Section: Anesthesiology

Research

COMPARATIVE OBSERVATIONAL PROSPECTIVE RANDOMIZED STUDY TO DETERMINE THE EFFECT OF CLONIDINE AS AN ADJUNCT TO INDUCTION AGENTS IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING SURGERY

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Abstract

Background: An alpha 2 adrenergic agonist, clonidine has been shown to have perioperative effects such as decreased anaesthetic needs, improved hemodynamic equilibrium, and analgesia, although its therapeutic utility in cardiac surgery remains understudied. We attempted to observe the effect of clonidine as an adjunct to induction agents and study the intraoperative hemodynamics in patients undergoing coronary artery bypass grafting surgery (CABG). **Materials and Methods:** Eighty subjects were recruited as per the eligibility criteria and subdivided into two groups with forty subjects each, i.e., the control group receiving normal saline and the case groups receiving I.V. clonidine as a pre-medication dose of 4µg/kg in the OT. The patients were then induced with injections of midazolam (0.1 mg/kg), fentanyl (5-10 µg/kg) and vecuronium (0.1mg/kg). For maintenance, a sevoflurance (2%) sedation mixture was used. Various intraoperative and hemodynamic parameters were monitored at various timepoints. **Result:** In control groups, parameters such as SBP, DBP, HR, MAP, and HCO3 significantly deviated from baseline, albeit the case group displayed the stabilised effect of clonidine over these parameters when compared to their baseline values. On the other hand, parameters like CVP, K+, PCO2, PO2, ACT, and HCT values significantly differed in both the groups upon intragroup comparison from baseline. **Conclusion:** Upon comparison, premedication treatment with intravenous clonidine as an adjunct to induction agents in patients undergoing coronary artery bypass grafting surgery (CABG) reduced hyperdynamic responses to anaesthesia and surgery.

INTRODUCTION

Patients with pre-existing heart illness and cardiac operations that involve strong surgical stimulation and cardiopulmonary bypass (CPB) present unique challenges for anaesthesia. Hypertension and tachycardia, together with enhanced sympathetic nervous system activity, may result in a discrepancy among myocardial energy demand and availability. Individuals experiencing coronary artery disease (CAD) or those at susceptibility of ischemic heart disorders (IHD) may experience myocardial ischemia.[1] Myocardial ischemia is a major preoperative risk factor for myocardial infarction, a potentially life-threatening event that can also reduce a patient's functional capacity.[1] Many different induction medications, including Pentothal sodium, propofol, etomidate, etc., have been employed, often in combinations with other medications like opioids and benzodiazepines. Reservations about using the full dose of these induction drugs have been highlighted by a number of researchers due to the absence of haemodynamic consistency.[2] Adjuvants such as benzodiazepines and opioids given before induction help control the patient's stress response and lower the overall dose of induction drugs needed during intubation.[3] As a result, it is usual practise to combine opioids and benzodiazepines for induction or as adjuvants with conventional induction drugs.

In therapeutic use, clonidine, a centrally acting 2-agonist, was initially implemented as a treatment for hypertension. Recently, the substance has been employed as an anaesthetic premedication due to its sedative, anxiolytic, and analgesic properties. In reaction to the stress of anaesthetics and surgical operations, clonidine reduces blood pressure, heart rate, and the hormone norepinephrine is released.[4] Clonidine has the potential to alleviate the need for anaesthetics and analgesics, to enhance perioperative hemodynamic stability, to minimise the risk of myocardial ischemia, to boost renal function, to induce sedation and relaxation, and to attenuate the

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neurohumoral stress response that often accompanies major surgical procedures. It has been suggested that pre-operative clonidine treatment, by increasing myocardial oxygen supply, can reduce the risk of myocardial ischemia in the operating room. [4,5] Thus, the present study aims to observe the effect of clonidine as an adjunct to induction agents and study the intraoperative hemodynamics in patients undergoing coronary artery bypass grafting surgery (CABG).

MATERIALS AND METHODS

Study Design, Approval and Duration

This comparative observational prospective randomised study was conducted in the Department of Anesthesiology, D Y Patil Deemed to be University, School of Medicine and Hospital, Nerul, Navi Mumbai. This study was duly approved by the Institutional Ethic Committee (IEC Ref no: DYP/IEBH/2021/007) before its commencement. The study duration was November 2020 to February 2022. The subjects were enrolled as per the pre-set eligibility criteria and informed consent was taken from all the participants post-providing detailed information about the study.

