J Anesth (2000) 14:138–142

Journal of
Anesthesia

Changes in left ventricular end-diastolic area, end-systolic wall stress, and fractional area change during anesthetic induction with propofol or thiamylal

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Abstract
Purpose. To elucidate the mechanisms of the more profound hypotensive effects of propofol relative to thiamylal, we monitored changes in left ventricular (LV) preload, afterload, and contractility during the course of anesthetic induction with propofol and thiamylal.
Methods. Thirty-two patients (ASA I) were randomly assigned into two groups and injected with propofol ($2\,mg\cdot kg^{-1}$) or thiamylal ($4\,mg\cdot kg^{-1}$) as anesthetic induction agents. Transthoracic echocardiography (TTE) was used to assess LV performance before and during induction by the two anesthetics. The LV end-diastolic area (EDA) and LV end-systolic wall stress (ESWS) were used as indices of LV preload and LV afterload, respectively, while LV contractility was assessed by the fractional area change (FAC).
Results. Both propofol and thiamylal significantly reduced EDA and ESWS without significant change in FAC. Propofol-induced reductions in EDA and ESWS were significantly greater than those of thiamylal.
Conclusion. The more profound hypotension observed during induction of anesthesia with propofol is due to the greater decrease in preload and afterload than with thiamylal, but not to a decrease in LV contractility.

Key words Left ventricular performance · Preload · Afterload · Intravenous anesthetic · Transthoracic echocardiography

Introduction

Propofol is used as an intravenous anesthetic agent; its action is similar to that of thiopental or thiamylal. It appears, however, that the induction dose of propofol causes a greater fall in arterial blood pressure than barbiturates [1–4]. The precise mechanism of propofol-induced hypotension remains unclear, despite several clinical and experimental studies [5–7]. Several mechanisms have been postulated, including a reduction in myocardial contractility, alterations in loading conditions, and changes in the central nervous system [5–11]. In humans, left ventricular (LV) performance has been assessed during infusion of propofol using transesophageal echocardiography (TEE) [2,12]. However, it is difficult to apply TEE in awake patients, and thus the reported cardiac actions of propofol studied by TEE are limited to those in anesthetized patients [2,12].

The purpose of the present study was to examine the effect of induction of anesthesia using propofol and thiamylal on LV performance in awake subjects. We used transthoracic echocardiography (TTE) for evaluation of LV performance in patients before and after anesthetic induction. As indices of preload, afterload, and myocardial contractility, we used LV end-diastolic area (EDA) with automated border detection, LV end-systolic wall stress (ESWS) using M-mode echocardiogram, and LV fractional area change (FAC).

Materials and methods

After institutional approval and informed consent had been obtained, 32 patients (ASA physical status I) undergoing ophthalmic or oropharyngeal surgery were enrolled in this study. The patients were randomly assigned to propofol ($n = 16$) or thiamylal ($n = 16$) groups. Each patient received $0.1\,mg\cdot kg^{-1}$ nitrazepam orally for sedation 1 h before induction. Atropine $10\,\mu g\cdot kg^{-1}$ was injected intramuscularly 30 min before induction. Anesthetic induction with propofol or thiamylal was performed after denitrogenation with 100% oxygen. All studies were performed while the patient was in the supine position.

The propofol group received a bolus dose of $2\,mg\cdot kg^{-1}$ propofol, whereas the thiamylal group received a bolus dose of $4\,mg\cdot kg^{-1}$ thiamylal. Patients in both groups received $0.1\,mg\cdot kg^{-1}$ vecuronium just after

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Received: December 8, 1999 / Accepted: April 19, 2000

the injection of the anesthetic agent and were then maintained on controlled ventilation with 100% oxygen to normocapnia. The echocardiographic parameters were measured simultaneously with hemodynamic variables before and at 1-min intervals for 4 min after injection of the test agent. Thereafter, the patients were intubated. All data were obtained at the end of the expiratory period, and five cardiac cycles for each patient were then chosen for analysis.

