

THE EFFECTS OF DURATION OF PROPOFOL INJECTION ON HEMODYNAMICS

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Abstract

Objectives: The aim of study was to see whether increasing the time of injection of standard dose of Propofol during induction can prevent fall in blood pressure in female patients; as is commonly observed with this anesthetic agent.

Design: Comparative, non-interventional, prospective, and randomized and single blind study.

Place and duration: The study was carried out on female in-patients admitted and surgically operated at a specialized, tertiary care hospital and was completed with in 6-months.

Patients and methods: The hemodynamic effects of Propofol were compared in three groups of patients undergoing minor surgical procedures. Each group comprised of 25 patients. A 2 mg/kg Propofol was administered for 30, 60 and 120 seconds in patients of group-A, group-B and group-C respectively. Baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressures were recorded before induction of anesthesia. The same hemodynamic variables were recorded after induction at one-minute intervals for 10-minutes. Anesthesia was maintained with 1.5% enflurane and 60% nitrous oxide in oxygen. Complications such as pain on injection, dystonic movements, erythema, laryngeal spasm, episodes of desaturation, hypoventilation and the number of additional boluses required to induce hypnosis were also recorded.

Results: The fall in blood pressure was statistically insignificant between the three groups of patients. The incidence of dystonic movements was the highest in group-A while pain on injection was highest in group-C. Additional boluses of Propofol to induce hypnosis were required for patients in group-B and group-C.

Conclusion: Varying the speed of injection of Propofol during induction of anesthesia in adult female patients does not cause any major difference in the drop of their heart rate, systolic blood pressure, diastolic pressure and mean arterial pressure.

Key words: Anesthetics, intravenous, Propofol, hemodynamics.

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Introduction

Propofol is a well accepted intravenously administered anesthetic agent and, by virtue of its pharmacodynamic properties, is considered a popular choice both for the induction as well as in the maintenance of anesthesia¹. Propofol was first introduced into clinical practice in about two decades back. Over the years, extensive clinical experiences with Propofol in a wide variety of patients during different surgical procedures have demonstrated its effectiveness².

Propofol has been claimed to be the best available drug because of its rapid and smooth induction, short duration of action and a swift and clear headed recovery³. The standard Propofol dose of 2 mg/kg given over the recommended time of 30-seconds to pre-medicated patients is associated with a few disadvantages. The patients may experience pain during injection of Propofol, some patients exhibit dystonic movements and in majority of patients, there is a significant drop in blood pressure on induction^{1,4,5}. The pain on Propofol injection can be treated in different ways, including mixing Propofol with Lidocaine, injecting Lidocaine into the same vein before injecting Propofol, injecting cold saline before the injection or refrigerating the emulsion before injection. The pain on Propofol injection can also be reduced by selecting large size veins for administration of the drug⁶⁻⁹. Dystonic movements occur in a small percentage of patients, which are usually transient¹⁰.

The fall in blood pressure in patients remains a major problem during induction with Propofol, especially in hypertensive patients, patients having ischemic heart disease and those with cerebro-vascular disease, where a fall in blood pressure can lead to myocardial or cerebral ischemia. The aim of this study was to see whether increasing the time of injection of a standard dose of Propofol prevents the fall in blood pressure.

Methods

The study was initiated after approval from the hospital's project review board and ethics committee. Seventy five American society of anesthesiologists (ASA) grade I & II patients undergoing dilatation and

curettage (D & C) were randomly allocated to one of the three groups of patients. Patients with an ASA class-III or higher, patients with history of hypertension, peripheral vascular disease, diabetes and those with a history of sensitivity to egg proteins were excluded from the study. A written consent was obtained from all the patients who participated in the study. Patient demographics, including age, height and weight were recorded.

