Original Research Article

Comparison of induction characteristics of 1 percent propofol versus 2 percent propofol during induction in elective plastic surgery procedures

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ABSTRACT

Context: Propofol is the most widely used and available agent. Due to its complex formulations many preparations of propofol existed in the market.

Aim: Compare the induction characteristics of 1% propofol with 2% propofol in adults undergoing elective plastic surgery procedures.

Settings and Design: Randomized double blind prospective study conducted after institutional ethics committee in our institute.

Materials and Methods: We have recruited sixty adult patients of either sex and age between eighteen to sixty year for the study who were randomly allocated in to two groups. Group one (1% propofol) and group two (2% propofol) of thirty patients each. Induction characteristics like time to loss of consciousness, entropy less than forty, incidence of hypotension, bradycardia, involuntary movement as well as the total dose required was calculated in both groups.

Results and Conclusion: Time to loss of verbal response and entropy less than 40 was less in the two percent propofol group. Overall incidence of hypotension was 15% but the incidence was much higher in group one 26.6% (p value < 0.05). The incidence of bradycardia was around 16%, the incidence was much more in group 1 as compared to group 2 (p < 0.05).

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1. Introduction

Intravenous induction is the most widely accepted method of induction. Propofol owing to its many desirable effects like easy titration, early onset, good hemodynamic tolerance, minimal side effects, short duration and early recovery is considered the best among the existing intravenous anaesthetics. Due to its complex formulations basically for the lipid contents and hydrophobic nature many preparations of propofol existed in the market.^{1,2} 2% propofol contains mixture of medium chain triglycerides. 2% propofol seems to be advantageous because of high drug concentration, low volume and lesser time required for induction. 2% Propofol is advantageous in ICU sedation.

Few studies have described induction characteristics in elderly and children.^{3,4} This study was under taken to compare the induction characteristics of 1% and 2% propofol.

2. Materials and Methods

After institutional ethics committee approval, subjects were recruited into the study following written informed consent. The study included 60 adult patients in the age group of 18 to 60 years of ASA 1 and 2 of either sex, mallampati grade 1 and 2 undergoing elective plastic surgery procedures. Patients of age less than 18 year or >65 year, undergoing emergency surgery and who denied consent were excluded from the study. Patients who were allergic to propofol, severe hypotension or had other comorbidities like severe

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cardiac or lung disease were also excluded from the study. There were two groups of 30 patients each, group 1 and group 2. Group 1 was assigned for 1% propofol whereas group 2 for 2% propofol in a prospective randomised double blinded manner. Randomisation was done with the help of computer generated random table.

All the patients recruited into the study group were explained about the procedure in the preoperative counselling one day prior to surgery. They had received 0.5 mg alprazolam, 150 mg ranitidine on the day before and on the morning of surgery. After shifting to operation theatre routine monitors like non-invasive blood pressure, electrocardiograph, end tidal carbon dioxide, pulse oximetry were attached along with bispectral index. Baseline hemodynamics were recorded and IV line was secured. All the patients were premedicated with fentanyl (2 mcg/kg) and xylocard 2mg/kg. Group 1 patients received 1% propofol and group 2 patients 2% propofol in a syringe pump at 99ml/hour. Time of beginning of infusion and time to loss of consciousness was noted in both cases.

Unconsciousness was defined as absence of a reaction to verbal stimulation, observer assessment alertness or sedation scale.⁵ (OASS) <2 or bispectral index less than 40. Time to induction was defined as the time of beginning of infusion to time of loss of consciousness. Total induction dose of Propofol was calculated in each case.

Observer assessment alertness or sedation scale has a range of 1 to 5. Score 5 was given when patient was fully active – responded readily to name spoken in normal tone and has normal speech and facial expression and no ptosis. Score of 4 was allotted when patient had lethargic response to name and mild ptosis was present. Score 3 when the patient responded after loud repeated calling of name and there was slurring of speech and marked ptosis. Score of 2 when the patient responds only after mild podding or shaking and there were only few recognisable words. Score 1 when he did not respond on shaking too.

All the patients were intubated with appropriate size of endotracheal tube via direct laryngoscopy, bilateral air entry was confirmed and connected to mechanical ventilation. The quality of intubation was evaluated according to a valid score (1 -excellent, 2-good, 3-unsatisfactory, 4-bad) and maintained with air, oxygen and sevoflurane.

Hemodynamic changes like systolic and diastolic blood pressure, heart rate, respiratory rate, pulse oximetry, endtidal carbon dioxide were recorded before induction, at the end of induction and 5 minutes after induction. Any hypotension and bradycardia was recorded. Hypotension was defined as SBP<90 or MAP <60. Bradycardia was defined as HR <50. Hypotension was treated with mephenteramine 3 mg doses incrementally. Bradycardia was treated with atropine 0.3 mg. No of episodes of bradycardia and hypotension was noted.

Pain on injection was considered when patients complained about it or when they withdrew their hand during injection. Abnormal movements was defined as purposeless movements of any part of the body during or immediately after injection of propofol. Abnormal movements were classified as A: movement of hand or finger, B: movement of forearm and C: movement of arm and shoulder.

