Original Article

A randomized comparative study of preloading with Ringers lactate and intravenous ephedrine for the prevention of hypotension due to propofol during induction of general anesthesia

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Abstract

Background: The ideal method to prevent hypotension due to intravenous propofol for induction of anesthesia is still debatable. The aim of the study was to compare the hemodynamic response of ephedrine and volume loading with ringer lactate in preventing the hypotension caused by propofol as inducing agent in patients scheduled for elective surgeries requiring general anesthesia with endotracheal intubation.

Methods: This was prospective randomized study conducted in 40 patients of ASA physical status I, aged 20-50 years, scheduled for elective surgeries requiring general anesthesia with endotracheal intubation. Group I received intravenous ephedrine sulphate (70 mcg/kg) just before induction of anaesthesia, and patients assigned to Group II received preloading with Ringer's lactate (12 ml/kg) over the 10-15 minutes before the administration of propofol. The variables compared were heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure following induction of anesthesia till 10 minutes after intubation of trachea.

Results: We found that there were increase in systolic blood pressure, diastolic blood pressure and mean arterial pressure after induction in both the groups but the difference between the groups was not significant. The increase in heart rate was found to be significantly higher in ephedrine group in comparison to volume loading group.

Conclusion: Our study showed that both the methods used were equally effective in preventing hypotension induced by propofol in the adult ASA physical status I patients requiring general anesthesia with endotracheal intubation. However, the heart rate was significantly higher in patients receiving ephedrine in comparison to volume loading group.

Key words: anesthetic agents; ephedrine; hypotension; propofol; ringer's lactate.

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Introduction

Propofol is widely used in clinical practice because of its favorable recovery profile and infrequent side effects.[1] Propofol provides fast onset of action[2], potent attenuation of pharyngeal, laryngeal and tracheal reflexes[3] and adequate depth of anesthesia during intubation.[2,4] It also posses antiemetic activity at low dose.[5] However, Induction of anesthesia with propofol is often associated with a significant decrease in arterial blood pressure.

So far, various methods that have been studied to prevent hypotension induced by propofol during induction of anesthesia, include preloading with fluids (colloids and crystalloids)[6,7] and use of various vasopressors including dopamine, dobutamine, phenylephrine, ketamine and metaraminol.[8] The ideal method to prevent hypotension is still debatable. Therefore, this study was designed to determine the efficacy of two prophylactic approaches, either with fluid loading or intravenous ephedrine against the anticipated propofol induced hypotension.

Methods

Following Institutional Review Board approval and written informed consent, consecutive patients undergoing any elective surgery who needed general anaesthesia with endotracheal tube intubation were accessed for inclusion in the study. The inclusion criteria were ASA Physical Status I of both sexes of aged 16 - 50 years weighing 40 - 80 kg scheduled for elective surgeries requiring general anaesthesia with endotracheal intubation. The exclusion criteria were patients with known allergy to Propofol, morbid obesity and pregnancy.

All patients included in the study were admitted to the hospital at least a day before surgery in their respective ward. Informed written consent was taken from each patient who was included in the study and thorough pre- anaesthetic check-up was done. The heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) taken at pre-anaesthetic check-up were considered as baseline. Patients were pre-medicated with Tab Diazepam 10 mg for those weighing ≥ 50 kg and five mg for those weighing < 50 kg in the night before surgery and were kept nil per orally after midnight.

In operation theatre, intravenous access was achieved with 18 gauge cannula and was secured. Monitors: ECG (Electrocardiogram), non-invasive blood pressure (NIBP) and pulse-oximeter were connected to the patient. Inj. Ephedrine (Fedrine 5mg/ml of Jayson Pharmaceticals) were prepared by the doctor or nurse not involved in the study by diluting 1 ml of Ephedrine with 4 ml of distilled water making the concentration of 1mg/ml. Patients included in the study were allocated randomly into two groups by lottery method: patients assigned to Group I received ephedrine sulphate (70 μg/kg iv) just before induction of anaesthesia, and patients assigned to Group II received preloading with Ringer's lactate (12 ml/ kg) over the 10–15 minutes before the administration of propofol.

