During CPB, a membrane oxygenator was used, primed with 2000 ml of crystalloid solution, 100 ml of 20% mannitol, and 5000 IU of heparin, with a roller pump providing circulation. The initial heparin dose was 300 IU/kg, maintaining an activated coagulation time (ACT) of 480 seconds or more. Hematocrit levels were kept between 25-30%, while pH control followed the alpha-stat strategy. Mean blood pressure was regulated between 40 and 70 mmHg, and nasopharyngeal

temperature was reduced to 32°C. The pump flow rate was maintained between 2.4 and 3 L/min/m², with a flow rate of 1.6 L/min/m² during hypothermia.

To achieve electromechanical quiescence, 15 ml/kg of cold antegrade crystalloid cardioplegia solution containing potassium and magnesium was administered. Heparin was neutralized with protamine based on the patient's ACT after the completion of CPB. Post-surgery, the patient was transferred to the critical care unit for sedation, intubation, and ventilation, with the study medication infusion discontinued at the conclusion of the procedure.

Study Outcomes:

The following time intervals were used to record heart rate, SBP, and DBP: baseline measurement upon admission to the preparation room, 5 minutes after administering the study drug's loading dose, 5 minutes post-endotracheal intubation, and 5 minutes after sternotomy, at the start of skin closure, and 10 minutes had passed since detachment from CPB.

All procedures were conducted in the morning, except during CPB, when mean arterial pressure MAP was monitored every 10 minutes, along with the requirement for vasoactive or vasodilator agents, the total amount of opioid medication (Fentanyl) administered, and serum cortisol levels were measured at baseline, 10 minutes post-sternotomy, and 10 minutes after CPB. Each patient was connected to a Holter ECG with two bipolar leads (CC5 and modified CM5) starting just before induction and continuing for 48 hours post-operation to monitor recovery rhythms, use of DC shock, and detection of any arrhythmias or ischemic events. A single cardiologist, blinded to patient identity, treatment, and clinical outcomes, independently reviewed all ischemic events.

The baseline S-T segment level was defined as the average S-T segment level taken over an extended period during the initial registration phase while the patient was in a supine position. An ischemic episode was characterized by a reversible deviation in the S-T segment of more than 1 mm (0.1 mv) below baseline or more than 2 mm above baseline, lasting at least 1 minute, the development of new Q waves, or an increase in creatine kinase MB isoenzyme activity to more than 100 U/l during surgery or more than 70 U/l at any point after 12 hours post-surgery, and continuing for up to 48 hours.

End Points*:* patient refusal at any time, acute hemodynamic instability, mortality and appearance of allergy to dexmedetomidine.

Ethical Considerations:

This study was conducted following approval from the Research Ethics Committee at Ain Shams University. Written informed consent was obtained from all participants prior to their enrolment in the study, ensuring that they were fully aware of the study's purpose and their rights, including the confidentiality and privacy of their data. The consent form also covered permission for the publication of results. This research adhered to the ethical guidelines outlined in the Declaration of Helsinki for studies involving human subjects.

Data Management and Statistical Analysis:

Data management and statistical analysis were conducted using SPSS version 26 (IBM, Armonk, New York, United States). Normality of quantitative data was assessed using the Kolmogorov–Smirnov test, the Shapiro-Wilk test, and direct data visualization methods. Quantitative data were summarized as means, standard deviations, and ranges. Categorical data were presented as numbers and percentages. For comparisons between the study groups, the independent t-test was used for normally distributed quantitative variables, while the Mann-Whitney U test was applied for non-normally distributed variables. Categorical data were compared using the Chi-square or Fisher's exact test. All statistical tests were two-sided, and P values less than 0.05 were considered significant.

RESULTS

The 2 groups were matched as regard age, sex and weight. Weight of the study group was significantly lower than the control group.

Table 1: Comparison between control group P and study group D as regard demographic data.

		Control group P	Study group D	Test value	P-value	Sig.
		No. = 25	No. = 25			
Age (Years)	Mean ± SD	58.16 ± 6.39	57.52 ± 6.63	-0.348	0.730	NS
	Range	49 – 70	45 – 70			
Sex	Female	7 (28.0%)	8 (32.0%)	0.095	0.758	NS
	Male	18 (72.0%)	17 (68.0%)			
Weight (kg)	Mean ± SD	89.6 ± 15.87	80.8 ± 13.04	-2.142	0.037	S
	Range	60 – 130	55 – 100			

SD: standard deviation, Sig.: Significance, NS: Not Significant, S: Significant

The 2 groups were matched as regard basal heart rate in different occasions. The heart rate of the study group was significantly lower than the control group.

