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.

Introduction

Propofol is widely used in clinical practice because of its favorable recovery profile and infrequent side effects. Propofol provides fast onset of action, potent attenuation of pharyngeal, laryngeal and tracheal reflexes and adequate depth of anesthesia during intubation. It also possesses antiemetic activity at low dose. 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) and use of various vasopressors including dopamine, dobutamine, phenylephrine, ketamine and metaraminol. 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-anesthetic 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-anesthetic 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 Pharmaceuticals) 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 1 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 l/ 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. 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

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5 (25%)</td>
<td>4 (20%)</td>
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<tr>
<td>Female</td>
<td>15 (75%)</td>
<td>16 (80%)</td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Weight(kg)</td>
<td>52.7±5.2</td>
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</tbody>
</table>

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 0.36) whereas after induction systolic 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 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 more than the baseline.
The study done by Michelsen et al showed that the hypotension induced by propofol is 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). 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. 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. 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.

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 up to 23.5% from the baseline.

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

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