The doctor directly involved in the study came to operation room only after the test drug or the preloading was given. At that point of time, patients in both the groups received Ringer's lactate only to keep vein open. After pre-oxygenation for three minutes, propofol (2.5 mg.kg^{-1} bolus with lidocaine at 1mg/ml was administered in < 10 sec followed by inj. Vecuronium at 0.1 mg.kg^{-1} for laryngoscopy, and orotracheal intubation. Assisted ventilation was done by 100% oxygen for 3 minutes, laryngoscopy and intubation was done by the doctor who was involved in the study after 3 minutes of vecuronium administration and assisted ventilation with 100% oxygen. After intubation and confirming the position of the endotracheal tube, intermittent positive-pressure ventilation was started with the administration of oxygen at 6 lit/min and 2 % halothane for 2 minutes and maintenance was done with 1% halothane till 10 minutes.

During the perioperative period, HR and SBP, DBP and MAP were measured just before induction, after the administration of propofol, just after intubation and at 3, 5, 7, 10 minutes after intubation using an automatic non-invasive blood pressure monitor. No surgical stimulation was performed until the first ten minutes after induction was completed to ensure no untoward extraneous effect on patients' physiological variables during the study period. Anesthesia maintenance was done by Halothane, IPPV, oxygen, vecuronium and pethidine. At the end of surgery with the attempt of spontaneous breathing, the effects of muscle relaxant were reversed with intravenous 0.05mg/kg of neostigmine and 0.02mg/kg of atropine. Extubation of trachea was done when the respiration was adequate and protective reflexes were intact. Any complications during induction, i.e., somatic movements, vomiting, convulsions, laryngospasm and coughing, were excluded from the study.

The number of patients required in each group was determined by using power analysis based on the previous study.[9] The sample size required detecting 20% reduction in MAP from baseline at 5% level of significance and 80% power was 20 patients in each group. All the data were analyzed using SPSS software. Chi-square test, independent and paired t test, different tables and diagrams were used in proper context in the process of data analysis.

Results

A total of 40 patients were enrolled in the study. Both the groups were comparable with respect to demographic data (Table 1).

Table 1: Demographic data

	Group I n=20	Group II n=20	P value
Male	5 (25%)	4 (20%)	0.70
Female	15 (75%)	16 (80%)	
Age (years)	29.7±7.4	29.3±6.4	0.87
Weight(kg)	52.7±5.2	53.2±5.4	0.76

Figure 1: Comparison of heart rate between the two groups

The mean HR ± SD before induction in both the groups were statistically not significant (p value 0.64) whereas after induction heart rate increased in both the groups and was statistically significant (p value 0.007). The heart rate further increased significantly after intubation till ten minutes after intubation in both the groups, but the increment were more in group I than group II and were statistically significant.
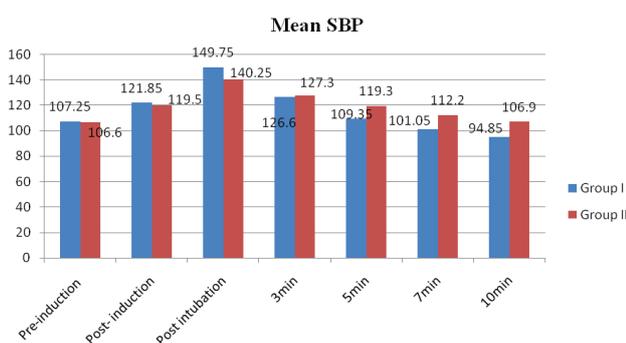

Figure 2: Comparison of mean systolic blood pressure between the two groups

The mean systolic blood pressure ± SD before induction in both the groups were statistically not significant (p value 0.76) whereas after induction systolic blood pressure had increased in both the groups and were not statistically significant (p value 0.33). There were further rise in systolic blood pressure in both the groups immediately after intubation which were statistically significant (p

value 0.02). Then after the systolic blood pressure started decreasing in both the groups but more were noted in the ephedrine group and were statistically significant. In the volume loading group the systolic blood pressure had came to normal after ten minutes of intubation but in ephedrine group it had decreased more than the baseline.
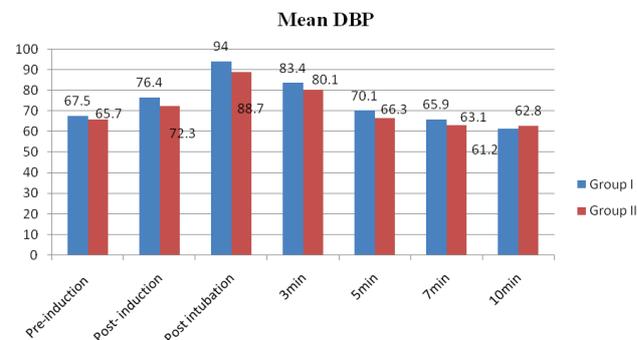