Table 2: Comparison between control group P and study group D as regard heart rate.

		Control group P	Study group D	Test value	P-value	Sig.
		No. = 25	No. = 25			
HR basal (beat per minute)	Mean ± SD	78.2 ± 9	75.8 ± 4.49	-1.193	0.239	NS
	Range	60 – 90	65 – 80			
HR 5 after loading dose	Mean ± SD	80 ± 7.22	63.8 ± 3.89	-9.877	<0.001	HS
	Range	70 – 90	60 – 70			
HR 5 after ETT	Mean ± SD	96.8 ± 6.27	72.6 ± 5.61	-14.377	<0.001	HS
	Range	85 – 110	65 – 85			
HR 5 after Stern	Mean ± SD	92.6 ± 5.8	70.8 ± 4.49	-14.867	<0.001	HS
	Range	80 – 100	65 – 80			
HR 10 after separation CPB	Mean ± SD	95.8 ± 6.24	83 ± 5.2	-7.878	<0.001	HS
	Range	90 – 110	75 – 100			
HR skin closure	Mean ± SD	91.8 ± 6.44	81.6 ± 3.14	-7.124	<0.001	HS
	Range	85 – 110	75 – 90			

HR: Heart Rate, SD: Standard Deviation, ETT: Endotracheal Tube, CPB: Cardiopulmonary Bypass, Sig.: Significance, NS: Not Significant, HS: Highly Significant.

The 2 groups were matched as regard systolic blood pressure. Systolic blood pressure of the study group was significantly lower than the control group.

Table 3: Comparison between control group P and study group D as regard systolic blood pressure (SBP).

		Control group P	Study group D	Test value	P-value	Sig.
		No. = 25	No. = 25			
SBP basal(mmHg)	Mean ± SD	136.8 ± 23.4	138 ± 14.43	0.218	0.828	NS
	Range	110 – 170	110 – 160			
SBP 5 min. after loading dose	Mean ± SD	140.8 ± 12.22	109.4 ± 18.84	-6.992	<0.001	HS
	Range	115 – 160	60 – 140			
SBP 5 min. after ETT	Mean ± SD	164.6 ± 13.61	131.4 ± 18.57	-7.210	<0.001	HS
	Range	145 – 190	80 – 160			
SBP 5 min. after Sternotomy	Mean ± SD	150.6 ± 14.02	119.6 ± 19.68	-6.415	<0.001	HS
	Range	110 – 170	60 – 150			
SBP 10 min. after CPB	Mean ± SD	88.6 ± 10.75	82.4 ± 8.31	-2.281	0.027	S
	Range	60 – 110	60 – 100			
SBP Skin closure	Mean ± SD	111.72 ± 13.44	97.6 ± 8.79	-4.396	<0.001	HS
	Range	80 – 130	80 – 110			

SBP: Systolic Blood Pressure, SD: Standard Deviation, ETT: Endotracheal Tube, CPB: Cardiopulmonary Bypass, Sig.: Significance, NS: Not Significant, HS: Highly Significant, S: Significant.

The 2 groups were matched as regard diastolic blood pressure. Diastolic blood pressure of the study group was significantly lower than the control group.

Table 4: Comparison between control group P and study group D as regard diastolic blood pressure (DBP).