Eligibility Criteria

All consenting patients in the age range of 30-65 years, ASA grade II or III of either sex, undergoing CABG with ejection fraction > 40% without pulmonary hypertension were included in the study. Whereas all non-consenting patients with age < 30years and > 65 years and ejection fraction < 40% were excluded from the study. Also, any subjects with a history or cases of pregnancy, pulmonary hypertension, valvular heart disease, bronchial asthma, or on treatment with anti-psychotic drugs were also not allowed to participate in the study.

Study Procedure

Pre-operative evaluation encompassing undertaking history, clinical examination, routine investigation, stress test, 2D-ECHO, and coronary angiography was performed for all the enrolled subjects. On the day of surgery, the study participants were randomly allocated to two groups using the sealed envelope technique, with each group containing forty patients.
Control (Placebo), n= 40: Patients allocated to this group received I.V. 0.9% normal saline in the OT
Cases (Clonidine), n= 40: Patients allocated to this group received I.V. clonidine as a pre-medication dose of 4µg/kg in the OT.
Pre-operative vitals were recorded in the form of baseline pulse and blood pressure. After arriving in the OT, monitors were attached to a manual BP cuff, pulse oximeter, ECG leads, temperature probe, and cardioscope. Inspired air was supplemented with oxygen at 5-6 liters/min. Further veins were canulated with appropriate intracath (16G or 18G) on the dorsum of the hand and an injection of I.V. clonidine (4µg/kg) was given over a period of 10 mins to the case group. Internal jugular vein was canulated with triple lumen and radial artery was canulated for intra-arterial blood pressure monitoring. The patients were then induced with injections of midazolam (0.1 mg/kg), fentanyl (5-10 µg/kg) and vecuronium (0.1mg/kg). The doses of injection propofol were given and any additional doses required during the procedure were considered and duly noted. For maintenance, sevoflurance (2%) sedation mixture (Inj Fentanyl+ Inj. Midazolam+ Inj. Vecuronium) was used. Rescue maintenance requiring sevoflurance in incremental doses of 4-6% was considered and noted. Intraoperatively, parameters such as electrocardiogram (ECG), pulse, oximetry, EtCO, intra-arterial blood pressure, central venous pressure (CVP), nasopharyngeal temperature, serial arterial blood gas (ABG), and activated clotting time (ACT) were thoroughly monitored. Hemodynamic parameters like heart rate (HR), systolic arterial pressure (SBP), diastolic arterial pressure (DBP), and mean arterial pressure (MAP) were also recorded at various time points. The level of sedation was assessed using a sedation scale as: 0-Awake and alert, 1-Minimally sedated, 2-Moderately sedated, 3-Deeply sedated, and 4-Unarousable. Other parameters such as levels of bicarbonate (HCO_3^+), potassium (K^+), partial pressure of CO2 (PCO_2) and O2 (PO_2) were also measured at different time points. Further bypass and cross clamp time along with total cardiac output were also measured in all the subjects of both the groups.

Statistical Analysis

The data are presented as Mean ± SD. All the data was analyzed by using Student's t test, Chi-square test, Wilcoxon Sign Rank Test as appropriate. A p value <0.05 was considered to be statistically significant.

RESULTS

The demographic data of all the patients of both the groups was recorded. Parameter like mean age, height and weight showed no significant difference when compared between both the group suggesting unbiased allocation of the enrolled subject in control and case group. In medicine, two common measurements are body mass index (BMI) and body surface area (BSA). Both are measures of size, yet they convey information regarding different things. A patient's level of overweight can be estimated using their body mass index (BMI), which has a direct relationship to their fat proportion. While body surface area (BSA) is employed in the assessment and dosing of medical treatments. These parameters were found to be significantly different in case group when compared to controls. An array of biochemical test was performed as a part of routine investigation such as hemoglobin (HB), total leukocyte count (TLC), platelet count (PC), creatinine, prothrombin

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time (PT), international normalized ratio (INR), bilirubin, liver function test, left ventricular ejection fraction (LVEF). The mean of all the parameters were found to be non-significantly different in both the groups [Table 1].

