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STUDY OF EFFECT OF PRIMING OF PROPOFOL ON HAEMODYNAMIC CHANGES DURING INTUBATION

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Abstract

Background: Propofol auto co-induction or the Priming Principle has also been proposed to lower Propofol requirements. The purpose of this study was to see if using the 'Priming Principle' for the propofol induction, 2 minutes before actual induction would attenuate the pulse rate to laryngoscopy and intubation, as opposed to the reflex tachycardia due to increased sympathetic activity. **Material and Methods:** Present study was Comparative, randomized, prospective, observational study, conducted patients belonging to age groups 18-35 years, to either gender, belonging to ASA physical status 1 and 2, scheduled for elective surgical procedures requiring general anaesthesia with endotracheal intubation. Patients were randomly allocated into two groups of 25 each and were subjected to the Group A (priming of propofol with 25% of the calculated dose) & Group B (No priming of propofol). **Results:** In the group that was administered with primed dose of propofol it was noted that the administered dose was much less compared to the originally calculated dose. The dose of propofol that was administered in the primed group was much less compared to the control group with a statistical difference having a P value of 0.00. The pulse rate at 1 minute post laryngoscopy and intubation in the case group was lower than that of the control group with the p value of 0.010. The SBP was higher in cases when compared to controls with statistical significance. The p values at laryngoscopy, post laryngoscopy and intubation at 1-,3- and 5 minutes are 0.000, 0.000, 0.000 and 0.001 respectively. **Conclusion:** Priming of propofol with 25% of the calculated dose two minutes before the induction is effective in attenuating the pulse rate at 1 minute post intubation. The group with priming required doses lesser than the calculated dose with better hemodynamic stability.

Keywords: glycosylated hemoglobin, mortality, need of mechanical ventilation, critically ill patients, ICU care

Introduction

One of the most crucial steps in general anaesthesia is inducing anaesthesia. Induction of general anaesthesia required the inhalation of gases or vapours prior to the injection of intravenous anaesthetic drugs, which was an unpleasant experience for the majority of patients.[1] It was also discovered that laryngoscopy alone resulted in an elevation in blood pressure. This effect was amplified by intubation, which was potential cause of arrhythmias.[2]

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Thus, creating a need for smoother induction and intubation with minimal hemodynamic changes.

Propofol has recently gained acceptance as a viable alternative to the tried-and-true thiopentone for intravenous induction. In comparison to thiopentone, propofol induction is smoother, faster, with faster awakening and orienting times, better intubating circumstances, and better upper airway integrity.[3] However, a key drawback of rapid Propofol induction is a moderate decrease in systemic arterial blood pressure as a result of decreased systemic vascular resistance. It is necessary to carefully titrate the medicine toward its (slightly delayed) anaesthetic effect.[4]

Propofol auto co-induction or the Priming Principle has also been proposed to lower Propofol requirements.[5,6] However, due to a lack of sufficient proof, anaesthesiologists rarely use this approach. The priming principle has been well documented in the use of non-depolarizing muscle relaxants, where priming accelerates the onset of neuromuscular blockade, optimizes intubating circumstances, and reduces total drug intake.[7,8] The purpose of this study was to see if using the 'Priming Principle' for the propofol induction, that is, by administering 25% of the calculated dose (2mg/kg body weight) 2 minutes before actual induction would attenuate the pulse rate to laryngoscopy and intubation, as opposed to the reflex tachycardia due to increased sympathetic activity.

Material And Methods

Present study was Comparative, randomized, prospective, observational study, conducted in Department of anaesthesia, at A.J institute of medical sciences and research centre, Mangalore, India. Study period was of one and half years (from November 2019- April 2021). The study was initiated after obtaining approval from the institutional ethics committee.

Inclusion criteria

- Patients belonging to age groups 18-35 years, to either gender, belonging to ASA physical status 1 and 2, scheduled for elective surgical procedures requiring general anaesthesia with endotracheal intubation, willing to participate in present study.

Exclusion criteria

- Patients who refused to participate in the study.
- Patients with history of hypertension or IHD or patient on blocker drugs.
- Patient with BMI >25kg/m^2
- Patients with known difficult airway or requiring more than 1 attempt of intubation or duration of laryngoscopy for more than 1 minute
- Patients who are known to be allergic to propofol or having food allergy.