		Control group P	Study group D	Test value	P-value	Sig.
		No. = 25	No. = 25			
DBP basal(mmHg)	Mean ± SD	81.4 ± 10.95	80.4 ± 9.35	-0.347	0.730	NS
	Range	60 – 100	60 – 90			
DBP 5 min. After loading	Mean ± SD	82.4 ± 8.67	61.6 ± 11.43	-7.247	<0.001	HS
	Range	65 – 95	40 – 80			
DBP 5 min. after ETT	Mean ± SD	96.8 ± 8.02	74.6 ± 11.72	-7.816	<0.001	HS
	Range	80 – 110	50 – 90			
DBP 5 min. after Sternotomy	Mean ± SD	88.2 ± 10.09	67.8 ± 12.42	-6.373	<0.001	HS
	Range	50 – 100	40 – 90			
DBP 10 min. after separation from CPB	Mean ± SD	48.8 ± 7.4	47 ± 14.14	-0.564	0.575	NS
	Range	30 – 60	30 – 90			
DBP at skin closure	Mean ± SD	59.4 ± 6.82	54 ± 5.77	-3.022	0.004	HS
	Range	50 – 80	40 – 60			

DBP: Diastolic Blood Pressure, SD: Standard Deviation, ETT: Endotracheal Tube, CPB: Cardiopulmonary Bypass, Sig.: Significance, NS: Not Significant, HS: Highly Significant.

The 2 groups were matched as regard mean arterial blood pressure. Mean arterial blood pressure of the study group was significantly lower than the control group.

Table 5: Comparison between control group P and study group D as regard mean arterial blood pressure (MBP) every 10 minutes during cardiopulmonary bypass.

Every 10 minutes during CPB		Control group P	Study group D	Test value	P-value	Sig.
		No. = 25	No. = 25			
MBP basal(mmHg)	Mean ± SD	72.8 ± 8.3	52.8 ± 8.3	8.518	<0.001	HS
	Range	50 – 85	50 – 85			
10 minutes	Mean ± SD	54.6 ± 7.76	47.6 ± 6.14	-3.536	0.001	HS
	Range	35 – 70	40 – 70			
20 minutes	Mean ± SD	59.68 ± 6.52	51.8 ± 10.09	-3.279	0.002	HS
	Range	50 – 75	40 – 90			
30 minutes	Mean ± SD	59 ± 7.22	49.8 ± 9.84	-3.77	<0.001	HS
	Range	50 – 70	40 – 90			
40 minutes	Mean ± SD	60.8 ± 7.31	48.2 ± 5.38	-6.94	<0.001	HS
	Range	50 – 75	40 – 60			
50 minutes	Mean ± SD	60.2 ± 6.84	50 ± 4.33	-6.298	<0.001	HS
	Range	50 – 70	45 – 60			

MBP: Mean Blood Pressure, CPB: Cardiopulmonary Bypass, SD: Standard Deviation, Sig.: Significance, HS: Highly Significant.

The 2 groups were matched as regard opioid usage. Opioid usage of the study group was significantly lower than the control group. But vasoactive drugs were used more significantly higher in study group.

Table 6: Comparison between control group P and study group D as regard usage of vasoactive, vasodilator medications, and total opioid medication (fentanyl) used to maintain hemodynamics around 20-30% basal values.

Vasoactive, vasodilators, or opioids used to maintain hemodynamics around 20-30% basal values		**Control group P**	**Study group D**	**Test value**	**P-value**	**Sig.**
		No. = 25	**No. = 25**			
Vasoactive	No	7(28.0%)	2 (8.0%)	10.965	0.001	HS
	Yes	18 (72.0%)	23 (92.0%)			
Vasodilator	No	9 (36.0%)	22 (88.0%)	14.346	<0.001	HS
	Yes	16 (64.0%)	3 (12.0%)			
Total fentanyl (mic/kg)	Mean ± SD	10.4 ± 1.44	7.64 ± 1.58	-6.453	<0.001	HS
	Range	8 – 14	5 – 10			

Sig.: Significance, HS: Highly Significant, SD: Standard Deviation.

The 2 groups were matched as regard cortisol level. Cortisol level. of the study group was significantly lower than the control group.

Table 7: Comparison between control group P and study group D as regard cortisol level.

		Control group P	**Study group D**	**Test value**	**P-value**	**Sig.**
		No. = 25	**No. = 25**			
Cortisol level Basal(mcg/dl)	Mean ± SD	13.8 ± 2.14	11.6 ± 1.63	-4.089	<0.001	HS
	Range	9 – 17	9 – 15			
Cortisol level 10 min. after sternotomy	Mean ± SD	31.96 ± 1.93	17.84 ± 1.28	-30.533	<0.001	HS
	Range	29 – 36	15 – 19			
Cortisol level 10 min. after CBP	Mean ± SD	29.76 ± 1.67	15.84 ± 0.99	-35.957	<0.001	HS
	Range	27 – 33	14 – 18			

SD: Standard Deviation, CPB: Cardiopulmonary Bypass, Sig.: Significance, HS: Highly Significant.

