Effect of Calcium Gluconate on Mean Arterial Pressure after Induction of Anesthesia with Propofol in Patients undergoing Coronary Artery Bypass Graft Surgery

Vali Imantalab[1] MD; Abbas Seddighinejad[1] MD; Ali Mir Mansouri[1] MD; Alimohammad Sadeghi Meibodi [2] MD; Heidar Dadkhah[2] MD; Said Farzam MD;[2] Kambiz Forghan-Parast [3]

Introduction: A combination of Propofol and Fentanyl is used as a method for inducing general anesthesia. Although Propofol is widely used for the induction and maintenance of anesthesia, it has a significant effect on reducing arterial blood pressure. It has been suggested that Calcium Gluconate, when administered simultaneously with Propofol, may reduce the inotrope negative effect of Propofol on heart function.

Objective: To determine the effect of Calcium Gluconate in decreasing the negative effect of Propofol.

Materials and Methods: This randomized, controlled, double-blind, clinical trial divided 70 patients undergoing elective coronary artery bypass graft surgery (CABG) into two groups: Group A (Calcium Gluconate) and Group B (placebo). Each patient was injected with Fentanyl (4 µg/kg), Pancuronium (0.1 mg/kg), and Propofol (1.5 mg/kg) within 60 seconds via a central vein line. Calcium Gluconate (30 mg/kg) and saline (placebo) were administered to Group A and Group B, respectively. Homodynamic data were obtained at baseline (T0), 4 minutes after anesthesia induction (T1), and 2 minutes after tracheal intubation (T2). The data were analyzed using descriptive statistics, repeated measurement, and T tests; a p value < 0.05 was considered statistically significant.

Results: The mean and SD of mean arterial pressure at T0 was 101.11 ± 13.63 for Group A and 107.142 ± 14.59 for Group B (non-significant). These figures for T1 (4 minutes after anesthesia induction) and T2 (2 minutes after tracheal intubation) were 70.14 ± 14.67 and 80.22 ± 23.29 for Group A and 72.05 ± 15.45 and 82.42 ± 14.86 for Group B (non-significant).

Conclusion: The findings of this research indicated no differences between the two groups. Calcium Gluconate appeared to exert no impact on reducing the negative effect of Propofol. ***(Iranian Heart Journal 2013; 13 (2):30-36).***

Keywords: Cardiac surgery■ Calcium Gluconate■ Propofol■ Fentanyl■ Blood pressure

Coronary artery bypass graft surgery (CABG) has been one of the most popular operations in recent years. Anesthesia for CABG has many aspects, first and foremost amongst which is the induction of anesthesia. Many drugs such as opioids and hypnotics can induce anesthesia in CABG. Among hypnotics, Propofol is routinely administered but it may cause hypotension.[1] Propofol-induced hypotension may be caused by decreasing afterload and systemic vascular resistance (SVR)[2] and blocking baroreceptor reflex.[3]

[1] Fellowship of Cardiac Anesthesia, Assistant Professor of Guilan University of Medical Sciences, Department of Cardiac Anesthesia, Heshmat Hospital, Rasht University of Medical Sciences, Rasht, IRAN.
2 Cardiac Surgeon, Assistant Professor of Guilan University of Medical Sciences.
3 PhD, Associate Professor of Microbiology, Guilan University of Medical Sciences.
Corresponding: Abbas Seddighi Nejad, MD; Department of Cardiac Anesthesia, Heshmat Hospital,Rasht University of Medical Sciences, Rasht, IRAN.
Tel:00989111325712 **E-mail:** A_ sedighinejad@yahoo.com **Address:** Heshmat Hospital, Rasht, Guilan, IRAN.

Negative inotropic effect of Propofol may be dependent on a reduction in myocardial intracellular ionized Ca^{++} availability,[4,5] which might be due to calcium-channel block and also due to disturbance in reticulum sarcoplasmic calcium uptake.[6] In one study, the administration of calcium chloride and Propofol during the induction of anesthesia reduced the negative inotropic effect of Propofol.[4] In our study, we sought to evaluate the effect of Calcium Gluconate on the negative inotropic effect of Propofol during the induction of anesthesia in CABG.