All the patients were pre-medicated orally with 3 – 4 mg Lorazepam, 2 hours before administering anesthesia. Baseline measurement of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded with a non-invasive automatic blood pressure measuring machine (Dinamap Pro 400 V2, GE healthcare, USA). One 18 gauge canula was inserted into a large peripheral vein in one of the patient's forearm. Two-milliliters of 2% Lidocaine was injected through the same vein before starting the injection of Propofol. The patients in group-A, group-B and group-C were administered a 2 mg/kg dose of Propofol for 30, 60 and 120 seconds respectively, using an infusion pump (Imed Gemini PC-1, Alaris Medical systems, San Diego, CA, USA). The heart rate, systolic blood pressure, diastolic blood pressure and arterial pressures were recorded every minute after induction of anesthesia for 10 minutes. In all the groups, after the loss of verbal contact with patient, anesthesia was maintained with 1.5% enflurane and 60% nitrous oxide in oxygen via face mask. An additional 10 mg bolus of Propofol was given to patients with whom verbal contact was not lost after a full induction dose of Propofol. The number of boluses required in each group were noted. Pain on injection and any other side effect including erythema at the site of injection or dystonic movement were also documented. Endotracheal intubations, patient's positioning and surgery were delayed for 10 – 12 minutes after induction in order to avoid any kind of stimulus which could affect the hemodynamics. The quality of anesthesia was ensured by monitoring laryngo-spasm, episodes of apnea, desaturation, hypoventilation and any abnormal movements.

SPSS version 14 was used to analyze the data of the study. Numerical data was analyzed by one way analysis of variance (ANOVA) and expressed as mean

and standard deviation. Non-parametric data were compared with chi-square test. The values of statistical significance were taken as $p < 0.05$.

Results

The data was successfully obtained in all cases. The demographic data was comparable between the three groups. No statistically significant differences were found between the groups with respect to age, weight and height (Table I). The baseline hemodynamic variables including the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were also comparable and statistically insignificant (Table II).

Soon after induction of anesthesia, a 15 – 20% decrease in the heart rate from the base line was generally observed in all patients. The drop in the heart rate was comparable between the three groups and there was no statistically significant difference between them ($p > 0.05$) (Fig. 1A). The systolic blood pressure decreased generally by 20 – 25% from the base line in patients of all groups and no statistically significant difference was observed between the three groups ($p > 0.05$) (Fig. 1B). The diastolic blood pressure in patients of all groups also decreased after induction of anesthesia by 22 – 28% from the base line. The decrease in diastolic

blood pressure was gradual and a maximum decrease was observed at the last minute of recording. There was no statistically significant difference in the decrease of diastolic blood pressure among the three groups ($p > 0.05$). However, the percent decrease in mean diastolic pressure was slightly different (22 – 28 %) than the percent decrease in mean systolic blood pressure (20 – 25%) among the three groups of patients (Fig. 1C). A general decrease in the mean arterial pressure by 20 – 25% from the base line was also noted parallel to the decrease in systolic and diastolic blood pressures, but no statistically significant difference was noted between the three groups ($p > 0.05$) (Fig. 1D).

Moderate to severe pain was observed on injection of Propofol in 8 (32%) patients in group-A, 9 (36%) in group-B and 11 (44%) in group-C. This was despite the fact that all these patients were injected with Lidocaine in the same vein before the injection of Propofol. Erythema at the site of injection was noted in only one patient in group-C. Dystonic movements were observed in 6 (24%) patients in group-A, 4 (16%) in group-B and 3 (12%) in group-C. Other complications including laryngeal spasm, apnea (longer than 30 seconds), desaturation ($SpO_2 < 90\%$) and hypoventilation (End tidal carbon dioxide > 45 mmHg) were not observed in any patient among the three groups. Verbal contact by the end of 2 mg/kg Propofol injection was lost with

Table I
Demographics of patients included in the study

| | Group A | Group B | Group C | P-Value |
|----------------------|--------------|--------------|-------------|---------|
| Age (Years) | 28.68 ± 4.5 | 29.0 ± 6.1 | 28.91 ± 6.1 | 0.95 |
| Weight (Kilograms) | 62.1 ± 8.1 | 62.30 ± 9.34 | 59.4 ± 6.1 | 0.34 |
| Height (Centimeters) | 153.96 ± 6.5 | 154.28 ± 6.6 | 154.0 ± 6.2 | 0.98 |