All patients who required oro-tracheal intubation as part of their anesthetic management and had given informed written consent to participate in the study, were randomly allocated into two groups of 25 each and were subjected to the following regimen-

Group A- priming of propofol with 25% of the calculated dose (n=25)

Group B- No priming of propofol (n=25)

Prior to the day of surgery, we performed a detailed pre-anesthetic assessment and noted the demographic details, baseline vitals, airway and laboratory investigations. We obtained a written informed consent from all the included patients. All the patients were premedicated with Ranitidine 150mg orally on the night prior to surgery. Patients were advised a fasting period of 8 hours for solids, 4 hours for semi- solids and 2 hours for clear liquids.

After arrival to the anesthetic room, preinduction monitors were connected- 5 lead ECG

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with automated ST segment analysis, pulse oximetry, non-invasive blood pressure, temperature probe, was initiated and basal reading noted. Appropriate i.e. access secured. Following pre-medications were given- inj. Fentanyl 2mcg/kg, inj. Glycopyrrolate 0.05mg/kg. All patients were preoxygenated for 3 minutes. Anesthesia was induced with propofol 2mg/kg and loss of response to verbal stimuli was confirmed. Endo tracheal intubation was facilitated using vecuronium 0.1mg/kg after confirming the ability to mask ventilate.

Patients belonging to group A received 25% of the calculated dose of propofol 2 mins prior to induction. Remaining dose of propofol was administered until the loss of verbal commands. The administered dose of propofol was noted. Patients belonging to group B received the entire calculated dose of propofol.

The primary investigator who is unaware as to which group the patient belongs to performs the laryngoscopy and endotracheal intubation. Another investigator, a consultant anesthesiologist / anesthesiology resident who gives the drug as per the protocol and noted down all the data. Anesthetic plane deepened with Isoflurane and anesthesia maintained with isoflurane, O_2:N_2O (40%:60%).

Residual neuromuscular blockade will be reversed with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg. Endo tracheal tube will be extubated after adequate recovery of muscle power and patients will be monitored post operatively. Heart rate, SBP, DBP and MAP were measured before laryngoscopy and intubation and immediately after intubation at 1, 3 and 5 minutes. Any side effects associated with the administration of propofol was noted.

The following treatments were provided: 0.5 mg atropine sulphate was administered for bradycardia (HR <50 beat min^{-1}), 5 mg ephedrine or 5 mg mephentermine was administered for hypotension (systolic arterial pressure <100 mmHg). For patients in whom intubation time (laryngoscopy + intubation) is more than 1 min were excluded from the study. Patients requiring more than one attempt of laryngoscopy attempt were excluded from the study.

The collected data was summarized by frequency and percentage of categorical data such as gender, Mallampati score. Quantitative data was summarized by mean and standard deviation. Comparison between cases and controls of categorical data was performed by chi-square test. Comparison of quantitative data of case and control was performed by independent t- test. Level of significance in the present study is 5% and analysis was performed using SPSS software.

Results

For all statistical purpose Group A was referred to as cases and Group B as Control. The mean age, gender distribution, mean weight & Mallampati score between the two groups were comparable with no significant statistical difference between the two groups (P value > 0.05)

Table 1: Comparison of general characteristics

	Cases (%)	**Controls (%)**	**P value**
Mean Age (in years)	29.44 ± 5.92	29.00 ± 5.60	0.788
Gender			
Female	8 (32.0 %)	9 (36.0 %)	0.765
Male	17 (68.0 %)	16 (64.0 %)	
Mean Weight (kg)	61.48 ± 11.26	65.56 ± 15.53	0.293
Mallampati score (MP)			
MP 1	17 (68.0 %)	21 (84.0 %)	0.185
MP 2	8 (32.0 %)	4 (16.0 %)	

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In the group that was administered with primed dose of propofol it was noted that the administered dose was much less compared to the originally calculated dose. Applying t-test to the given data the p vale was 0.000 suggesting a high significance between the administered dose and the calculated dose.

Table 2: Comparison of the administered dose and the calculated dose in the group with priming of propofol

Dose of propofol	n	mean	Standard deviation	P value
Calculated dose	25	122.64	22.73	0.000
Administered dose	25	83.80	11.8	

The dose of propofol that was administered in the primed group was much less compared to the control group with a statistical difference having a P value of 0.00.

Table 3: Comparison of the administered dose between the cases and controls.