Methods

Our study was a double-blind, randomized, clinical trial (RCT). After approval by the Ethics Committee of Guilan University of Medical Sciences and approval of IRCT (number 545), seventy patients undergoing CABG were selected. Having provided written informed consent, the patients were randomly enrolled in two groups- each with 35 patients.

The inclusion criteria were composed of elective CABG, having enough consciousness, not having any allergic reaction to Propofol and Calcium Gluconate, not having cardiac heart failure and congenital heart disease background or past history of myocardial infarction (MI), having ejection fraction more than 40%, and finally a spared left main coronary artery.

By using a randomized closed-envelop system, the patients received Calcium Gluconate (Group A) and saline (Group B). The patients received anesthetic premedication one hour before surgery - which included Morphine Sulfate (0.1 mg/kg) intramuscularly and Lorazepam (1 mg) orally. On the arrival of the patient at the operating room, electrocardiographic monitoring was started (leads II and V5). After sterilization and infiltration of local anesthesia, an intra-arterial catheter was placed in the radial or brachial artery. Additionally, a central vein (CV) catheter was placed through the right subclavian vein. Anesthesia was induced by an experienced anesthesiologist in both groups by means of Fentanyl (4 µg/kg) and Pancuronium (0.1 mg/kg), followed by Propofol (1.5 mg/kg) in 60 seconds. At the same time and at the same speed (60 seconds), a blinded anesthesiologist administered Calcium Gluconate (30 mg/kg) to Group A and saline to Group B via another CV line port.

These patients were ventilated with 100% oxygen for 4 minutes, and tracheal intubation was done. Hemodynamic data were obtained at baseline, 4 minutes after induction, and 2 minutes after intubation by one of our colleagues. The data included mean arterial pressure (MAP), heart rate (HR), and central venous pressure (CVP).

Data analysis was done with SPSS (version 16) using repeated measurement and T-test.

Results

Seventy patients were allocated to two groups of 35 - with no difference in terms of age, American Society of Anesthesiologists (ASA) class, sex, and ejection fraction (Table 1).

Evaluation of data and usage of general linear model with repeated measuring revealed that there were significant differences between HR at different time intervals in each group (p value < 0.0001 and p value < 0.0001). However, a comparison of the mean HR between the two groups revealed no statistically significant differences in all the time points of the study (p value = 0.23) (Table 2 and Figure 1).

There were significant differences between MAP at different time intervals in each group (p value < 0.0001 and p value < 0.0001). Nevertheless, a comparison of the mean MAP between the two groups demonstrated no statistically significant differences in all the study time points (p value = 0.316) (Table 3 and Figure 2).

There were no significant differences as regards CVP at different time intervals in each of the two groups (p value = 0.138 and p

value = 0.184). A comparison of the mean CVP between the two groups showed no statistically significant difference in all the study time points (p value = 0.795) (Table 4 and Figure 3).

Also, a comparison of the mean CVP between the two groups revealed no statistically significant differences at each study time point (before induction, four minutes after the induction of anesthesia, and 2 minutes after intubation) (p value = 0.402, p value = 0.693, and p value = 0.688) (Table 5).

A comparison of MAP at different time points demonstrated no statistically significant differences between the two groups at each time point (before induction, four minutes after the induction of anesthesia, and 2 minutes after intubation) (p value = 0.079, p value = 0.597, and p value = 0.639) (Table 6).

A comparison of HR at different time points demonstrated no statistically significant differences between the two groups at each time point (before induction, four minutes after the induction of anesthesia, and 2 minutes after intubation) (p value = 0.462, p value = 0.098, and p value = 0.44) (Table 7).

