Prevention of hypotension during propofol induction: A comparison of preloading with 3.5% polymers of degraded gelatin (Haemaccel®) and intravenous ephedrine

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ABSTRACT

The present study compared the efficacy of preloading with colloid "Haemaccel®" with vasoconstrictor (intravenous ephedrine sulphate) in preventing hypotension during propofol induction. This prospective, randomized study included 120 patients of Amercan Society of Anaesthesiologists (ASA) physical status I and II ageing 21 to 50 years of both gender coming for routine surgery. Patients were randomly allocated into three groups with 40 patients in each. Group A (control) did not receive any study medication, group B received Haemaccel® (10ml/kg intravenously over 10-15 minutes) and group C received injection ephedrine (0.2mg/kg iv) prior to induction of anaesthesia. Propofol (2.5mg/kg iv) was used for induction of anaesthesia. Heart rate and blood pressure were recorded before induction (baseline) and then every minute for 5 minutes after administering propofol. Anaesthesia was continued with standard technique thereafter. Hypotension was defined as fall in systolic blood pressure more than 20% from the basal value. The incidence of hypotension in Haemaccel® (23.1%) or ephedrine group (22.5%) was significantly less than the control group (67.5%, P<0.01). We conclude that though preloading with colloid (Haemaccel®) or prior injection of sympathomimetic (ephedrine) are not fully efficacious in preventing hypotension caused by propofol induction, both decrease the incidence in significant number of patients with heart rate less than baseline value in the colloid group.

Keywords: preloading, hypotension, propofol, ephedrine, Haemaccel®.

INTRODUCTION

Anaesthesia induction with propofol is often associated with a significant decrease in arterial blood pressure especially in patients with advanced age (>50 years), prior hypotension (mean arterial pressure <70mmHg) and higher American Society of Anaesthesiologists' Physical Status (ASA-PS) class (> II).[1-4] This decrease in blood pressure may not be clinically significant in young and healthy individuals, but significant hypotension during induction has been reported to correlate with longer postoperative stay and/or death than those without it.[3] So far, various measures to prevent hypotension include preloading with fluids (colloids and crystalloids)[5,6] and use of vasopressors including ephedrine, dopamine, dobutamine, and metaraminol.[7-9] Preloading with colloid (500ml or more) has been shown to be more effective at maintaining arterial blood pressure than crystalloid in parturient undergoing spinal anaesthesia for caesarean section.[10] Preloading with fluids (including Haemaccel®) prevents hypotension by increasing venous return and filling pressure of the right atrium and left ventricle to augment cardiac output but can have many disadvantages including long administration time, high cost, risk of haemodilution, fluid overload and anaphylactoid reactions.[11] Similarly sympathomimetics (including ephedrine) prevent and correct 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.[12] Thus, ideal method to prevent hypotension is still debatable. This study was designed and carried out to compare the efficacy of preloading with 3.5% polymers of degraded gelatin (Haemaccel®) and intravenous ephedrine in prevention of hypotension during induction of anaesthesia with propofol.

MATERIALS AND METHODS

This was an open prospective, randomized, comparative study conducted on 120 American Society of Anaesthesiologist (ASA) physical status I and II patients aged between 21-50 years, undergoing routine surgery. Approval for the study was obtained from the institute's ethical committee and written and informed consent was taken from the patients after explaining the nature of the study. Patients with history of hypertension (controlled or uncontrolled), any cardiac disease, cerebrovascular disease, thyrotoxicosis, any respiratory, hepatic or renal diseases, allergy to the study medications, therapy with vasoactive medications, morbid obesity (BMI> 40kg/m^2) and pregnancy, or any hypovolaemic condition (like therapy with diuretics) were excluded from the study.

All the patients enrolled in the study received 10mg diazepam as premedication the night before and 2 hours prior to surgery. The peripheral venous access was secured with 16G intravenous cannula. Patients were randomly allocated into three study groups of 40 patients in each using sealed envelope technique. In group A (control group) neither any colloid nor any vasoconstrictor medication was given. In group B Haemaccel® (10ml/kg) was given intravenously over 10-15 minutes and in group C injection ephedrine (0.2mg/kg) was given intravenously prior to induction of anaesthesia with propofol (2.5mg/kg iv over 20-30 seconds). The usual maintenance and replacement fluid (Ringer's Lactate solution) was started at the rate of 2ml/kg in all the patients. All patients were monitored using continuous electrocardiography, pulse oximetry and non-invasive arterial blood pressure at one minute interval. We noted down the heart rate and arterial blood pressure (systolic, diastolic and mean) every minute, starting before induction till 5 minutes after propofol injection. In this period, bag and mask ventilation was used to maintain oxygen saturation >95% and no orotracheal intubation was done. We also observed for the incidence of hypotension that is fall in systolic blood pressuree"20.0% from baseline and any other side effects. Hypotension was treated with rapid infusion of Ringer's Lactate. At the end of study period vecuronium and morphine was given to continue anaesthesia and surgery.