Figure 3: Comparison of mean diastolic blood pressure between the two groups

The mean diastolic blood pressure ± SD before induction in both the groups were statistically not significant (p value 0.36) whereas after induction diastolic blood pressure had increased in both the groups and were not statistically significant (p value 0.13).There were further rise in diastolic blood pressure in both the groups immediately after intubation which were statistically significant (p value 0.02). Then after the diastolic blood pressure started decreasing in both the groups but more were noted in the ephedrine group than volume loading group and were not statistically significant.
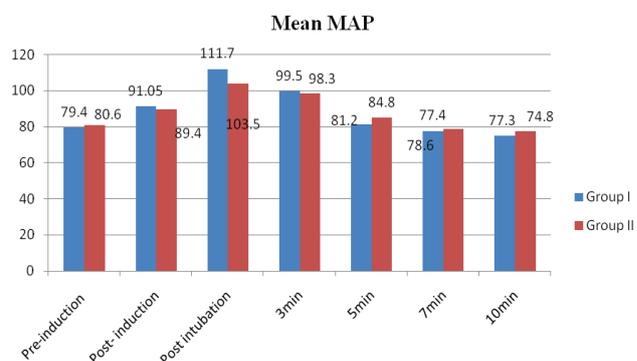

Figure 4: Comparison of mean arterial pressure between the two groups

The mean arterial pressure ± SD before induction in both the groups were statistically not significant (p value 0.62) whereas after induction mean arterial pressure had increased in both the groups and were not statistically significant (p value 0.42).There were further rise in mean arterial blood pressure in both the groups immediately after intubation which were statistically significant (p value 0.045). Then after the mean arterial pressure had

decreased in both the groups but more were noted in the ephedrine group and were not statistically significant.

Discussion

Induction of general anaesthesia can have significant hemodynamic consequences and many strategies have been used for the induction of anesthesia. There is evidence that hypotension and hypertension during general anaesthesia are independently associated with adverse outcome in patient having both noncardiac and cardiac surgery. One of the intervals of general anaesthesia during which hypotension is prevalent is the period after the induction of anaesthesia but before the onset of surgical stimulation. This period is particularly prone to decreased vigilance with regard to hemodynamic changes. The choice and dosage of intravenous anesthetic drugs influence the occurrence of hemodynamic instability in the period after induction.

Propofol and thiopentone are the two most commonly used drugs for induction of general anaesthesia in our part of the world. Propofol is gaining popularity and is the most common agent for induction of anesthesia. Propofol has a rapid onset of action and fast recovery in comparison to thiopentone. It also provides good intubating condition, and also has significant anti-emetic property in low doses.[10] Therefore, we had chosen this drug in our study.

Besides these advantages and favorable effects, it has certain side effects which cause the limitation in its use. The most prominent and important side effect of propofol is a decrease in arterial blood pressure during induction of anesthesia irrespective of the presence of cardiovascular disease. The decrease in arterial pressure is mostly associated with decrease in cardiac output and decrease in the peripheral vascular resistances. The hypotensive effect of propofol is due to decrease in systemic vascular resistance[1,11] or on cardiac output[12] caused by a combination of venous and arterial vasodilatations[12,13,14], impaired baro-reflex mechanism[15], and depression of myocontractility.[10]

Though there are many other factors that influence the hemodynamic stability during the induction period like anxiety, dose of the drugs, speed of injection, age, preoperative vitals etc. Taking all these factors into consideration, all the patient included in our study were given anxiolytic drugs i.e. Tab. Diazepam night before surgery during pre-anesthetics check up.

The study done by Michelsen et al[16] found that there was increased sensitivity of propofol in the elderly patient so in our study we had chosen the subject between the ages of 16 years to 50 years and there were no statistically significant difference in the age of the patient included in the study group as shown in the table I. All the patients included in the study were of ASA I. The hemodynamic instability during induction may also depend on the baseline hemodynamic condition. In our study, there were also no statistically significant differences in the baseline heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure.

The study done by Hossan El-beheiry et al[17] showed that the hypotension induced by propofol was also dependent on the speed of injection given so, considering that into account in our study we had also given the drug within 10 seconds to all the patients included in the study.