Table 1. Demographics as well as American Society of Anesthesiologists and ejection fraction parameters

Variable		N	%
Sex	Male	33	47.1
	Female	37	52.9
Age (year) (Mean ± SD)		60.24 ± 8.14	
ASA Class	II	56	80
	III	14	20
EF (Mean ± SD)		55.8 ± 6.83	

*ASA, American Society of Anesthesiologists *EF, ejection fraction

Table 2. A comparison of the mean heart rate at different time points in separate study groups

Group	Time	N	Mean	SD	F value	P value	P value between groups
Propofol +Ca	Before induction	35	83.37	17.72	11.96	P=0.0001	P=0.23
	4 min after induction	35	74.97	14.9			
	2 min after intubation	35	76.68	15.36			
Propofol +Placebo	Before induction	35	81.8	10.42	27.25	P=0.0001	
	4 min after induction	35	69.71	11.03			
	2 min after intubation	35	74.48	6.67			

Table 3. A comparison of the mean arterial blood pressure at different time points in separate study groups

Group	Time	N	Mean	SD	F value	P value	P value between groups
Propofol +Ca	Before induction	35	101.11	13.63	36.55	P<0.0001	P=0.316
	4 min after induction	35	70.14	14.67			
	2 min after intubation	35	80.22	23.29			
Propofol +Placebo	Before induction	35	107.14	14.59	126.91	P<0.0001	
	4 min after induction	35	72.05	15.45			
	2 min after intubation	35	82.42	14.86			

Table 4. A comparison of the mean central vein pressure at different time points in separate study groups

Group	Time	N	Mean	SD	F value	P value	P value between groups
Propofol +Ca	Before induction	35	5.91	2.27	2.3	P=0.138	P=0.795
	4 min after induction	35	5.91	2.79			
	2 min after intubation	35	6.54	3.19			
Propofol +Placebo	Before induction	35	6.31	1.64	1.83	P=0.184	
	4 min after induction	35	5.68	1.96			
	2 min after intubation	35	5.68	1.96			

Table 5. A comparison of the mean central vein pressure between the two study groups at separate time points

Group	Time	N	Mean	SD	F value	P value
Before induction	Propofol +Ca	35	5.91	2.27	0.842	P=0.402
	Propofol +Placebo	35	6.21	1.64		
4 min after induction	Propofol +Ca	35	5.91	2.79	0.396	P=0.693
	Propofol +Placebo	35	5.68	1.96		
2 min after intubation	Propofol +Ca	35	6.54	3.19	0.404	P=0.688
	Propofol +Placebo	35	5.68	1.96		

Table 6. A comparison of the mean arterial blood pressure between the two study groups at separate time points

Group	Time	N	Mean	SD	F value	P value
Before induction	Propofol +Ca	35	101.11	13.63	1.87	P=0.079
	Propofol +Placebo	35	107.14	14.59		
4 min after induction	Propofol +Ca	35	70.14	14.67	0.532	P=0.597
	Propofol +Placebo	35	72.05	15.45		
2 min after intubation	Propofol +Ca	35	80.22	23.29	0.471	P=0.639
	Propofol +Placebo	35	82.42	14.86		

Table 7. A comparison of the mean heart rate between the two study groups at different time points

Group	Time	N	Mean	SD	F value	P value
Before induction	Propofol +Ca	35	83.37	17.72	1.67	P=0.462
	Propofol +Placebo	35	81.8	10.42		
4 min after induction	Propofol +Ca	35	74.97	14.9	0.777	P=0.098
	Propofol +Placebo	35	69.71	11.03		
2 min after intubation	Propofol +Ca	35	76.68	15.36	0.842	P=0.44
	Propofol +Placebo	35	74.48	6.67		