The 2 groups were matched as regard age and sex. Weight of the study group was significantly lower than the control group.

Table 8: Comparison between control group P and study group D as regard recovery rhythm, DC shock usage, and cardiac complications up to 48 hours postoperative.

		Control group P	**Study group D**	**Test value**	**P-value**	**Sig.**
		No. = 25	**No. = 25**			
Recovery rhythm	Sinus	14 (56.0%)	18 (72.0%)	1.389	0.239	NS
	Arrhythmic	11 (44.0%)	7 (28.0%)			
DC shock usage	No	14 (56.0%)	18 (72.0%)	1.389	0.239	NS
	Yes	11 (44.0%)	7 (28.0%)			
Cardiac complications	No	13 (52.0%)	17 (68.0%)	1.333	0.248	NS
	Yes	12 (48.0%)	8 (32.0%)			

DC: Direct Current, Sig.: Significance, NS: Not Significant.

DISCUSSION

CAD remains the leading cause of morbidity and mortality globally. CABG is a key therapeutic option but is associated with significant rates of morbidity and mortality. The causes of these adverse outcomes are complex, with the surgical stress response playing a major role [3].

The stress response to surgical trauma triggers a significant neuroendocrine and cytokine reaction, marked by increased levels of catecholamines and steroid hormones, which in turn produce expected metabolic effects. This stress response is considered an essential homeostatic mechanism that helps the body adapt and build resilience to harmful stimuli. However, in individuals with comorbidities, the presence of such pronounced physiological changes can be dangerous. A prolonged stress response can result in fatigue, reduced resistance, delayed recovery, and increased morbidity and mortality due to a sustained hypermetabolic state caused by the depletion of essential resources [5,6].

Alpha-2 receptors, a subset of noradrenergic receptors, play a key role in regulating the sympathetic nervous system. These presynaptic receptors, when activated, do not trigger or inhibit the release of epinephrine, and can be therapeutically utilized to achieve sympatholysis. Dexmedetomidine, an alpha-2 adrenergic agonist, was approved by the FDA in 1999 for sedation in adult patients in the intensive care unit. Previous studies in non-cardiac surgery have demonstrated that dexmedetomidine reduces the need for intravenous and inhalational anesthetics, maintains intraoperative hemodynamic stability, and decreases the requirement for postoperative opioid analgesics. Several clinical studies have explored its use in the ICU, showing its potential to enhance the quality of sedation, improve pain management for postoperative heart surgery patients, and assist in weaning patients off mechanical ventilation. However, there is limited knowledge regarding the intraoperative use of dexmedetomidine as an adjunct to anesthesia in cardiac surgeries [7,8].

The present clinical trial tried to demonstrate the effectiveness and safety of dexmedetomidine usage in CABG surgeries as an adjuvant to anesthesia in order to attenuate stress response including its accompanied adverse effect, and decrease doses of anesthetics, which helps in more safe CABG surgeries.

Two groups of patients (Group D and group P), 25 patients in each group, were selected randomly and were administered dexmedetomidine to group D and placebo to the other group P. Then the results of the two groups were compared as follow.

In terms of demographic data, no statistically significant differences were identified between the two groups. All patients met the inclusion criteria, having no major comorbidities, and received the same standard anti-ischemic treatments, including beta-blockers, antiplatelet agents, statins, and nitrates as necessary.

This study found no significant differences between the two groups in terms of the hemodynamic effects of dexmedetomidine. However, heart rates in group D were significantly lower than those in control group P at the following intervals: 5 minutes after the loading dose, 5 minutes post-sternotomy, 10 minutes after separation from CPB, and at the start of skin closure, with a P-value of less than 0.001.

Baseline systolic and diastolic blood pressure measurements showed no notable differences. However, group D displayed significantly lower systolic and diastolic blood pressure compared to group P at the same intervals: 5 minutes post-loading dose, 5 minutes after sternotomy, 10 minutes post-CPB separation, and during skin closure, also with a P-value of less than 0.001, following administration of the study drug and placebo.