All the data were entered and analyzed using statistical package SPSS version10 (Chicago University, Illinois, USA). One way analysis of variance (ANOVA) and Students t test were used to compare continuous data. Chi-square test was used to compare proportions. At 95.0% confidence interval, the calculated value of p< 0.05 was considered statistically significant difference.

RESULTS

As one patient developed anaphylaxis following administration of Haemaccel®, only 39 patients remained in group B for analysis. Demographic characteristics (age, sex distribution, body weight and height) and baseline haemodynamic parameters of the patients were similar in the three groups (Table-1).

There was decrease in blood pressure from the baseline in all the three groups. The decrease in systolic blood pressure (SBP) from the baseline was significant in group A ($p<0.0001$) from the first minute onwards till the end of observation. In group B, the decrease in SBP was significant ($p<0.05$) from the first minute onwards while the decrease in group C became significant ($p<0.05$) only three minutes onwards. While comparing among the three groups, SBP was lowest in group A and highest in group C at all observation times (Table-2).

Although the heart rate decreased from the base line following administration of propofol in both groups A and B, the reduction was statistically significant at 4 and 5 minutes intervals in group B. The increase in heart rate in group C was statistically insignificant during study period (Table-3).

The incidence of hypotension (67.5%) in group A was significantly ($P<0.0001$) more than group B (23.1%) or group C (22.5%). There was no difference in between group B and group C. The median time interval at point of hypotension was longest in group C but the difference did not reach the level of statistical significance ($p>0.05$) (Table-4).

DISCUSSION

Our study confirmed significant reduction in arterial blood pressure during induction of anaesthesia in our patients. We also found that the heart rate is also reduced

Table-1: Demographic data and baseline haemodynamic parameters

Parameters	GroupA mean± SD (n=40)	GroupB mean± SD (n=39)	GroupC mean± SD (n=40)	p value
Age (years)	34.3±11.1	36.8±10.2	35.2±11.1	0.59
Weight (Kg)	49.9±8.3	49.7±6.8	50.0±9.3	0.987
Male: female ratio	11:29	9:30	9:31	0.85
Heart rate (beats per minute)	83.6±15.8	82.1±13.2	81.3±15.8	0.790
Systolic blood pressure (mmHg)	123.8±11.3	120.7±11.0	126.0±12.4	0.138
Diastolic blood pressure (mmHg)	78.8±8.3	77.6±9.2	79.1±8.2	0.720
Mean blood pressure (mmHg)	93.8±8.6	92.4±9.5	96.2±10.0	0.202

Table-2: Comparison of systolic blood pressure (mmHg) during study period

Time (min)	Group A mean± SD (n=40)	Group B mean± SD (n=39)	Group C mean± SD (n=40)
0	123.8± 11.3	120.7± 11.0	126.0± 12.4
1	101.4± 10.4**	113.0± 14.8*#	124.4± 18.0##¥
2	100.0± 11.2**	110.8± 15.1*#	119.7± 20.3##¥
3	98.8± 10.8**	107.0± 11.8**#	117.0± 16.4*##¥
4	99.8± 10.3**	107.3± 11.5**#	114.6± 14.6*##¥
5	100.8± 10.2**	106.6± 11.3**#	111.8± 12.5**##¥

Note: comparison with the base line (within group): * (p<0.05), ** (p<0.001); comparison with the placebo group (between group): # (p<0.05), ## (p<0.001); comparison between Haemaccel® and ephedrine group: ¥ (p<0.05),

in this period but was significantly less in colloid preloaded patients. We have also demonstrated a significant reduction in the incidence of propofol induced hypotension with Haemaccel® preloading and prior administration of ephedrine. However, hypotension was still present in almost one fourth of the patients.