Echocardiography was performed using a 3.5-MHz transducer and an ultrasound system (Sonos 2500, model 2406A, Hewlett-Packard, Andover, MA, USA) with the M-mode and an automated border detection system. The echocardiographic data and electrocardiogram were recorded simultaneously on S-VHS videotapes. Arterial blood pressure was measured by an automated cuff pressure device (JENTOW, Colin Electronics, Komaki, Japan) using a corrected size cuff on the upper arm. ESWS was obtained from the LV long-axis view of the parasternal position with M-mode tracing (sweep, 100 $mm \cdot s^{-1}$). FAC and EDA were obtained from the short-axis view of the LV at the papillary muscle level using the automated border detection system. Because ESWS and EDA could not be simultaneously obtained on the same view, each group ($n = 16$) was subdivided into those examined by ESWS only ($n = 8$) and those examined by EDA and FAC only ($n = 8$). These parameters were recorded during five cardiac cycles at the end of the expiratory period. FAC was defined by the equation $FAC\ (\%) = [(EDA - ESA) \cdot EDA^{-1}] \cdot 100$, where ESA is the end-systolic area. ESWS was calculated by the formula $ESWS = 0.334 \cdot P \cdot d \cdot h^{-1} \cdot [1 + (h \cdot d^{-1})]$, where P is systolic blood pressure, d is systolic left ventricular diameter, and h is systolic posterior wall thickness. These parameters were measured with the automated cuff pressure and M-mode technique of transthoracic echocardiography. Prior to these measurements, we confirmed the absence of gradient across the aortic valve by the color Doppler technique. The systolic LV diameter and systolic posterior wall thickness were obtained using the M-mode dimensions.

All data are presented as mean ± standard deviation (SD). Changes from baseline values were compared by one-way analysis of variance with repeated-measures ANOVA followed by Scheffe multiple comparison tests. A two-way analysis of variance was performed to compare the two groups. If the F test showed a significant difference, an unpaired t-test was performed. $P < 0.05$ indicates statistical significance.

Results

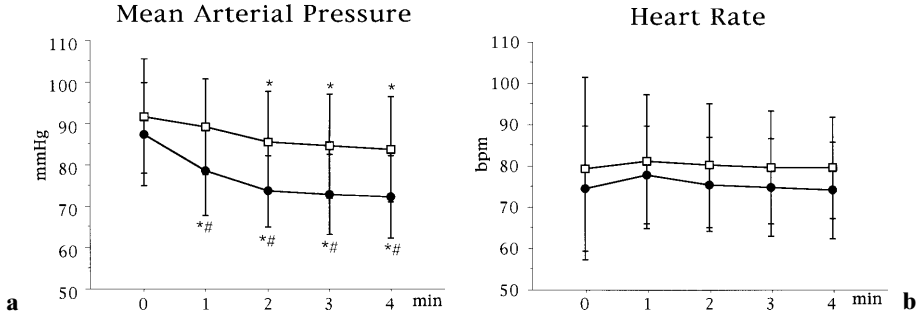
Table 1 shows the anthropometric data from the patients. There were no significant differences between the groups in age, sex, weight, or height.

Administration of propofol or thiamylal resulted in a significant decrease in the mean arterial pressure (MAP), which was greater after administration of propofol than of thiamylal. The heart rate remained stable in both groups (Fig. 1).

Propofol and thiamylal did not influence FAC (Fig. 2). The EDA index (EDA divided by body surface area: EDAI) significantly decreased from 5.5 ± 0.5 to 4.1 ± 0.5 $cm^2 \cdot m^{-2}$ after administration of propofol and from 5.8 ± 0.4 to 5.1 ± 0.2 $cm^2 \cdot m^{-2}$ after administration of thiamylal. The percent change in EDAI from baseline