During cardiopulmonary bypass, the mean arterial pressure in group D was consistently lower every 10 minutes compared to control group P, with a P-value of less than 0.001. This indicates that patients in group D maintained better hemodynamic stability during stressful periods compared to those in control group P.

The results of our study are consistent with those reported by **Jaakola *et al.*** [9], who investigated the analgesic effects of dexmedetomidine. Their study demonstrated that dexmedetomidine enhances hemodynamic stability by modulating the sympathoadrenal responses triggered by intubation during surgery and awakening from anesthesia. They found that dexmedetomidine reduced the typical increases in blood pressure and heart rate associated with intubation, using a dosage similar to the one we applied in our study.

Additionally, our findings are in agreement with **Sulaiman *et al.*** [10], who studied the effects of dexmedetomidine in reducing the stress response to endotracheal intubation in patients undergoing elective off-pump CABG. Their research showed that pretreatment with dexmedetomidine at a dose of 0.5 μg/kg, administered as a 10-minute infusion before anesthesia induction, decreased the hemodynamic response to laryngoscopy and intubation.

Dexmedetomidine administration is associated with a biphasic cardiovascular response. In young, healthy individuals, a temporary increase in arterial blood pressure followed by a reflexive decrease in heart rate is observed after administering a 1 μg/kg bolus. This initial response is due to the activation of vascular smooth muscle via α2 receptors. A slow infusion over 10 minutes can significantly reduce this effect. In our trial, this reaction was not observed because the drug was administered gradually over a 10-minute period [11].

Jalonen *et al.* [12] reported that the intraoperative incidence of bradycardia requiring intervention was not higher in the dexmedetomidine group compared to the control group in CABG patients on beta blockers. Since long-acting beta receptor antagonists had already inhibited beta receptors, any additional sympathetic blockade from dexmedetomidine was minimal. As a result, dexmedetomidine significantly reduced the

responses of systolic and diastolic blood pressure, as well as heart rate, to stress during surgery.

Our findings indicated that 92% of patients in group D required vasoactive agents, such as ephedrine, adrenaline, and noradrenaline, compared to only 72% in group P. Additionally, group D received more fluid challenge boluses to maintain systolic pressure above 90 mmHg. In contrast, 64% of patients in group P required vasodilators like glyceryl trinitrate, while only 12% of patients in group D needed similar interventions to prevent hypertensive responses to surgical stress.

The results of our study align with those of **Jalonen *et al.*** [12], who investigated the impact of dexmedetomidine on coronary hemodynamics and myocardial oxygen balance. They found that the median dose of ephedrine required in the dexmedetomidine group was roughly double that of the placebo group, while the median glyceryl trinitrate dose was lower in the dexmedetomidine group. The FDA has labeled dexmedetomidine as "analgesia-sparing" due to its ability to stabilize hemodynamics.

In this study, the placebo group (group P) required 8-14 mcg/kg of opioids to manage stressful events and control the hemodynamic response, whereas the dexmedetomidine group (group D) needed only 5-10 mcg/kg. The average opioid doses for group P and group D were 10.4 mcg/kg and 7.64 mcg/kg, respectively, reflecting a 30% reduction in fentanyl usage with dexmedetomidine, confirming its analgesia-sparing effect and facilitating faster cardiac surgery procedures.

The primary goal of accelerated anesthetic protocols is to achieve patient extubation within 1 to 6 hours after ICU admission. These protocols are associated with improved postoperative hemodynamics, lower rates of atrial fibrillation, fewer postoperative respiratory infections, reduced healthcare costs, and more efficient use of hospital resources. The findings of this study suggest that dexmedetomidine could serve as an anesthetic agent for accelerated surgical procedures [13].

Afanador *et al.* [14] conducted a study investigating the impact of intraoperative dexmedetomidine on anesthetic requirements and the time to tracheal extubation in patients undergoing elective adult cardiac surgery. Their findings were consistent with the current study, demonstrating that dexmedetomidine reduced opioid consumption by 48% in CABG patients compared to the placebo group.