Ephedrine is the mixed acting drug that acts by increasing the endogenous release of non-epinephrine (indirect acting) and also directly stimulant the effects on adrenergic receptor (direct acting).[9] It increases myocardial contractility and also increases the systemic vascular resistance by peripheral venous and arterial vasoconstriction. Prophylactic use of ephedrine, as vasopressor, attenuates the hemodynamic response to the bolus administration of propofol.[9] Therefore sympathomimetics including ephedrine prevent hypotension by increasing peripheral vascular resistance and / or cardiac contractility with their advantages of low cost and ease of administration. But they also have disadvantages including tachycardia and increased risk of arrhythmias with concomitant use of volatile anaesthetics.

Preloading with fluids prevents hypotension by increasing venous return and filling the pressure of right atrium and left ventricle to augment cardiac output.[18] Since one of the mechanism of hypotension caused by propofol induction is sympathetic blocked that causes vasodilatation and reduction in venous return to heart therefore additional fluid infusion in the form of preloading can maintains cardiac preload and help to attenuate the drop in the blood pressure.

In this study, we compared the effect of iv ephedrine and preloading for the prevention of hypotension induced by propofol when given in the bolus dose for induction. Ephedrine and volume loading were used as the test drug because many studies showed that the decrease in arterial blood pressure was associated with decrease in cardiac output, decrease in stroke volume and systemic vascular resistance.[3,10,11]

The patient's variables (Table I) in relation to age, sex, weight were not statistically significant in these two study groups. There were also no statistically significant differences among the two study groups in baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure. Our study showed that the administration of ephedrine sulphate immediately before induction produced modest post-induction hypertension, enhanced the post intubation hypertension but showed the delayed decrease in blood pressure. There was also considerable increment in heart rates with a maximum increased of 47.2% from the baseline just after intubation. On the other hand, pre-induction volume loading with ringer lactate had also prevented the post induction hypotension and also abolished the ten minutes hypotension. There were also

slight increase in heart rate in the volume loading group but less than those from the ephedrine group, maximum increment reached upto 23.5% from the baseline.

Our study was comparable to the study done by Hossan El-Beheiry et al[17] in 1995, administration of ephedrine sulphate immediately after induction produced modest post- induction increase in blood pressure, enhanced the post intubation increased in arterial blood pressure but failed to protect against the delayed hypotension. There were also considerable increased in the heart rates with maximum upto mean of 41.9%from baseline just after intubation, where as in our study similar result had come but the maximum heart rate increased upto mean of 47.2 % from baseline.

In the same study in other hand pre-induction volume loading group with ringer's lactate abolished the post induction decrease in arterial blood pressure and ten minutes post intubation hypotension. In our study also there was increased in blood pressure post induction which went to peak immediately after intubation and had came to nearly to baseline after ten minutes of intubation. The same study also showed that there was slight increased in heart rate in volume loading group which were not different from the preoperative values, which was similar to our study.

Our study showed that there was increased in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure in both the groups after induction with propofol bolus. So we found that both the methods used in our study for the prevention of hypotension induced by propofol in general anesthesia were found to be effective. In our study, we found that there were statistical significant differences between the two groups in terms of heart rate. In ephedrine group heart rate nearly increased by 50% from the baseline after intubation whereas in volume loading group the heart rate did not increase as high as ephedrine. Therefore, because of more increase in heart rate in ephedrine group, it should be use with caution in high risk patient like elderly and patient with heart disease. So the prophylactic measure for the prevention of hypotension induced by propofol with volume loading found to be better in such high risk patient in comparison to ephedrine, though there were no statistically significant differences were found between the two groups. However, for the applicability of the results to such high risk patients, we suggest another randomized trial in such a population. The results of this study should be cautiously applied to patients of ASA physical status II and more.

The limitations of the study might be the fact that the observations of hemodynamic variables were completed within 10 minutes. Ephedrine may have arrhythmogenic effect after the 10 minutes period also.

In conclusion, we found that both ringer's lactate infusion and bolus ephedrine used in our study were equally effective in preventing the hypotension induced by propofol in ASA physical status I patients requiring general anesthesia. However, increase in the heart rates was more in the ephedrine group.