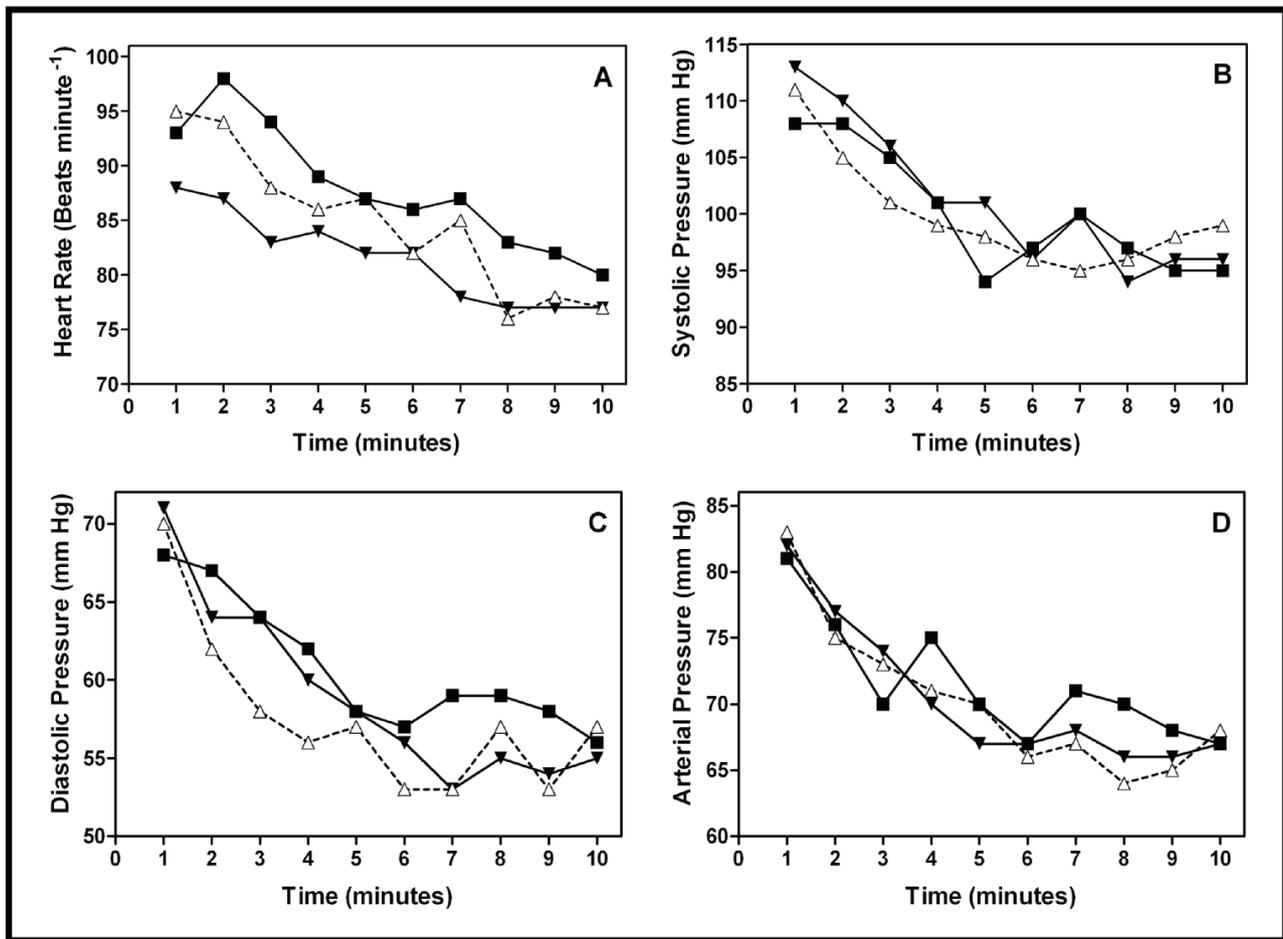
The data is the mean ± standard deviation (SD) of 25 patients (n = 25) in each group.

Table II
Baseline hemodynamic variables included in the study

| | Group A | Group B | Group C | P-Value |
|---------------------------------|---------|---------|---------|---------|
| Heart Rate min^{-1} | 93 | 90 | 88 | 0.99 |
| Systolic blood pressure (mmHg) | 120 | 127 | 116 | 0.98 |
| Diastolic blood pressure (mmHg) | 77 | 79 | 73 | 0.92 |
| Mean Arterial pressure (mmHg) | 88 | 93 | 85 | 0.90 |

The data is the mean of at least three readings from each of the 25 patients.

Fig. 1



Heart rate (Fig. 1-A), Systolic blood pressure (Fig. 1-B), Diastolic blood pressure (Fig. 1-C) and Mean Arterial pressure (Fig. 1-D) were recorded in female patients for 10 minutes after induction with Propofol in patients in group-1 (—■—), group-2 (---△---) and group-3 (—▼—).

all patients in group-A. However, 3 patients in group-B and 5 patients in group-C required additional boluses of 10 mg and 20 mg of Propofol respectively before they lost verbal contact.