[Table 2] represents mean SBP, DBP, and HR at various time intervals from baseline to the shifting of subjects to the ICU. Mean SBP levels were found to increase slightly from the baseline and were found to be significant ($p<0.05$) in control groups, albeit intragroup comparison of SBP at various time points to the baseline yielded no significant difference in the group who received clonidine (case group). The SBP parameter intergroup comparison revealed a significant difference ($p<0.05$) in values, which is mostly attributed to changes observed in control groups. A very comparable trend of increase in DBP of control subjects was observed being significantly different from case subjects were DBP was observed to be in lines with the baseline values (non-significant). These results indicate that clonidine drug is stable and attenuate stress response. In addition to SBP, HR is a significant element in determining myocardial work and oxygen consumption. Every effort is made to keep the heart rate as low as possible, which in turn reduces myocardial work and oxygen consumption. In our study, HR increased significantly in the control group at various timepoints when compared to baseline whereas it was found to stable in case again point out towards to efficacy of the clonidine adjunct.

MAP is the tissue perfusion pressure. In patients with coronary artery disease, an increase in MAP induces a rise in systemic vascular resistance, which can further aggravate the left ventricle's burden. During intubation, every effort is taken to manage the MAP, as it is a proxy marker for left ventricular strain. MAP was found to increase significantly in the control group whereas in case group it was revealed to statistically indistinguishable from the baseline. Inter group comparison also yielded significant ($p<0.05$) difference in the MAP values of both the group [Table 3]. CVP is the pressure in the thoracic vena cava close to the right atrium. CVP is an important element in critical care medicine since it can be used to measure a patient's fluid status, cardiac function, and right ventricle function. In our study, intragroup comparison of CVP at various time points against base line was found to be statistically different in both the groups except just before induction. The baseline CVP was almost similar in both groups as no intervention was done [Table 3].

Levels of HCO_3 and K^+ ions were also measured along with the partial pressure of CO_2 and O_2. These parameters were assessed at the baseline, before, on, and off pump timepoints. In control patients, the levels of HCO3 and K^+ were significantly different before and after pumping when compared to baseline values. These ions levels appeared to be in conjunction with the baseline while on-pumping. Furthermore, in cases, these ion levels were found to be stable before and on pump timepoint, albeit deviated slightly when the pump was removed. This shows the tendency of clonidine to have an ameliorative effect on fluctuating levels of ions in subjects. Recording partial pressure of CO_2 and O_2 is the primary measurement used to determine the partial pressure of these gases is arterial blood. In our study, it was observed that the levels of PCO_2 significantly decreased in both the groups when compared to its respective baseline. Likewise, the levels of PO_2 were significantly deviated from its baselines in both the groups [Table 4].

[Table 5] represents ACT and HGT measurements at baseline, before bypass and after protaminisation in both control and cases. It was found out the mean ACT time before bypass significantly increased in both the groups and tends to stabilize after protaminisation albeit remained statistically significant when compared to baseline values. On the other hand, HCT increased marginally after protaminisation and was found to be statistically significant in cases. Furthermore, bypass and cross-clamps time did not differ in cases when compared to control. Both pre-operative and post-operative, cardiac output was also found to be slightly less in cases when compared to control [Figure 1].

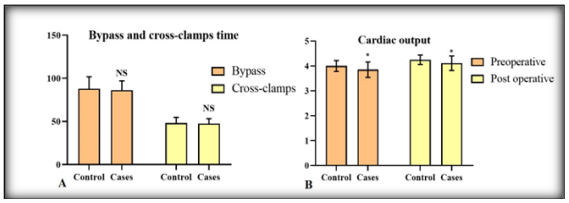

Figure 1: Comparison between A. By-pass time and cross-clamps time; B. Preoperative and post-operative cardiac output in control and case subjects.

Table 1: Demographic data of all the participants enrolled in the study

Mean parameter	Control	Cases	p value
Age (years)	53.7 ±6.94	55.7 ±5.58	0.132
Height ()	1.56 ±0.09	1.54 ±0.08	0.245
Weight (kgs)	60.9 ±8.39	57.2 ±4.99	0.451
BSA (M2)	1.61 ±0.10	1.48 ±0.16	0.001
BMI (Kg/m2)	23.6 ±1.49	24.5 ±1.20	0.005
ASA	2.72 ±0.45	2.65 ±0.48	0.245
HB (g/dl)	11.3 ±1.15	11.2 ±1.04	0.895
TLC (mm3)	6287 ±1696	6362 ±1987	0.856
Platelet count (per cubic mm)	355500 ± 66984	36075 ±71050	0.735
Creatinine (mg/dl)	0.74 ±0.19	0.75 ±0.19	0.995
PT (sec)	13.7 ±1.80	12.8 ±1.96	0.040