Table 1. Anthropometric data from the patients in each group

Characteristiz	Propofol ($n = 16$)	Thiamylal ($n = 16$)
Age (yr)	26 ± 12	32 ± 14
Sex (M/F)	9/7	7/9
Weight (kg)	57 ± 11	55 ± 10
Height (cm)	166 ± 8	161 ± 9



a **b**

Fig. 1. Changes in mean arterial blood pressure and heart rate. **a** Mean arterial blood pressure (MAP) decreased significantly after injection of propofol (*Solid circles*) and thiamylal (*open squares*) ($P < 0.05$). Note that the propofol-induced fall in MAP was significantly greater than that induced by thiamylal ($P < 0.05$). **b** Heart rate remained stable in both groups. Data are means ± standard deviation. *$P <$ 0.05 vs. baseline. #$P < 0.05$ vs. thyamylal

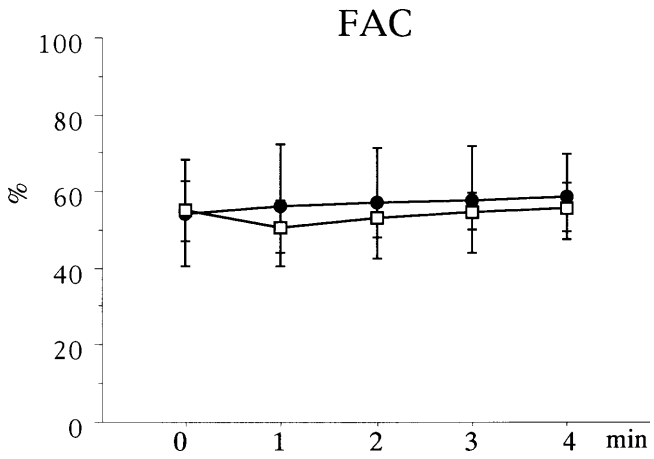


Fig. 2. Effects of propofol (*solid circles*) and thiamylal (*open squares*) on left ventricular fractional area change (*FAC*). Neither anesthetic agent significantly changed left ventricular FAC. Data are means ± standard deviation

also significantly decreased by 25 ± 4% after administration of propofol and by 11 ± 2% after administration of thiamylal. Propofol caused a more significant decrease in EDAI than thiamylal (Fig. 3).

Propofol and thiamylal significantly reduced ESWS from 56.7 ± 5.2 to 40.2 ± 2.8 g·cm^{-2} and from 56.6 ± 9.0 to 51.9 ± 10.4 g·cm^{-2}, respectively. The percent change in ESWS from baseline also significantly decreased after propofol and thiamylal by 29 ± 5% and 13 ± 10%, respectively. The propofol-induced decrease in ESWS was significantly greater than that induced by thiamylal (Fig. 3).

Discussion

Our study of LV performance during the course of anesthetic induction demonstrated that propofol caused a more pronounced decrease in the LV preload and afterload than thiamylal but had no significant effect on LV contractility.

The equipotent doses of propofol and thiopentone or thiopental have been reported to be 1:1.6–1:2.6 in previous human studies [3,13,14] and 1:2 in an animal study [15]. Therefore, we administered propofol at a dose of 2 mg·kg^{-1} in comparison with thiamylal at a dose of 4 mg·kg^{-1} as a bolus dose for anesthetic induction.

We showed that the more profound hypotensive effects of propofol relative to thiamylal were mainly due to reduced cardiac output as shown by reduced stroke area and reduced EDA, without concomitant changes in HR and FAC.

The reported propofol-induced changes in LV preload varied among studies [4,16,17]. The LV end-diastolic volume (EDV) obtained from the modified Simpton's rule with TEE remained unchanged with propofol and thiopental [2,12]. Lepage et al. [5,10], using gated radionuclide ventriculography, however, obtained decreased EDV with propofol. Propofol was infused in already anesthetized patients in the former study and in awake patients in the latter. We used propofol in awake patients, and our results are compatible with Lepage's results [5,10]. We measured EDA using TTE with automated border detection. Automated border detection can measure LV cavity area on line in real time. Estimation of LV volume by this method has been shown to be accurate and useful [18–21].

