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Original research article

A study to evaluate the postoperative recovery profile of sevoflurane anaesthesia with an intravenous subhypnotic dose of propofol added at the time of closure: A prospective single blinded randomised controlled study

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Abstract

Background: Emergence from general anaesthesia with long duration use of inhalational agents like Sevoflurane is often associated with turbulent emergence. A subhypnotic dose of propofol (0.5mg/kg) given at the time of skin closure is known to be associated with a faster, clearer headed recovery, with adequate anxiolysis and anti-emesis.

Methodology: This was a Prospective single-blinded Randomized controlled study carried out at Department of anaesthesiology, Nizam's institute of medical sciences (NIMS), India between March 2021 to February 2022. After ethics committee approval, this prospective randomised controlled single blinded study was carried out with 50 adult (18-60) patients, of either gender, posted for elective surgeries under general anaesthesia with sevoflurane, who were divided into two groups, (Group P n= 25) patients receiving 0.5 mg/kg Propofol IV bolus after discontinuing sevoflurane at the time of skin closure (but no antiemetic) and (Group C n= 25) patients receiving 0.15 mg/kg ondansetron +0.08 mg/kg Dexamethasone IV bolus at the time of skin closure. The parameters observed were Emergence time (min), extubation time (min), mental status, SOMCT score, Aldrete score and incidence of nausea and vomiting at different time intervals in the immediate postoperative period. Results were analysed using paired and unpaired student's T test and Chi square test. (p<0.05 was significant).

Results: The mean emergence time and mean extubation time was seen to be statistically significantly higher in the control group as compared to the propofol group. Postoperative mental status was seen to have higher number of confused and agitated patients in the control group. Patients in propofol group performed better than the control group with respect to short orientation memory concentration test results. Modified Aldretes scores and incidence of Nausea and Vomiting was comparable in both the groups.

Conclusion: A subhypnotic dose of propofol (0.5mg/kg), given at skin closure in patients receiving sevoflurane as maintenance agent under general anaesthesia, significantly reduces emergence time, extubation time and also gives a calm, oriented, and clear-headed recovery with lesser incidence of postoperative nausea and vomiting, in the absence of an antiemetic.

Keywords: Extubation time, propofol, dexamethasone, antiemetic

Introduction

Early emergence from anaesthesia facilitates early neurological examination and immediate post-operative intervention. Anaesthetic technique that facilitates early awakening with clear higher mental function is highly desirable in anaesthesia and anaesthetic agents are the major determinants of the time of emergence and extubation, thus, making short acting anaesthetic agents preferable as maintenance agents [1]. The inhalationl agent, Sevoflurane, has gained popularity as maintenance agent of choice for ambulatory anaesthesia due to its significantly lower blood gas partition coefficient (0.45), thus promising faster recovery than most of the easily available agents [2]. Recovery from sevoflurane, however, is known to be associated with emergence agitation, delirium, and increased postoperative nausea and vomiting [3, 4]. Sub hypnotic dose of the intravenous agent propofol given just before closure

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has been shown to reduce emergence agitation in paediatric population [5]. Its anxiolytic effect has been postulated to offer a calm and clear headed recovery [6]. The property of propofol to attenuate airway reflexes [7] is also a boon to the anaesthetist during extubation, especially in areas of work where raised intra-cavity pressures are a major concern. Reducing the incidence of postoperative cough also benefits in prevention of wound dehiscence or internal bleeding.

The antiemetic properties of propofol used in sub hypnotic doses has been proved to be effective for the prevention and treatment of chemotherapy induced emesis and also in the post-surgical period (8). The weak anti serotonin properties of propofol and their effect on the chemoreceptor trigger zone have been postulated as one of the reasons behind this action. Recent studies have attributed analgesic properties to propofol by its action on NMDA receptors [9]. This, in addition to routine multimodal agents, improves postoperative analgesia and subsequently the recovery profile, especially in patients with in situ urine catheters and painful wide bore intravenous cannulae.

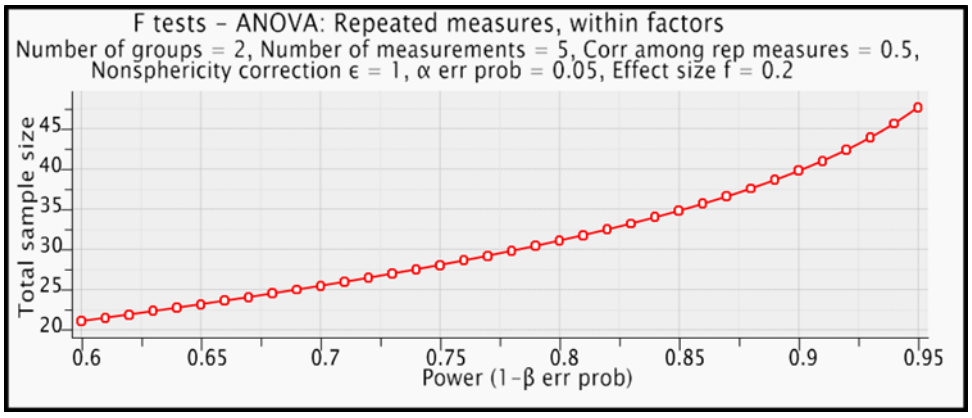
In the present study, we have been evaluated the effectiveness of a sub hypnotic dose of propofol (0.5mg/kg) given at the time of surgical closure, on the time required for emergence and extubation, the quality of emergence from anaesthesia seen by short orientation memory concentration test (SOMCT), modified Aldrete's score and also on reducing the incidence of PONV.