2.1. Statistics

Sample size was calculated using Statistical Software G Power. The effect size of 0.66 was calculated from from previous studies taking into consideration the difference in heart rate and blood pressure between baseline and intubation between the two groups. With this effect size and a power of 80% and an alpha error of 0.05 the sample size was calculated to be 54 (27 patients in each group). However, considering the drop outs in the study because of unanticipated difficult intubations we have selected 30 in each group and total 60 subjects. Statistical analysis was performed using IBM SPSS (version 20, IBM, IL). The descriptive analysis of normally distributed continuous variables was expressed as mean with standard deviation. The categorical variables were expressed as frequencies with percentages. The statistical analysis for comparison of continuous variables between the groups was performed using ANOVA and a two tailed significance of $p < 0.05$ was considered as significant difference. The comparison of categorical variables between the groups was performed using chi-square test or Fisher exact test when the expected cell values were < 5 . A two tailed p -value of ≤ 0.05 was considered as significant difference between the groups.

3. Results

Total sixty patients (30 patients in each group) were recruited for the study who underwent elective surgery under general anaesthesia in plastic surgery. The data was collected, tabulated, analysed and following observation were made.

Out of total 60 patients 1/3 rd were female and 2/3 rd were male. All other demographic data like age, sex, height and weight were similar in both the groups as described in Table 1. Mean age was 34.37 for group 1 and 38.1 was for group 2. Similarly mean height was 161.8 cm in group 1 compared to 164.83 in group 2, mean weight was 65.33 and 69.67 kilogram in group 1 & 2 respectively.

Total dose required in both groups were comparable. The mean dose required for group 1 was 141.32 mg and that of group 2 was 139.33 mg. As described in Table 2 time taken to loss of verbal response and to entropy less than 40 there was no statistical significance in the two groups though the 1% group required little more time compared to 2% group. Mean time to achieve loss of verbal response was 2.4 min

in group 2 compared to 3.13 min in group 1. Similarly time taken for entropy to fall below 40 was 5.7 min in group 2 compared to 7.4 minute in group 1. This may be due to the pharmacokinetics of the drug as 2% propofol has more drug concentration as compared to 1% formulations.

Figure 1 and 2 depicted the heart rate and blood pressure variations in both the groups. In all these cases systolic blood pressure, mean arterial pressure and diastolic blood pressure there was fall from the base line value which was most marked at the point where entropy value was less than 40. In case of 1 % propofol the fall was little more than 2% group but it was not statistically significant. Similarly in group 1 there was increase in heart rate following intubation and after that which may be due to hemodynamic response or due to reflex tachycardia associated with hypotension. Figure 3 and 4 depicts the variation in response and state entropy values in both groups.

Table 3 Describes the different adverse effects associated with propofol. The incidence of Hypotension, bradycardia associated with 2% propofol was less compared to that of 1% group. Incidence of laryngospasm, abnormal movement following injection was more with 1% propofol when compared to 2% propofol. Though there was no statistical significance in the pain associated with 1% or 2% group. The quality of intubation following 2% intubation was better than 1% group.

Fig. 1: Heart rate variation

Demographic variables like age, height weight were comparable in both groups. Time to loss of verbal response and that for entropy less than 40 was less in second group, which may be due to the pharmacokinetics of the drug as 2% propofol has more drug concentration as compared to 1% formulations and we have administered the drugs through a syringe pump.

Time to induction was characterized either clinically by loss of verbal response or by entropy value less than 40. In our study we have found that induction time was faster with 2% propofol as compared to 1% propofol. Infusing propofol 2% led to administration of the induction dose in a short time, and to a higher propofol concentration

Fig. 2: Mean arterial pressure variation

Fig. 3: Variation in response entropy

Fig. 4: Variation in state entropy

gradient between plasma and the effect site. Which might have facilitated the passage of propofol into the effect compartment, thereby shortening the exit rate constant from the central compartment. But we did not find any significant difference in doses. Separate studies tell that dose requirement may be higher in case of entropy guided induction to achieve same depth.⁶ Whereas Snehaddeep Arya et al in a comparative study found no significant difference in dose of propofol when assessed clinically or by BIS

Table 1: Demographic variables between 1 % and 2 %propofol

		Mean	Standard Deviation
Age	1 % propofol	34.37	12.02
	2% propofol	38.1	12.1
Height	1% propofol	161.83	5.33
	2% propofol	164.97	6.76
Weight	1 % propofol	65.33	7.64
	2% propofol	69.67	6.97

Table 2: Total dose requirement of protocol and time to loss of verbal response and entropy less than 40 in both groups

		Mean	Standard Deviation
Dose of propofol	1 % propofol	141.32	21.5
	2% propofol	139.33	17.1
Time to loss of verbal response (in Minutes)	1% propofol	3.13	0.97
	2% propofol	2.4	0.62
Time to entropy < 40 (in minutes)	1 % propofol	7.4	2.6
	2% propofol	5.7	1.05