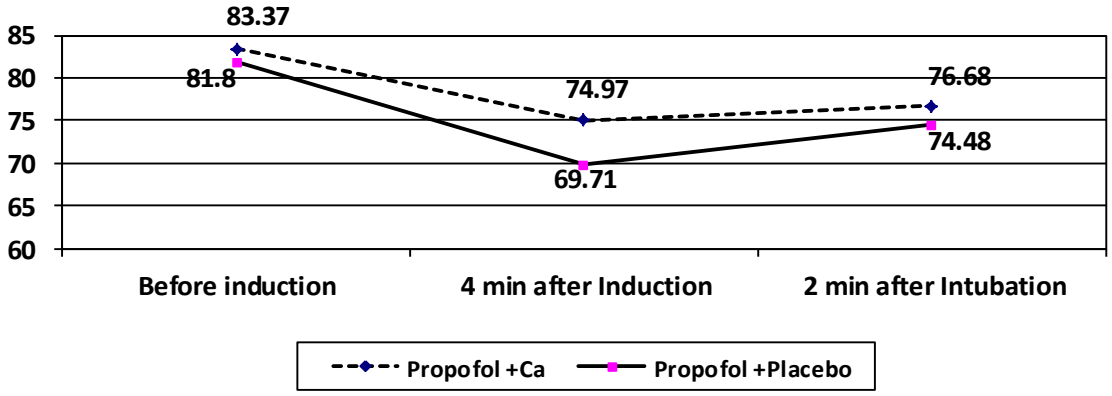

Fig. 1. A comparison of the mean heart rate at different time points in separate study groups

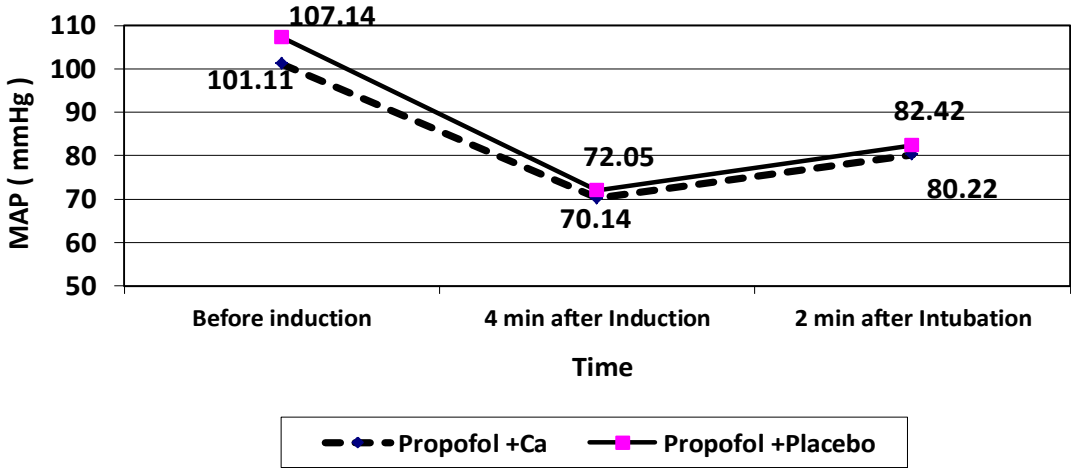

Fig.2. A comparison of the mean arterial blood pressure at different time points between the two study groups