Discussion

Propofol induced hypotension has been thought to act by different mechanisms. Propofol may lead to a reduction in the systemic vascular resistance and cardiac output is decreased by less than 20%⁴. Propofol induced hypotension is mediated by inhibition of the sympathetic nervous system and impairment of the baroreflex regulatory mechanism¹¹. Similarly Propofol is considered to have a direct relaxant effect on venous smooth muscles and in this way an increase in venous capacitance may contribute to the hypotension in

patients¹². Propofol also has a negative inotropic effect on the heart and moderately depresses cardiac function (more than thiopentone and ketamine). The mechanism is thought to be the attenuation of the auto-regulation of the heart which also leads to coronary vasodilatation¹³.

In our study, no significant difference between the three groups of patients was observed with respect to the established hemodynamic effects of propofol, while a fall in systolic blood pressure, diastolic blood pressure and mean arterial pressures were comparable to other reported studies¹⁴. Rapid administration of Propofol probably results in an early peak drug concentration in plasma, thus providing a larger gradient for Propofol uptake into the central nervous system and for drug redistribution to other body tissues. This observation was studied by Rolly et al, 1985 who failed to induce

anesthesia in 10% of his non-premedicated patients who received 2 mg/kg Propofol injected over 60 seconds, whereas the same dose was effective in all patients when injected for over five seconds¹⁵. This explains the need for additional boluses in our study in some patients in group-B and group-C. On the other hand, the slow increase in plasma drug concentration associated with a slow infusion provides a lower but more sustained gradient for uniform drug delivery throughout the central nervous system. However, by slow infusion a larger total dose may be required to maintain a sustained gradient of drug delivery into central nervous system.

Increasing the duration of induction delayed the loss of verbal contact in some patients in group-B and group-C in the present study, however, the hemodynamic response was similar in all the three groups of patients. Our results confirm the reported observations of Gillies and Lees, 1989 where they found that 2.5 mg/kg Propofol injected over 20, 40 or 80 seconds resulted in a significantly slower induction compared to Etomidate (0.3 mg/kg) injected at equivalent rates¹⁶. They also found that although increasing the length of injection resulted in a slower induction, the hemodynamic response was not different between the 20, 40 and 80 seconds groups of the Propofol administered patients.

Some studies have observed an initial tachycardia in patients after Propofol administration. However, most of the studies reported no change or decrease in the heart rate of patients after a bolus or infusion of Propofol¹⁵. In our study, the heart rate generally decreased by 15 – 20% in all groups of patients, which may be due to the absence of baroreflex activity and direct vagotonic effects of Propofol¹⁷.

The overall reported incidence of pain on injecting Propofol is 17.5 – 74%, however, the incidence varies with the technique of administration¹⁸. The size and site of the vein, temperature and concentration of the solution and the use of Lidocaine can help in pain reduction in patients injected with Propofol to 34%¹⁸⁻¹⁹. In our study, the incidence of pain in group-A and

Group-B was comparable with the generally accepted incidence, however the frequency was higher in group-C compared to other studies⁵. Theoretically, patients in group-A and B had a lower incidence of pain because the effect was transient due to shorter duration of induction. However, patients in group-C had a delayed loss of consciousness due to longer period of induction and therefore experience of pain was also probably longer.

The reported incidence of excitatory effects, including spontaneous movements, twitching, tremor, hypertonus and hiccups in patients as a result of Propofol induction is 14%¹. We noticed similar complications among 6 (24%) patients in group-A, 4 (16%) in group-B and 3 (12%) in group-C. The incidence of excitatory effects was comparable in group-B and C but was slightly higher in-group-A. These observations indicate towards the possibility of an indirect correlation between the speed of injection of Propofol and dystonic movements. Further studies with larger sample size may be required to firmly correlate the incidence of pain on injection and dystonic movements with the speed of injection of Propofol.

Conclusions

Propofol is a well accepted intravenously administered anesthetic agent but it causes a significant drop in blood pressure on induction. From the results obtained in this study we may conclude that varying the speed of injection of Propofol for induction of anesthesia in adult female patients does not prevent the decrease in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure. Administration of induction dose of Propofol (2 mg/kg) in 60 seconds and 120 seconds is associated with increased requirement for additional boluses to induce complete hypnosis. Incidence of pain at the site of injection is also higher in this group of patients, while injecting the same dose of Propofol in 30 seconds is associated with a relatively higher incidence of dystonic movements.

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