Group		N	Mean	Standard Deviation	p value
ADMINISTERED DOSE(MG)	Cases	25	83.80	11.48	0.000
	Controls	25	131.12	31.06	

The mean pulse rate between the cases (group with priming of propofol) and the controls (non-primed group) was compared using independent t test. The p value (0.925) was not significant pre-induction indicating that the heart rate was comparable between both the groups. The pulse rate at 1 minute post laryngoscopy and intubation in the case group was lower than that of the control group with the p value of 0.010. The heart rate during laryngoscopy and at 3- and 5- minutes post intubation was comparable with the p value of 0.051, 0.612 and 0.179 respectively.

Table 4: Comparison of the pulse rate between the two groups

Pulse rate	Cases (Mean ± SD)	Controls (Mean ± SD)	P value
Preinduction	77.80 ± 9.862	78.08 ± 11.120	0.925
During laryngoscopy	81.24 ± 9.892	75.12 ± 11.649	0.051
At 1 min	83.24 ± 9.888	75.28 ± 11.100	0.010
At 3 min	77.08 ± 8.911	75.72 ± 9.910	0.612
At 5 min	73.72 ± 7.903	76.88 ± 457	0.179

The mean systolic blood pressure between the two groups were compared using independent t test. The preinduction SBP was comparable between the two groups with a p value of 0.054. The SBP was higher in cases when compared to controls with statistical significance. The p values at laryngoscopy, post laryngoscopy and intubation at 1-,3- and 5 minutes are 0.000, 0.000, 0.000 and 0.001 respectively.

Table 5: Comparison of the SBP between the cases and controls

SBP	Cases (Mean ± SD)	Controls (Mean ± SD)	P value
Preinduction	129.76 ± 13.800	122.04 ± 12.212	0.054
During laryngoscopy	132.92 ± 13.115	110.16 ± 18.520	0.000
At 1 min	134.32 ± 13.937	110.08 ± 20.764	0.000
At 3 min	129.76 ± 12.269	110.88 ± 17.372	0.000
At 5 min	126.60 ± 11.951	113.88 ± 14.446	0.001

The DBP between the cases and the controls were compared using independent t test. The

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preinduction DBP was comparable with no statistical significance having a p value of 0.269. The DBP during laryngoscopy and post intubation at 1- and 3- minutes was higher in the cases group with a statistically significant p value of 0.001, 0.001 and 0.003 respectively. The DBP 5 minutes post intubation was again comparable with no statistical significance and a p value of 0.136

Table 6: Comparison of the DBP between the cases and controls

DBP	Cases (Mean ± SD)	Controls (Mean ± SD)	P value
Preinduction	73.20 ± 9.574	70.56 ± 6.899	0.269
During laryngoscopy	75.80 ± 9.060	66.92 ± 9.037	0.001
At 1 min	76.84 ± 9.227	67.36 ± 8.958	0.001
At 3 min	74.28 ± 8.590	67.20 ± 7.365	0.003
At 5 min	72.24 ± 8.151	69.08 ± 6.480	0.136

To identify any statistical significance between the MAP of the cases and controls the independent t test was applied. The MAP between the two groups was comparable preinduction and at 5 minutes post intubation with a p value of 0.102 and 0.217 respectively. The MAP was lower in the control group during laryngoscopy, at 1- and 3- minutes post intubation with statistically significant p value of 0.000, 0.000 and 0.000 respectively.

Table 7: Comparison of the MAP between the cases and controls

MAP	Cases (Mean ± SD)	Controls (Mean ± SD)	P value
Preinduction	91.96 ± 10.648	87.68 ± 7.186	0.102
During laryngoscopy	94.72 ± 9.927	81.48 ± 11.336	0.000
At 1 min	96.04 ± 10.438	81.68 ± 12.206	0.000
At 3 min	92.64 ± 9.534	81.60 ± 10.112	0.000
At 5 min	118.44 ± 137.253	84.00 ± 8.401	0.217

Out of the 50 subjects, 18 of the patients had side effects associated with propofol. Of which 11% were from the cases and 89% from of the controls. 8% of the cases and 64% of the controls showed side effects. Out of the 50 subjects in the study, 18 experienced pains on administration of propofol. Among the 18, 2 belonged to the case group and 16 to the control group. In this study 6 patients showed incidence of hypotension. There was no incidence of hypotension noted in the case group while 6 patients from the control group had incidence of hypotension.