Table 3: Comparison of adverse effects in both groups

		1% Propofol	2% propofol	P value
Hypotension	Yes	8	1	0.012
	No	22	29	
Bradycardia	Yes	9	1	0.006
	No	21	29	
Laryngospasm	Yes	18	0	0.000
	No	12	30	
Quality of intubation	Excellent	2	23	0.000
	Good	28	7	
Abnormal movement	Yes	21	1	0.000
	No	9	29	
Pain during injection	Yes	4	3	0.500
	No	26	27	

monitoring.⁷ In our study we have found the incidence of hypotension was 15% overall. But the incidence was much higher in 1% group 26.6% (p value < 0.05). Different studies state incidence of hypotension for propofol is between 25 to 60%. Ephedrine, phenylephrine or fluid preloading can prevent the incidence of hypotension. We have not used preemptively ephedrine or phenylephrine, after hypotension mean arterial pressure less than 60 only we have used mephenteramine 3 milligram in incremental doses.^{8–10}

Normally there can be bradycardia following induction with propofol. In our study population incidence bradycardia was around 16%. The incidence was much more in group 1 as compared to group 2 (p < 0.05) this was well in concordance with study by Trammer et al. In literature the incidence of bradycardia following propofol induction varies from 6.4 to as high as 20%.^{11,12} Bradycardia was treated with atropine 0.3 milligram. In our study group we had avoided muscle relaxant to look for the quality of intubation so the dose requirement was more. The mean dose required for group 1 was 141.32 mg and that of group 2 was 139.33 mg which was more than

standard 2mg/kg dose.

Intubating and ventilating conditions were excellent or good in all our patients. In none of the patients it was unsatisfactory or bad. Quality of intubation was excellent in 2 group in 76.6% compared to 6.6% in group 1 and good in 23.3% cases in group 2 compared with 93% in group 1. Quality of intubation was better in group 2 compared to group 1 (p value < 0.05) This was well in concordance with study by M. Pellégrini et al who have studied the induction characteristics of propofol 1% and 2% in children undergoing ENT surgery.¹³ Intubating conditions were satisfactory in 87% and 96% of children receiving propofol 1% or 2%, respectively (P=0.19). A Borgeat et al had found that induction with 2% propofol 4 mg/kg was associated with ease of performing manual ventilation. Manual ventilation was assessed as very easy and comfortable in 88% of children. Pedersen et al observed that sedation with propofol in patients with hyperactive airway disease provided marked Broncho dilatation.^{14,15}

Propofol is known to be associated with involuntary movements or seizure like phenomena. Spontaneous

movements observed during induction of anaesthesia in adults and children, but a higher incidence appears in the children group. This depends on the dose, pre-existing condition and rate of infusion. The incidence of involuntary movements is as high as 16% to 45% in different studies. In our study the incidence was as high as 33%. The high incidence of involuntary movement in our study can be due to slow rate of infusion in syringe pump. Hae Keum kil et al has studied the effect of different rates of infusion and its effect on hemodynamic and involuntary movement in case of children and concluded that slow injection may increase the incidence of involuntary movement during propofol induction in children.¹⁶

Other excitatory events such as cough and hiccup during induction with propofol though rare but can occur with slow incomplete induction. In our study we have found the overall incidence was 20% and it was marked in the 1% propofol group as high as 40%. This can be due to incomplete or low dosage of propofol probably requiring more time for higher brain concentration and complete suppression of all reflexes including hiccups. Surprisingly Borgeat et al observed more incidence of cough in the group with 5mg/kg of propofol 2% compared to 4mg/kg of propofol 2% which they had explained as a sudden high propofol brain concentration might have led to some excitatory effects on the cough centre.

A potential advantage of propofol 2% might have been a lower incidence of pain on injection owing to its content of medium chain triglyceride but this was not detected in our study. The incidence of pain was low in our study (overall incidence was 11.6%) and there was no statistical difference between the two groups. The overall low incidence can be due to slow rate of infusion in a syringe pump and all patients were premedicated with opioid fentanyl and lidocaine was given to all patients prior to starting of propofol. Our study is in concordance with M. Pellégrini et al who had also failed to show any difference in incidence of pain in 2% versus 1% propofol group. They had also small incidence of pain due to slow rate of infusion.¹³

Dewandre J et al compared 2% and 1% formulations of propofol during anaesthesia for craniotomy and concluded that both preparations were associated with a similar incidence of injection pain and venous thrombosis or thrombophlebitis at 24 hour.¹⁷ Servin FS in a study on comparison of 2% and 1% formulations of propofol for the induction and maintenance of anaesthesia in surgery of moderate duration found that discomfort on injection occurred in 40% and 52% of those given 1% (n = 55) and 2% (n = 55) propofol respectively; there was no statistically significant group difference in severity.¹⁸ Our study was in accordance with Servin et al.

4. Conclusion

Present study shows that induction of anaesthesia with propofol 2% can provide comparable clinical conditions as

that of 1% propofol with fewer side effects like involuntary movements, laryngospasm and have a rapid onset of loss of consciousness.

5. Limitation of the study

We have not studied the effect on fat level following induction.

6. Source of Funding

None.

7. Conflict of Interest

None.

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