Propofol and Fentanyl Take Longer for Induction of Anesthesia in Aortic Regurgitation: A Case-Controlled Prospective Study

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Objectives: **This study was conducted to determine if induction time of anesthesia in patients with aortic regurgitation (AR) is different from patients with a normal aortic valve (AV).**

Design: **A prospective, case-control study.**

Setting: **A single institutional study conducted in a tertiary care teaching hospital.**

Participants: **Twenty-four male patients scheduled for cardiac surgery, group I (n = 12) patients with competent AV and group 2 (n = 12) with severe AR.**

Interventions: **General anesthesia was induced by intravenous infusion of propofol and fentanyl.**

Measurements and Main Results: **Continuous measurements of heart rate, intra-arterial blood pressure, and bispectral index were recorded. Induction doses of propofol and fentanyl were analyzed and compared. There was significant difference between the 2 groups in terms of induction time of anesthesia (mean ± SD 308 ± 68.2 seconds in group 1 *v* 445 ± 97.9 seconds in group 2). The patients in group 2 (AR) required significantly larger doses of propofol (0.91 ± 0.40 mg/kg) than the patients in group 1 (0.49 ± 0.17 mg/kg). Similarly, fentanyl dose was increased in the group 2 patients (20.8 ± 15.9 μg/kg) compared with the group 1 patients (9.2 ± 2.9 μg/kg).**

Conclusion: **The authors concluded that there was a significant prolongation of the induction time of anesthesia and the need of larger doses of propofol and fentanyl by slow intravenous infusion regimen in patients with AR compared with patients with a competent aortic valve.**

KEY WORDS: aortic regurgitation, bispectral index, induction time, propofol, fentanyl

AORTIC REGURGITATION (AR) is associated with a hyperdynamic circulation.[1] However, the effective stroke volume (the forward flow) is decreased with increased in left ventricular end-diastolic volume (LVEDV).[2,3] This implies that the anesthetic drugs administered intravenously might take more time to attain effective concentration in the brain. Characteristically, administration of a large bolus of intravenous drug can blur this difference. However, a bolus dose of intravenous anesthetic drug may lead to a precipitous fall in the arterial blood pressure in patients with compromised cardiac diseases (eg, coronary artery diseases,[4,5] valvular diseases,[6] and cardiomyopathy[7]). Therefore, slow administration of drugs is advocated in these patients. The authors hypothesized that, in patients with AR, intravenous administration of anesthetic drugs might be associated with a delay in induction of anesthesia. There are no reports in the literature to suggest that the induction of anesthesia takes longer in patients with AR than in patients with a normal aortic valve (AV); thus, the aim of this study was to compare the induction of anesthesia by slow infusion of intravenous propofol in patients with AR with the patients with normal AV function.

MATERIALS AND METHODS

Approval was obtained from the institute's ethical committee, and written informed consent was obtained from all participating patients. The authors referred to the Tripathi et al study,[8] in which the slow propofol infusion in patients with normal valve function had a mean induction time of 142 seconds and a standard deviation (SD) of 25 seconds. Assuming that a difference in induction time of 40 seconds would be clinically significant, with the power analysis at 95% confidence interval (CI) and the level of significance of 0.05, the calculated sample size came to 11 patients in each of the 2 study groups. Twenty-four patients were recruited for the study: 12 consecutive adult male patients with coronary artery disease scheduled for coronary artery bypass grafting (CABG), and 12 consecutive adult male patients with chronic AR (grades 3 and 4) planned for aortic valve replacement. Patients with left mainstem coronary artery stenosis, left ventricular dysfunction, ventricular aneurysm, concomitant mitral valve diseases, aortic stenosis (grade >4), significant hepatic or renal dysfunction, and increased risk of aspiration were excluded.