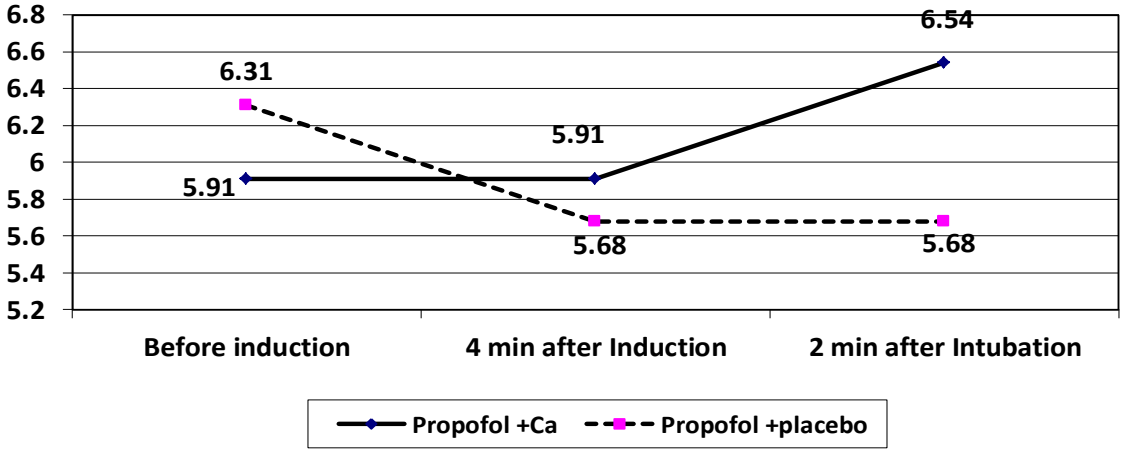

Fig. 3. A comparison of the mean central vein pressure at different time points in separate study groups

Discussion

One of the most popular forms of anesthesia induction is by using a high dosage of narcotics; this is likely to be associated with undesirable side effects such as long-lasting respiratory depression, delayed extubation time, long stays in the Intensive Care Unit (ICU), and increased hospital costs.

Recently Propofol has become the most frequently used intravenous anesthetic agent. The combination of Propofol and Fentanyl for the induction of anesthesia in patients undergoing CABG is common. This combination blunts hemodynamic responses to laryngoscopy and intubation of trachea but might be associated with severe decreases in SVR, preload, and cardiac work.[7,8] The most prominent effect of Propofol is a decrease in arterial blood pressure during the induction of anesthesia. Independent of the presence of cardiovascular disease, an induction dose of 2-2.5 mg/kg produces a reduction in systolic blood pressure,[8,9] mean and diastolic blood pressure, cardiac index (15%),[9,10] stroke volume index (≈20%),[9,11] and SVR (15-25%).[10,11] Propofol in patients with valvular heart disease reduces pulmonary capillary wedge pressure and pulmonary artery pressure, which can decrease both preload and afterload.[12] Propofol at high concentrations (10 μg/ml) abolishes the inotropic effect of α but not β-adrenoreceptor stimulation, and enhances the lusitropic (relaxation) effect of β stimulation.[13]

It seems that the vasodilatory effect of Propofol is due to a reduction in sympathetic activity,[14] a direct effect on intracellular smooth muscle calcium mobilization,[15] inhibition of prostacyclin synthesis in endothelial cells,[16] reduction in angiotensin II-elicited calcium entry,[17] activation of k^+ adenosine triphosphate channels, and stimulation of nitric oxide.

Since the negative inotropic effect of Propofol may depend on a reduction in the intracellular calcium, the administration of calcium chloride simultaneously with Propofol during the induction of anesthesia can lessen its negative inotropic effect on the cardiac function.

In 1992, Lugigi Trapepe et al.[4] - in a study on 58 patients undergoing CABG - showed that the administration of CaCl2 decreased the negative inotropy of the cardiac function. Other investigators demonstrated Ca++ mediated improvement in myocardial oxygen consumption and no creation of coronary vasospasm.[17]

In this study, we selected 70 patients and divided them into two groups: one group receiving Propofol plus Calcium Gluconate and the other group receiving Propofol plus placebo. The choice of Calcium Gluconate in our study was because there is no calcium chloride in Iran's pharmacopeia. According to our results, there were no significant differences between the two groups' hemodynamic parameters such as MAP, HR, and CVP. However, in each group - there were significant differences in terms of hemodynamic parameters (MAP and HR). These findings were different from those reported by another study.[4,18] This difference may be in consequence of the special effect of Calcium Gluconate (different from CaCl2), rapid injection of Calcium Gluconate, or differences in race and geography of our people.

Myocardial ischemia secondary to Ca++ ion administration has been reported,[19] and this effect may arise from hypotension due to Calcium Gluconate administration.

In our study, Calcium Gluconate could not maintain cardiovascular stability and the patients treated with Calcium Gluconate had no significant differences with the placebo group. Furthermore, Calcium Gluconate could not prevent cardiovascular depression induced by Propofol.

Conclusion

Our study revealed that adding Calcium Gluconate as an agent for attenuating the cardiac depressant effect of Propofol was

ineffective and it could not prevent hypotension after the injection of Propofol.

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