Previous studies have shown that propofol or thiopentone does not alter the effective arterial elastance, an index of afterload [2]. Other studies, in which systemic vascular resistance (SVR) was used as an index of afterload, showed that propofol either significantly reduced SVR by 20% [4,16] or did not significantly reduce it [17,22]. During in vivo animal studies [23,24], propofol induced little or no change in indices of LV afterload such as SVR, LV systolic wall-thickness frac-

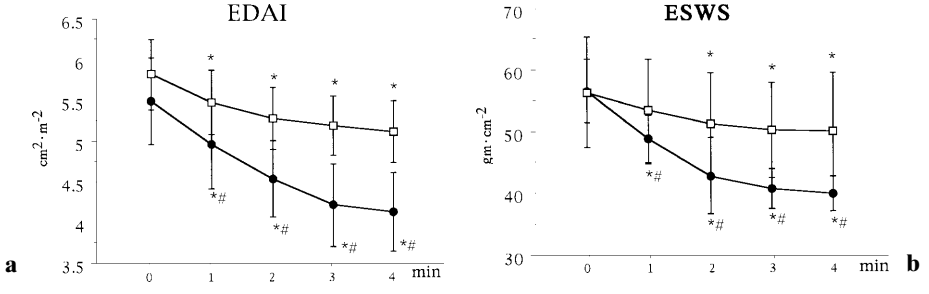


Fig. 3. Effects of propofol (*solid circles*) and thiamylal (*open squares*) on left ventricular end-diastolic area index and end-systolic wall stress. Both anesthetic agents reduced left ventricular end-diastolic area index (*EDAI*; **a**) and end-systolic wall stress (*ESWS*; **b**) relative to baseline. The propofol-induced reduction of EDA and ESWS was significantly greater than that induced by thiamylal ($P < 0.05$). Data are means ± standard deviation. *$P < 0.05$ vs. baseline. #$P < 0.05$ vs. thyamylal

tion, and effective arterial elastance. On the other hand, thiopentone does not reduce SVR [4]. The inconsistent results regarding the effects of these anesthetics on afterload may be due to different clinical and experimental settings. We adopted ESWS as an index of LV afterload using M-mode echocardiography and cuff systolic arterial pressure, which has been previously described by Reichek et al. [25]. Our results demonstrated that propofol decreased ESWS more than thiamylal in the course of anesthetic induction.

In studies of intact animals [6,7], propofol significantly reduced myocardial contractility, which was evaluated by dP/dt_{max} or end-systolic pressure-length relations (Ees). In an isolated heart preparation, both propofol and thiopental caused a dose-dependent reduction of myocardial contractility [24]. However, analysis of the relative anesthetic potencies demonstrated that thiopental was a more potent depressant of myocardial contractility than propofol [24–26]. Several methods have been used to assess the effect of anesthetics on LV contractility in humans. Mulier et al. [2,12] used the modified end-systolic pressure-volume relationship, whereas Gauss et al. [1] and Lepage et al. [10] used the end-systolic quotient. These studies showed that propofol was more potent than thiopentone with regard to depression of contractility. Our results showed that propofol and thiamylal did not change FAC. However, FAC may be influenced more or less by alterations of preload or afterload. Therefore, in our study the unaltered FAC, in spite of decreases in preload and afterload during anesthetic induction, could not be used to evaluate the effect on LV contractility accurately.

The decrease in preload and afterload by propofol may be attributable to direct and/or indirect vasodilatation due to inhibition of sympathetic nerve activity. Several animal studies have reported that propofol reduces the preload by a direct effect on venous smooth muscle tone [8,27]. In contrast, it has been reported that the mechanism of peripheral vasodilatation [28] and venodilatation [29] primarily involves the inhibition of sympathetic vasoconstrictor nerve activity. The concentration of propofol reported to have a direct vasodilatory effect in animal studies is much higher than that used clinically. Therefore, it is likely that the primary effect of propofol on circulation is due to an indirect vasodilatation of arterial and venous vascular beds due to a reduction in the sympathetic nerve activity.

In conclusion, we showed that propofol produces hypotension by eliciting a more pronounced reduction of the LV preload and afterload during the induction of anesthesia, as compared with thiamylal. On the other hand, we could not evaluate the effect of both anesthetic agents on LV contractility.

Acknowledgments. Supported by Grant-in-Aid 09470329 for Scientific Research, Ministry of Education, Science and Culture, Japan.

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