The preoperative medications of all patients scheduled for CABG included metoprolol and isosorbide dinitrate, and the preoperative medications of all patients scheduled for AR included digoxin and furosemide. All patients continued their medication until the morning of surgery. To facilitate arterial and jugular cannulation before induction of anesthesia, lorazepam (2 mg orally) was administered the night before surgery, and butorphanol (1-2 mg intramuscularly) was administered 2 hours before arrival in the operating room.[9] Patients were monitored by electrocardiogram (leads II and V_5), as well as for intra-arterial blood pressure and continuous cardiac output (CCO) by placing pulmonary artery pressure (Swan-Ganz CCO/VIP thermodilution catheter [7.5 Fr]; Edwards Lifesciences, Irvine, CA) and bispectral index (BIS) (A-2000 BIS monitoring system and BIS quatra sensor; Aspects Medical System, Inc, Norwood, MA). The invasive monitoring was started under local anesthesia before the induction of anesthesia.

The authors initiated induction of anesthesia with an infusion of propofol (1%; 0.5 mL/kg/hour) and fentanyl (25 μg/mL; 200 mL/hour). Oxygen was supplemented by facemask and assisted ventilation by bag and mask, when deemed necessary. The fentanyl infusion was stopped at BIS = 60 and the propofol infusion was titrated to maintain BIS between 60 and 40. To facilitate intubation, vecuronium bromide (0.1 mg/kg) was injected once the BIS value fell below 60.

An anesthesiologist, who was blinded to the patient type, noted the heart rate (HR), systolic (SAP), diastolic (DAP), mean arterial pressure (MAP), and BIS values before the start of infusions and continued every minute until BIS fell below 60, and then noted again at 1, 3, and 5 minutes after intubation. The time to loss of verbal response, time to onset of apnea, and the induction time to BIS = 60 were noted. The volume of propofol and fentanyl consumed until the BIS ≤ 60 also was noted. Although the attending anesthesiologist was not blinded for the

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Table 1. Patient Characteristics and Preinduction Hemodynamics in the Two Study Groups

Parameter	Group 1	Group 2	
Group Characteristic	Normal Aortic Valve (No AR)	Aortic Regurgitation (AR)	p Value
Number of patients	12	12	
Age (years)	59 ± 7.9	39 ± 15.5	0.001*
Height (m)	1.65 ± 0.07	1.61 ± 0.04	.096
Weight (kg)	60 ± 10.1	47 ± 8.3	0.003*
Body surface area (m^2)	1.63 ± 0.19	1.42 ± 0.15	0.006*
Heart rate (beats/min)	69 ± 18.9	94 ± 12.4	0.001*
Pulse pressure (mmHg)	60 ± 16.8	90 ± 18.4	0.001*
Stroke volume (mL)	63 ± 21.4	65 ± 18.6	0.848
Cardiac output (L/min)	4.1 ± 0.8	6.1 ± 1.5	0.01*
Stroke volume indexed (mL/m^2)	39.9 ± 15.5	46.3 ± 13.1	0.290
Cardiac index (L/min/m)	2.6 ± 0.6	4.3 ± 1.1	0.0001*
SVRI (dynes/cm/m)	2335 ± 386	1486 ± 308	0.005*
Bispectral index (%)	94 ± 6.0	95 ± 3.7	0.11
SQI (%)	92.8 ± 11.7	91.2 ± 12.6	0.12

NOTE: Values are mean ± SD.

Abbreviations: AR, aortic regurgitation; SVRI, systemic vascular resistance indexed; SQI, signal quality index of bispectral index; SD, standard deviation.

*Statistically significant difference.

patient type, the anesthesiologist who recorded all observations was blinded for the patient type. Phenylephrine was administered to correct hypotension.

All data were entered in the statistical package SPSS 19.0 (SPSS Inc, Chicago, IL). The Student's *t* test was used to compare the patients' characteristics, the propofol dose, and the fentanyl dose in the 2 study groups. BIS values and hemodynamic variables were analyzed using two-way analysis of variance (ANOVA) for repeated measurements. Kaplan-Meier analysis was performed to compare the induction times in the 2 study groups. The calculated value of $p < 0.05$ at 95% CI was considered statistically significant.