References

1. Smith I, White PF, Nathason M, Gouldson R. Propofol: an update on its clinical use. Anesthesiology 1994;81:1005-435. http://dx.doi.org/10.1097/00000542-199410000-00028 [PMID:7943815]

2. Hug Jr CC, McLeskey CH, Nahrwold ML, Roizen MF, Stanley TH, Thisted RA, et al. Hemodynamic effects of propofol: data from over, 25,000 patients. Anaesth Analg 1993;77:521-30. [PMID:8214693]

3. van Aken H, Meinshausen E, Prien T, Brussel T, Heinecke A, Lawin P. The influence of fentanyl and tracheal intubation on the hemodynamic effect of anaesthesia induction with propofol/N2O in humans. Anesthesiology 1988;68:157-63. http://dx.doi.org/10.1097/00000542-198801000-00031 [PMID:3257362]

4. Briggs MLP, Dundee JW, Bahar M, Clarke RSI. Comparison of the effect of disopropyl phenol and thiopentone on response to somatic pain. BJA 1982;54:307-11. http://dx.doi.org/10.1093/bja/54.3.307 [PMID:6978144]

5. Mc Collum JS, Milligan KR, Dundee JW. The antiemetic action of propofol. Anaesthesia 1988;43:239-40. http://dx.doi.org/10.1111/j.1365-2044.1988.tb05551.x [PMID:3259081]

6. Turner RJ, Gatt SP, Kam PC, Ramzan I, Daley M. Administration of a crystalloid fluid does not prevent the decrease in arterial blood pressure after induction of anaesthesia with propofol and fentanyl. BJA 1998;80:737-41. http://dx.doi.org/10.1093/bja/80.6.737 [PMID:9771299]

7. Al Ghamdi A. Hydroxyethyl starch 6.0% preload does not prevent the hypotension following induction with propofol and fentanyl. Middle East J Anaesthesiol 2004;17:959-68. [PMID:15449752]

8. Chiu CL, Tew GP, Wang CY. The effect of prophylactic metaraminol on systemic hypotension caused by induction of anaesthesia with propofol in patients over 55 years old. Anaesthesia 2001;56:893-9.http://dx.doi.org/10.1046/j.1365-2044.2001.02059-4.x [PMID:11531679]

9. Kasaba T, Yamaga M, Iwasaki T, Yoshimura Y, Takasaki M. Ephedrine, dopamine, dobutamine to treat hypotension with propofol during epidural anaesthesia. Can J Anaesth 2000;47:237-41. http://dx.doi.org/10.1007/BF03018919 [PMID:10730734]

10. Coates DP, Monk CR, Prys-Roberts C, Turtle M. Hemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anesthesia in humans. Anesth Analg 1987;66:64-70. http://dx.doi.org/10.1213/00000539-198701000-00011 [PMID:3492156]

11. Claeys MA, Gepts E, Camu F. Hemodynamic changes during anaesthesia induced and maintained by propofol. BJA 1988;60:3-9. http://dx.doi.org/10.1093/bja/60.1.3 [PMID:3257393]

12. Monk CR, Coates DP, Prys-Roberts C, Turtle MJ, Spelina K. Hemodynamic effect of the prolonged propofol infusion supplemented nitrous oxide anesthesia for peripheral vascular surgery. BJA 1987;59:954-60. http://dx.doi.org/10.1093/bja/59.8.954 [PMID:3498505]

13. Stephan H, Sonntag H, Schenk HD, Kettler D, Khambatta HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary heart disease. BJA 1986;58:969-75. http://dx.doi.org/10.1093/bja/58.9.969 [PMID:3489478]

14. Robinson BJ, Ebert TJ, O'brien TJ, Colinco MD, Muzi M. Mechanism whereby propofol mediates vasodialatation in humans: Sympathoinhibition or direct vascular relaxation? Anaesthesiology 1997;86:64-72. http://dx.doi.org/10.1097/00000542-199701000-00010 [PMID:9009941]

15. Ebert TJ, Muzi M, Berens R, Goff D, Kampine JP. Symphathetic response to induction of anaesthesia in humans with propofol or etomidate. Anesthesiology 1992;76:725-33. http://dx.doi.org/10.1097/00000542-199205000-00010 [PMID:1575340]

16. Michelsen I, Helbo-Hansen HS, Kohler F, Lorenzen AG, Rydlund E, Bentzon MW. Prophylactic ephedrine attenuates the hemodynamic response to propofol in elderly female patient. Anaesth Analg 1998;86:477-81. http://dx.doi.org/10.1097/00000539-199803000-00004 [PMID:9495396]

17. El Beheiry H, Kim J, Milne B, Seegobin R. Prophylaxis against the systemic hypotension induced by propofol during rapid sequence intubation. Can J Anaesth 1995;42:875-8. http://dx.doi.org/10.1007/BF03011034 [PMID:8706196]

18. Weeks S. Reflection of hypotension during caesarean section under spinal anesthesia: do we need to use colloid? Can J Anaesth 2000;47:607-10. http://dx.doi.org/10.1007/BF03018990 [PMID:10930197]