Surgical trauma triggers a cytokine cascade, a complex biochemical process that affects the injured host in various ways. Cytokines are immune mediators critical for wound healing and regulating the inflammatory response at the site of injury or infection. However, excessive production of proinflammatory cytokines from the primary injury site can lead to hemodynamic instability or metabolic imbalances. Under stress, the hypothalamus stimulates the release of ACTH, which rapidly elevates cortisol levels. Cortisol's metabolic effects are intended to help the body cope with stress. It plays a significant role in regulating the metabolism and utilization of glucose, amino acids, and fatty acids in both liver and peripheral tissues. Cortisol enables the quick release of amino acids and lipids from cellular stores, making them available for energy production and the synthesis of other essential molecules like glucose for various tissues [15].

In this study, cortisol level was used as a marker for stress response to the surgery, which was withdrawn in three occasions, first was basal reading on presentation to OR, second after 10 minutes of sternotomy, and finally after 10 minutes from weaning off CPB. It was found that there were no differences in basal readings especially that all operations were done at early morning to avoid variations of normal physiological circadian rhythm of cortisol. However, 10 minutes after the stress of induction of anesthesia, endotracheal intubation, skin incision, and sternotomy it was found that the range of cortisol level in study group D was significantly lower "range 15-19, mean 17.84" in contrast to control group P "range 29-36, mean 31.96" with P-value (<0.001). In addition, 10 minutes after weaning off CPB the cortisol level readings still had significantly lower values in study group D "range 14-18, mean 15.84" in contrast to control group P "range 27-33, mean 29.76" with P-value (<0.001).

Aho *et al.* [16] found that patients who received dexmedetomidine before surgery had significantly lower intraoperative cortisol levels compared to those who did not receive the drug. This observation is consistent with the current study, where dexmedetomidine was associated with reduced levels of stress response markers during surgery, reinforcing the findings of this research.

Uyar and colleagues [17] conducted a study on the attenuation of hemodynamic and neuroendocrine responses to the application of skull-pin head-holders during craniotomy using dexmedetomidine. Their results showed that plasma cortisol and glucose levels were significantly higher in the placebo group compared to the dexmedetomidine group. Our findings align with these results, demonstrating that dexmedetomidine effectively mitigated the neurohormonal effects of the stress response, thereby protecting patients from its negative consequences.

Studies suggest that the perioperative administration of dexmedetomidine may reduce the risk of adverse cardiac events, such as myocardial ischemia, by improving coronary blood flow during ischemic episodes. This is achieved by preventing the redistribution of transmural blood flow away from the ischemic endocardium through targeted epicardial vasoconstriction, which enhances endocardial perfusion (known as the reverse steal effect) and lowers heart rate. Dexmedetomidine also boosts the coronary vasodilation effect mediated by adenosine and raises cAMP levels, a mechanism referred to as preconditioning [11].

In the present study it was found that initial re-perfusion rhythm in study group D was not sinus rhythm in 28% of patients (7 patients) in the form of, supra-

ventricular tachycardia rhythm (SVT) in 3 patients, and ventricular fibrillation (VF) in 4 patients, through which all patients needed D.C shock to regain sinus rhythm. On the other side, control group P where arrhythmic rhythm was noted in 44% of patients (11 patients) in the form of, 3 patients was SVT and 8 patients was VF, and all regained sinus rhythm by D.C shock trial. This difference was not statistically significant but was considerable clinically. As regards postoperative cardiac complications, in study group D 32% (8 patients) of patients developed cardiac complications as 5 patients developed SVT rhythm, 2 patients developed atrial fibrillation (AF) rhythm, and one patient developed myocardial ischemia in first 4 hours postoperatively. On the other side group P, where 48% (12 patient) of patients developed postoperative cardiac complications as 4 patients developed SVT rhythm, 6 patients developed AF rhythm, and 2 patients developed ischemic episode in first 24 hour postoperatively. This difference was not statistically significant also but was considerable clinically.

The study did not demonstrate a statistically significant protective effect of dexmedetomidine on the myocardium, despite a clinically meaningful difference between the two groups.

Consistent with this study, **Geng *et al.*** [3] investigated the impact of perioperative dexmedetomidine in patients undergoing heart surgery. Their findings indicated no statistically significant benefit of preoperative dexmedetomidine administration in reducing postoperative major adverse cardiovascular events. However, from a clinical perspective in the operating room, the use of perioperative dexmedetomidine was still supported.