RESULTS

The patients in both study groups were male and were of similar height, but the patients in group 1 (No AR) (59 ± 7.9 years) were significantly older than the patients in group 2 (AR) (39 ± 15.5 years). The patients in group 1 (No AR) had heavier body weight (60 ± 10.1 kg in group 1 *v* 47 ± 8.3 kg in group 2) and, therefore, a larger body surface area (1.63 ± 0.19 m^2 in group 1 *v* 1.42 ± 0.15 m^2 in group 2) (Table 1). The preinduction heart rate (94 ± 12.4 bpm) and the cardiac index (4.3 ± 1.1 L/min/m^2) in the group 2 (AR) patients were significantly higher ($p < 0.05$) than in the group 1 (No AR) patients. However, the stroke volume index, BIS, and SQI values were similar in both study group patients (Table 1).

There was no significant difference in BIS values between the 2 groups at baseline and until 4 minutes past the start of the propofol infusion, but from 5 minutes onward the BIS value of the patients in group 1 was significantly reduced compared with group 2 patients (Fig 1). The median anesthesia induction time (7 minutes, 30 seconds) in group 2 (AR) patients was significantly longer ($p < 0.01$) than the median induction time of 4 minutes, 40 seconds in group 1 (No AR) patients (Table 2). The Kaplan-Meier analysis also showed a significant difference between the induction times of the patients in the 2 study groups (Fig 2). The dose of the propofol administered until BIS = 60 was significantly larger in the group 2 (AR) (0.91 ± 0.40 mg/kg) than in group 1 (0.49 ± 0.17 mg/kg) patients. Similarly, fentanyl dose also was larger in group 2 than in group 1 patients (Table 2). Because propofol infusion was stopped at different time intervals in different patients, subject to onset of BIS = 60 as seen in Figure 2, the hemodynamic data for only 6 minutes are presented, as up to this time point all patients were getting anesthetic infusion in both the study groups (Table 2).

The hemodynamic parameters characteristically showed that the diastolic arterial pressure was significantly lower in group 2 (AR) patients than group 1 (No AR). The other parameters, such as systolic arterial pressure and mean arterial pressures were similar during induction of anesthesia in both the study groups (Table 3). The incidences of hypotension and cardiac arrhythmia in the 2 study groups were similar. Phenylephrine was used to correct the hypotension in 8 patients (three in group 1 and five in group 2) (Table 4).

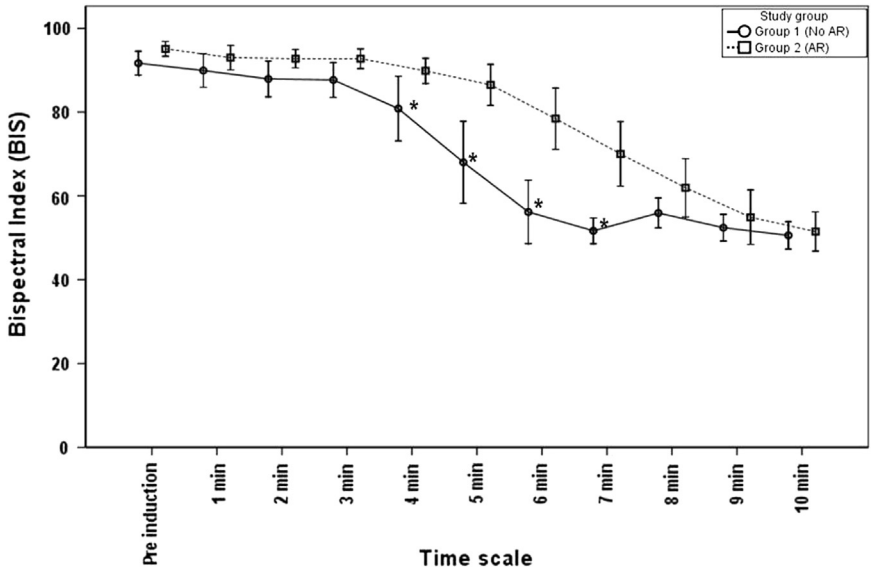

Fig 1. Trend of BIS in group 1 (no AR) and group 2 (AR), from preinduction to 10 minutes after induction; *p < 0.05 statistically significant difference from group 2 (AR).