Table 8: Other characteristics

	Cases (Mean ± SD)	Controls (Mean ± SD)	P value
Side effects	3 (12 %)	15 (60 %)	0.925
Pain on injection	2 (8 %)	16 (64 %)	0.051
Hypotension	0	6 (24 %)	0.010

Discussion

One of the most crucial events in the administration of general anesthesia is the induction of anesthesia. Induction of general anesthesia required inhalation of gases or vapors prior to the injection of intravenous anesthetic drugs, which was an unpleasant experience for the majority of patients.[9]

The sympathetic system is stimulated during laryngoscopy and intubation, causing an increase in heart rate and arterial blood pressure. Vasodilation and myocardial depression are

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common side effects of induction drugs, resulting in hypotension. This hypotension can be dangerous, especially in people who have a low cardiovascular reserve.

With the induction of anesthesia with propofol there is reduction in the systemic arterial pressure due to decrease in cardiac output, systemic vascular resistance or both.[10] With the use of non-depolarizing muscle relaxants, the 'Priming Principle' is well- established, with 'priming' shortening the onset of neuromuscular blockade and allowing for improved intubating conditions. [9]

In our study we evaluated, whether 'the priming principle' applied to the induction dose requirement of propofol could lower the overall induction dosage required and thus the accompanying hemodynamic alterations. We used 25% (0.5 mg/kg) of the calculated dose in our trial, with a normal propofol dose of 2 mg/kg. The majority of research on the priming principle were conducted in conjunction with the use of synergistic drugs, which we believed could have concealed the true efficacy of this strategy.

In this study the demographic data was comparable with respect to age, weight and gender. Both the groups were comparable with reference to ASA status, Mallampati score. The preinduction heart rate between the two groups was comparable. At one minute post induction the heart rate was significantly lower in Group B ($p<0.010$) which was similar to the study conducted by and Fairfield *et al.*,[10] but not in concordance to the study conducted by Maroof *et al.*,[11] & A. Kumar *et al.*,[12]

The mean induction dose of propofol was 83.80 ± 11.48 in the Group A when the priming principle was applied. We noted that there was 31.67% reduction in the dose required for induction when propofol was primed which was statistically significant. ($p< 0.000$). The reduction in the induction dose was more than that observed by Maroof *et al.*,[11] (21.4%), but lower than that observed by Naphade *et al.*,[13] (35%).

We also evaluated effects on other hemodynamic parameters after priming with propofol. The SBP was significantly higher in the Group A during and post laryngoscopy at 1-, 3- and 5 minutes with the p value of 0.000, 0.000, 0.000 and 0.001 respectively with comparison with the Group B which correlated with the study conducted by Pauline *et al.*,[14]

The DBP in the Group A during laryngoscopy and at 1- and 3- minutes post laryngoscopy was significantly higher than the Group B with the p value of 0.001, 0.001 and 0.003 respectively. The MAP in the Group A was significantly higher than in the Group B during laryngoscopy and at 1-, 3- minutes with a p value of 0.000, 0.000 and 0.000 respectively. This finding confirmed that the hemodynamic side effects were dose dependent as stated by Pauline *et al.*,[14] and Major *et al.*,[15].

The side effects of propofol were seen in 8% of the cases in Group A and 64% of the cases in the Group B. This higher incidence can be attributed to the cardiorespiratory depressant effects of propofol, which are dose dependent.[16] The main side effects that we noted in our study was pain during the administration of propofol and hypotension. The incidence of pain on injection was lower in the Group A when compared to Group B. This finding was similar to the study conducted by Tan CH *et al.* This pain on injection is attributable to the increased concentration of propofol in the aqueous phase.[17]

Propofol, because of its early onset and short duration of action, clear-headed recovery, superior intubating circumstances, and low postoperative sequelae has established itself as an ideal intravenous anaesthetic drug. Rapid induction with a standard dose of propofol, on the other hand, is linked to a drop in blood pressure (BP) and local discomfort, which is dose-dependent. A reduction in the induction dose would also cause a reduction in the associated complications and a better hemodynamic stability.

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Conclusion

Our findings suggest that priming of propofol with 25% of the calculated dose two minutes before the induction is effective in attenuating the pulse rate at 1 minute post intubation. There is a significant difference in the dose required when the propofol was primed. The group with priming required doses lesser than the calculated dose with better hemodynamic stability. The side effects of propofol induction such as pain on injection and hypotension was more common in the non-primed group.

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