Our results also align with those of **Jalonen *et al.*** [12], who studied the effects of dexmedetomidine on coronary hemodynamics and myocardial oxygen balance. However, their research did not confirm that the intraoperative use of dexmedetomidine would lower the incidence of postoperative atrial fibrillation in cardiac surgery patients.

One limitation of this study is the relatively small sample size of 50 patients, which may limit the generalizability of the findings. Additionally, the study was conducted in a single center, which may introduce bias related to institutional practices. The short follow-up period also restricted the ability to assess long-term outcomes and complications associated with dexmedetomidine use in CABG patients. Further multicenter studies with larger sample sizes and extended follow-up are needed to validate these findings.

CONCLUSION

Dexmedetomidine provides enhanced hemodynamic stability, reduces opioid requirements, and attenuates the stress response during CABG surgery, demonstrating its potential as an effective anesthetic adjuvant.

- **Financial support and sponsorship: Nil.**
- **Conflict of Interest: Nil.**

REFERENCES

1. **Lamy A, Devereaux P, Prabhakaran D *et al.* (2012)**: Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med., 366:1489-97.
2. **Shahian D, O'Brien S, Sheng S *et al.* (2012)**: Predictors of long-term survival after coronary artery bypass grafting surgery: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database (the ASCERT study). Circulation, 125:1491-500.
3. **Geng J, Qian J, Cheng H *et al.* (2016)**: The influence of perioperative dexmedetomidine on patients undergoing cardiac surgery: A meta-analysis. PLoS One, 11:e0152829.
4. **Venn R, Grounds R (2001)**: Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions. Br J Anaesth., 87:684-90.
5. **Finnerty C, Mabvuure N, Ali A *et al.* (2013)**: The surgically induced stress response. JPEN J Parenter Enteral Nutr., 37:21s-9s.
6. **Cusack B, Buggy D (2020)**: Anaesthesia, analgesia, and the surgical stress response. BJA Educ., 20:321-8.
7. **Hein L, Altman J, Kobilka B (1999)**: Two functionally distinct alpha2-adrenergic receptors regulate sympathetic neurotransmission. Nature, 402:181-4.
8. **Giovannitti J, Thoms S, Crawford J (2015)**: Alpha-2 adrenergic receptor agonists: a review of current clinical applications. Anesth Prog., 62:31-9.
9. **Jaakola M, Salonen M, Lehtinen R *et al.* (1991)**: The analgesic action of dexmedetomidine--a novel alpha 2-adrenoceptor agonist--in healthy volunteers. Pain, 46:281-5.
10. **Sulaiman S, Karthekeyan R, Vakamudi M *et al.* (2012)**: The effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. Ann Card Anaesth., 15:39-43.
11. **Saraf R, Jha M, Damani K *et al.* (2013)**: Dexmedetomidine, the ideal drug for attenuating the pressor response. Pediatric Anesthesia & Critical Care Journal, 1:3859-62.
12. **Jalonen J, Halkola L, Kuttila K *et al.* (1995)**: Effects of dexmedetomidine on coronary hemodynamics and myocardial oxygen balance. J Cardiothorac Vasc Anesth., 9:519-24.
13. **Horswell J, Herbert M, Prince S *et al.* (2005)**: Routine immediate extubation after off-pump coronary artery bypass surgery: 514 consecutive patients. J Cardiothorac Vasc Anesth., 19:282-7.
14. **Afanador C, Marulanda L, Torres G *et al.* (2009)**: Effect of intraoperative use of dexmedetomidine on anesthetic requirements and time to tracheal extubation in elective adult heart surgery patients. A retrospective cohort study. Internet J Anesthesiol., 22:2-10.
15. **Lin E, Calvano S, Lowry S (2000)**: Inflammatory cytokines and cell response in surgery. Surgery, 127:117-26.
16. **Aho M, Scheinin M, Lehtinen A *et al.* (1992)**: Intramuscularly administered dexmedetomidine attenuates hemodynamic and stress hormone responses to gynecologic laparoscopy. Anesth Analg., 75:932-9.
17. **Uyar A, Yagmurdur H, Fidan Y *et al.* (2008)**: Dexmedetomidine attenuates the hemodynamic and neuroendocrinal responses to skull-pin head-holder application during craniotomy. J Neurosurg Anesthesiol., 20:174-9.