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INR	0.99 ±0.32	1.08 ±0.35	0.280
Total bilirubin (mg/dl)	0.83 ±0.18	0.82 ±0.23	0.816
Direct bilirubin (mg/dl)	0.49 ±0.14	0.44 ±0.18	0.169
Indirect bilirubin (mg/dl)	0.35 ±0.16	0.38 ±0.13	0.416
sGPT (Units/l serum)	45.9 ±4.98	43.1 ±5.67	0.024
sGOT (Units/l serum)	43.8 ±5.41	43.6 ±6.87	0.885
ALPO4 (Units/l serum)	145 ± 16.83	154±26.64	0.075
LVEF (%)	54.3 ±3.83	54.8 ±3.95	0.587

Data represent value as Mean± SD and abbreviation are as follows,
BSA- Body surface area, BMI-Basal metabolic index, HB-Hemoglobin, TLC-Total leukocyte count, PT-prothrombin time, sGPT-Aspartate transaminase, sGOT-Alanine transaminase, ALPO4- alkaline phosphatase, LVEF- left ventricular ejection fraction.

Table 2: SBP, DBP and HR recorded in the subjects of both groups at various timepoints

Time Point	SBP (mmHg)		DBP (mmHg)		HR (beats per min)	
	Control	Cases	Control	Cases	Control	Cases
Baseline	126.7±9.1	124.1±10.6 ^{bNS}	75.7±6.3	71.7±6.7 ^{bNS}	83.2±10.9	79.8±13.9 ^{bNS}
Before induction	127.7±7 ^{aNS}	118.3±11.4 ^{a*,b*}	75.3±5.8 ^{a*}	71.5±5.7 ^{aNS,b*}	83.0±8.92 ^{aNS}	72.2±10.7 ^{a*,b*}
After intubation	145.4±8.7 ^{a*}	121.6±7.4 ^{aNS,b*}	91.4±5.0 ^{a*}	73.1±5.1 ^{aNS,b*}	127.1±10.6 ^{a*}	78.6±7.09 ^{aNS,b*}
After sternotomy	142.0±6.5 ^{a*}	122.0±6.9 ^{aNS,b*}	87.0±4.9 ^{a*}	72.8±4.7 ^{aNS,b*}	115.8±5.56 ^{a*}	80.8±6.42 ^{aNS,b*}
Before bypass	141.8±4.7 ^{a*}	123.0±5.7 ^{aNS,b*}	86.2±4.4 ^{a*}	71.4±4.2 ^{aNS,b*}	114.4±5.23 ^{a*}	81.7±5.44 ^{aNS,b*}
Immediately after bypass	137.0±17.4 ^{a*}	122.5±4.2 ^{aNS,b*}	84.8±3.7 ^{a*}	72.2±3.3 ^{aNS,b*}	122.2±7.22 ^{a*}	80.4±5.34 ^{aNS,b*}
After Protaminisation	137.8±5.6 ^{a*}	121.5±4.8 ^{aNS,b*}	84.3±4.2 ^{a*}	71.9±3.2 ^{aNS,b*}	123.1±6.32 ^{a*}	79.7±4.80 ^{aNS,b*}
After closure	136.3±5.8 ^{a*}	121.6±3.9 ^{aNS,b*}	82.2±3.7 ^{a*}	72.8±3.1 ^{aNS,b*}	121.9±5.68 ^{a*}	79.0±4.25 ^{aNS,b*}
After shifting to ICU	133.5±4.8 ^{a*}	122.2±3.4 ^{aNS,b*}	80.8±3.5 ^{a*}	73.6±3.1 ^{aNS,b*}	123.7±5.46 ^{a*}	79.9±3.56 ^{aNS,b*}

The symbols used in the table represents statistical significance and indicated as 'a'- when each timepoint is compared to the baseline (Intragroup) and 'b' when timepoints are compared between the group (Intergroup). NS-Non significant, *p <0.05.

Table 3: MAP and CVP recorded in the subjects of both groups at various timepoints