Propofol has been shown to cause hypotension due to its effects of peripheral vasodilatation by increased endothelial production and release of nitric oxide.[13] Significant decrease in systolic blood pressure from the baseline was observed in all the groups after propofol administration in our study also. We observed that both Haemaccel® and ephedrine effectively maintained significantly higher level of systolic pressure than control group. However, none of these two was fully effective in preventing the tendency of blood pressure reduction associated with propofol administration.

Table-3: Changes in heart rate (HR) during study period

Time (min)	Group A mean± SD (n=40)	Group B mean± SD (n=39)	Group C mean± SD (n=40)
0	83.6±15.8	82.1±13.2	81.3±15.8
1	84.7±13.2	81.9±12.9	85.7±16.5
2	80.5±12.8	79.2±14.0	85.6±18.4
3	79.4±13.9	76.6±14.4	85.6±16.2
4	78.1±14.3	75.9±13.5*	85.4±17.3
5	78.4±14.3	76.0±14.2*	87.0±16.7

Note: *comparison with the base line (within group): * (p<0.05)*

Our findings are consistent with the findings of Turner and colleagues[5] and Al-Ghamdi[6] who have shown lack of full effectiveness of preloading with crystalloid or colloids in preventing hypotension associated with propofol. Michelsen *et al*[7] have also observed attenuation of drastic fall of blood pressure but not complete abolition of hypotension associated with propofol induction with the use of prophylactic ephedrine. Similar effects have been observed with the use of metaraminol.[8] Recently, Gopalakrishna and colleagues[14] have reported ephedrine to be ineffective in preventing hypotension after induction of anaesthesia with propofol and rocuronium during rapid tracheal intubation. However, Gamlin *et al*[15] have reported full effectiveness in obtunding hypotensive effects of propofol when ephedrine was mixed with propofol. But, marked tachycardia was observed in majority of patients in their

Table-4: Number of patients developing hypotension and time of onset of hypotension

Parameters	Groups		
	A(n=40)	B(n=39)	C(n=40)
Number of patients developing hypotension(percentage)	27* (67.5%)	9 (23.1%)	9 (22.5%)
Median time (min) of onset of hypotension (Interquartile Range 25%-75%)	2 (1-5)	2 (1-4)	4 (1-5)

*Note: * (p<0.01)*

study. We also observed increase in the heart rates in patients' receiving ephedrine but it was less than 10.0% of the baseline mean, and it was statistically insignificant. The difference in observations could be correlated with higher dose of ephedrine (15mg, 20 mg and 25 mg) in their study than in ours (0.2mg/kg, mean dose 10mg). Unlike ephedrine, Haemaccel® preloading was associated with significant decrease in heart rates from the baseline (more pronounced than the control) in our study. Increasing the preload with volume probably prevented the reflex response (i.e. increase in heart rates) to hypotension in the Haemaccel® group. Besides, Win *et al*,[16] using heart rate variability analysis, a non-invasive and widely used technique to monitor autonomic nervous system activity, have reported that propofol enhances parasympathetic activity. This fact probably further contributed to the significant decrease in heart rate in Haemaccel® preloading group. Ephedrine seems to counteract and compensate for the decrease in heart rate associated with administration of propofol and the heart rate increased in ephedrine pre-treated patients.

Although both Haemaccel® and ephedrine significantly attenuated hypotensive effects of propofol administration in our study, ephedrine prevented immediate sudden fall in blood pressure more effectively. Interestingly, pressor response to intravenous ephedrine has been shown to be enhanced by propofol.[17] Contrary to our observation, El-Beheiry *et al*[18] observed pre-induction volume preloading to be more efficacious in maintaining haemodynamics than intravenous ephedrine during rapid sequence induction with propofol and succinylcholine. However, there are numbers of reasons for difference in their observations. First, their observation time was 10 minutes. Second, their observation was after endotracheal intubation and third, they used lower dose of ephedrine (0.07mg/kg) than in our study.

While preloading requires longer time to execute before induction of anaesthesia (15 to 20 mins) and impose volume overload to heart, ephedrine increases cardiac stress by tachycardia and increased afterload.[11,12] Our finding that ephedrine administration differed hypotension to longer time interval compared to Haemaccel® preloading indicates that pre-treatment with ephedrine might be a better option over preloading to avoid rapid fall of blood pressure during propofol induction.

We conclude that while preloading with Haemaccel® and ephedrine reduced the incidence of hypotension in significant number of our ASA I and II grade patients, their safety and efficacy need to be investigated in high risk group patients.

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