Time point	MAP (mmHg)		CVP (mmHg)	
	Control	Cases	Control	Cases
Baseline	74.35±6.4	67.20±4.5 ^{bNS}	5.88±1.4	4.88±0.9 ^{b*}
Before induction	76.30±6.3 ^{a*}	72.85±5.9 $^{aNS, b*}$	5.88±1.4 ^{aNS}	4.88±0.9 $^{aNS, b*}$
After intubation	81.38±5.4 ^{a*}	73.60±5.2 $^{aNS, b*}$	6.10±1.3 ^{a*}	5.33±1.0 $^{a*, b*}$
After sternotomy	83.90±4.1 ^{a*}	73.90±4.7 $^{aNS, b*}$	6.75±1.1 ^{a*}	5.75±0.4 $^{a*, b*}$
Before bypass	82.95±3.1 ^{a*}	72.60±4.3 $^{aNS, b*}$	6.93±1.0 ^{a*}	6.45±1.3 $^{a*, bNS}$
Immediately after bypass	81.25±3.0 ^{a*}	72.20±3.9 $^{aNS, b*}$	7.03±0.8 ^{a*}	5.18±0.9 $^{a*, b*}$
After Protaminisation	72.20±3.9 ^{a*}	72.20±3.2 $^{aNS, b*}$	7.10±0.8 ^{a*}	7.15±1.0 $^{a*, bNS}$
After closure	75.55±4.8 ^{a*}	71.45±2.8 $^{aNS, b*}$	7.20±0.7 ^{a*}	7.23±0.8 $^{a*, bNS}$
After shifting to ICU	76.40±4.1 ^{a*}	72.50±3.0 $^{aNS, b*}$	7.20±0.7 ^{a*}	6.32±0.9 $^{a*, b*}$

The symbols used in the table represents statistical significance and indicated as 'a'- when each timepoint is compared to the baseline (Intragroup) and 'b' when timepoints are compared between the group (Intergroup). NS-Non significant, *p <0.05.

Table 4: Levels of ions (HCO3 and K+) and partial pressure of gases (CO2 and O2) in both the groups at various time points.

Time point	HCO3 (mmol/l)		K+ (mmol/l)		PCO2 (mmol/l)		PO2 (mmol/l)	
	Control	Cases	Control	Cases	Control	Cases	Control	Cases
Baseline	24.0±2.4	21.9±1.5^{b*}	4.10±0.3	4.03±0.3^{bNS}	38.45±2.2	37.60±1.9^{bNS}	116±13	125±22^{b*}
Before pump	22.6±2.1^{a*}	21.3±1.4$^{aNS, b*}$	4.37±0.2^{a*}	4.23±0.2^{a,b*}	36.20±1.8^{a*}	35.40±2.5$^{a*, bNS}$	211±24^{a*}	216±22 $^{*a, bNS}$
On pump	24.0±2.4^{aNS}	21.5±1.4$^{aNS, b*}$	4.10±0.3^{NS}	4.23±0.2^{a*,bNS}	34.70±2.3+	35.63±2.1$^{a*, bNS}$	191±27^{a*}	227±17 $^{a*, b*}$
Off pump	21.9±1.5^{a*}	23.5±2.4^{a*} ^{b*}	4.03±0.3^{a*}	4.18±0.3^{a*,bNS}	37.60±1.9^{a*}	35.75±2.1^{a*,b*}	125±22 ^{a*}	217±19 $^{a*, b*}$

The symbols used in the table represents statistical significance and indicated as 'a'- when each timepoint is compared to the baseline (Intragroup) and 'b' when timepoints are compared between the group (Intergroup). NS-Non significant, *p <0.05.

Table 5: Estimation of ACT and HGT in both the groups

Time point	ACT (secs)		HGT (mg/dl)	
	Control	Cases	Control	Cases
Baseline	130.4±10.9	124.13±6.9 ^{b*}	147.9±21.4	160.45±24.6 ^{b*}
Before bypass	454.9±45.8 ^{a*}	461.25±49.9 $^{a*, bNS}$	146.6±20.3 ^{a*,}	177.50±27.4 $^{a*, b*}$
After Protaminisation	137.5±18.2 ^{a*}	122.43±5.9 $^{a*, b*}$	151.0±18.2 ^{aNS,}	176.20±26.7 $^{a*, b*}$

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The symbols used in the table represents statistical significance and indicated as ‘a’- when each timepoint is compared to the baseline (Intragroup) and ‘b’ when timepoints are compared between the group (Intergroup). NS-Non significant, *p <0.05.

DISCUSSION

Current data suggests that between 30-40 % of people who undergo CABG surgery also suffer from some form of depression (severe, mild, or dysthymia).[6] Long-term experimental research on the impact of psychological factors on patient’s outcomes following CABG surgery has revealed a link between these characteristics and an enhanced risk of both immediate and delayed complications. Although the behavioural and biological reasons are incompletely understood, recent findings indicate that both depression and anxiousness increase the risk of death and morbidity after CABG surgery independent of clinical considerations. [7, 8] Neither depression nor anxiety appears to have a significant effect on cognitive impairment, however depression does increase the risk for incident delirium.[9] Prominent injectable sedatives employed in the intensive care unit include benzodiazepines such lorazepam, diazepam, and midazolam; opioids like fentanyl, morphine, sufentanyl, remifentanyl, and alfentanyl; and propofol and dexmedetomidine. Unfortunately, whenever these treatments are combined, there is a greater chance of unwanted side effects[10]. One of the most recommended medicines is dexmedetomidine, a newer 2 receptor agonist that has been licenced for short-term (24 h) ICU sedation. Dexmedetomidine-sedated patients have good reflexes and awaken quickly with only mild respiratory distress. ICU patients might need some sedation for much longer than the allowed 24 hours for dexmedetomidine, however this medication could be highly pricey and may not be widely available, especially in developing countries. Though opioids are frequently utilised for their sedoanalgesic effects, they are not presently favoured as sedative medications of preference in the ICU. The potential for tolerance to these medications to develop could complicate their application in the ICU. [9,10] Clonidine is a α2 receptor agonist and is been regarded as an anaesthetic adjuvant because of its ability to decrease sympathetic nervous system output via a central α2 adrenergic mechanism..[9] It has been employed to alleviate a range of ailments, including hypertension, menopausal flushes, and opioid and alcohol withdrawal, among others, for quite some time. In addition to lowering blood pressure, it also reduces the need for inhaled anaesthetics, increases the effectiveness of sedative, anxiolytic, and analgesic medications, lessens the pressor reaction to laryngoscopy and intubation, and prevents postoperative nausea, vomiting, and shivering. [11-13] Clonidine can mitigate pain and induce sleep. Clonidine's sedative effects are likely the result of the drug's interaction with the locus ceruleus in the brain stem. [9]

Our results indicate the superior potential of clonidine as an adjunct to induction agent. Group administered with clonidine showed relative stable intraoperative hemodynamic parameters like baseline value. We observed relatively disturbed hemodynamic parameter values in group who did not received clonidine (control) suggesting its ameliorative and stability imparting nature in patients undergoing CABG surgery. The same authors looked at 40 patients who had suffered several traumas and were currently being treated with long-term mechanical breathing and fentanyl and midazolam for sedation due to their symptoms of sympathetic hyperactivity. The administration of clonidine resulted in a significant slowing in heart rate, from 90% of patients had a heart rate greater than 120/min after 24 hours, and their need for fentanyl and midazolam was reduced by 38% and 19% within the same time frame.[14]

In another short retrospective study conducted in thirteen ICU subjects, clonidine has been demonstrated to minimize the requirement for opioid and benzodiazepine use. With clonidine, the estimated average morphine dosage for nine patients decreased from 44.7 mg to 28.2 mg. Six of seven patients receiving concomitant clonidine and propofol demonstrated reduced necessity for propofol, and the daily dose of lorazepam in the eleven patients was 14.6 mg prior to and 3.9 mg following clonidine delivery.[15] Other report suggests that patients on mechanical ventilation who had been sedated were much less likely to experience withdrawal symptoms once the sedation was abruptly stopped after being given clonidine. This improved patient cooperation with the ventilator and expedited the weaning process, resulting in decreased breathing, metabolism, and cardiovascular requirements.[16] Likewise, Mandke et al with colleagues demonstrated high sedation score in clonidine group with non- significant different in the hemodynamics parameter and also patients received less isoflurance and nitroglycerin thereby supporting our study that clonidine appears to be a safe adjunct useful in anaesthesia for CABG surgery.[17] In conjunction to this surgery, premedication with 4 g/kg of IV clonidine is reliable and effective for establishing a bloodless surgical field during middle ear and nasal surgery. This report also presented that the dosages of isoflurane, fentanyl, and metoprolol for managed hypotension were lowered. However, clonidine at 5 g/kg was not more effective than clonidine at 4 g/kg in eliciting desired effects and was instead linked to certain unwanted side effects.

The main limitations of our study are its small sample size and its basic randomization, which prevented us from effectively stratifying subgroups such those with a history of drug misuse. Our results need to be confirmed in larger, multi-centeric trials.

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CONCLUSION

Low doses of frequently available induction drugs combined with midazolam, fentanyl, and vecuronium premedication, as well as slow and watchful induction, can provide safe induction in patients with coronary artery disease even without modern monitoring equipment. Clonidine administration has been linked to an increased incidence of hypotension in studies of patients undergoing noncardiac operations and CABG. Conversely, there was no intergroup difference in the incidence of hypotension following CPB in our investigation.

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