Methodology

Sample size estimation

The parameter, short orientation memory score, in a similar study, carried out by Kapil S et al. 2018, (1) was used for sample size calculation. The statistical software G*power3.1.9.2 (universistat, Dusseldorf, Germany) was used for the same, using A priori power analysis, and ANOVA repeated measures-within factors, as the statistical method. Effect size of 0.2, α error probability of 0.05, and Power (1-β error) of 0.95was taken.

A Sample size of 48, which was rounded off to 50 (25 each group) was derived.



This was a Prospective single-blinded Randomized controlled study carried out at Department of anaesthesiology, Nizam's institute of medical sciences (NIMS), India between March 2021 to February 2022. After Institutional Ethics committee approval, 100 ASA physical status class I and class II patients posted for elective surgery under GA were recruited for the study. After routine preanaesthetic check-up, and implementation of exclusion and inclusion criteria, patients' willingness to participate in the study was taken in the form of a written informed consent. The patient was explained in detail about the study procedure in his/her own native language. All patients were pre-medicated with Tab. Rantac 150mg and Tab. Alprax 0.25mg on the night before surgery.

On the day of surgery, Height (cm), weight (kg), BMI (kg/m2), and preoperative investigations were noted. After confirming fasting status for solids 8 hrs and clear fluids for 2hrs, and checking written and informed consent, patient was shifted to operation theatre.

Patient was connected to standard anaesthesia monitors: 5 lead ECG, Pulse oximetry, NIBP, skin temperature probe. Baseline Heart rate (HR), systolic, diastolic and mean blood pressure, spo2 and temperature were recorded. Intravenous cannulation with 16G/18G is secured in all patients and Ringers lactate fluid was started as maintenance IV fluid.

All patients were premedicated with fentanyl 1µgm/kg over 10min, glycopyrrolate (0.04mg/kg) and anaesthesia was induced with propofol (1-2mg/kg) until loss of verbal response. After endotracheal intubation anaesthesia was maintained with sevoflurane to maintain a MAC of 2 with fresh gas flow of 4 liters per min in a closed circuit on mechanical ventilation and Atracurium as muscle relaxant. A standard low dose IV infusion of Fentanyl (1-1.2mcg/kg/hr) was kept for intraoperative analgesia, which was later supplemented by IV acetaminophen 10mg/kg and topical anaesthesia with bupivacaine 0.25% at the end of surgical closure.

At the end of the surgery, and at the time of muscle closure, sevoflurane was switched off. The study

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drug was administered over 5 min as intravenous bolus according to randomisation. Patient was reversed with neostigmine and glycopyrrolate and thereafter extubated when response to verbal commands was found to be satisfactory with regular respiration generating adequate tidal volume ensuring complete reversal of neuromuscular blockade.

Inclusion critera

- ASA grade 1 or 2.
- Age 18-60yrs.
- Both genders.
- Elective surgeries.
- Anticipated extubation at the end of surgery.
- Patient Willingness to participate.

Exclusion criteria

- ASA grade 3&4.
- Preoperative Glasgow coma score <15/15.
- Patient scheduled for Craniotomy.
- History of allergy.
- Previous History of PONV, motion sickness.
- History of snoring.
- History of obstructive sleep apnoea.
- Patient with anticipated difficult intubation or difficult mask ventilation.
- Patient with uncontrolled hypertension, uncontrolled Diabetes mellitus, cardiac disorders.
- Patient with poor pulmonary reserve where early desaturation is expected.
- Patient with BMI>30kg/m2.
- Pregnant females.
- C-spine fractures or other cervical disorders with restricted neck movements or unstable cervical spine.
- Patient on regular use of sedatives/abuse substances/alcohol addiction/antipsychotics.

Aims and Objectives

To compare the effect of a sub hypnotic dose of propofol (0.5mg/kg) given at the time of surgical closure, on the time required for emergence and extubation, the quality of emergence from anaesthesia seen by mental status, short orientation memory concentration test score (SOMCT), modified Aldrete's score and the incidence of postoperative nausea and vomiting, with a control group in patients receiving sevoflurane as anaesthetic agent.

Results

Demographic data such as Age, gender, height, weight, ASA classification were found to be comparable in both the groups

Table 1: Age in years-Frequency distribution in two groups of patients studied

Age in Years	Group P	Group C	Total
<30	1(4%)	4(16%)	5(10%)
30-40	10(40%)	4(16%)	14(28%)
>40	14(56%)	17(68%)	31(62%)
Total	25(100%)	25(100%)	50(100%)

p>0.05 not significant.

Table 2: Gender-Frequency distribution in two groups of patients studied

Gender	Group P	Group C	Total
Female	11(44%)	13(52%)	24(48%)
Male	14(56%)	12(48%)	26(52%)
Total	25(100%)	25(100%)	50(100%)

p>0.05 not significant

Table 3: Comparison of Clinical Variables in two Groups of Patients Studied

Variables	Group P	Group C	Total	P Value
Age in Years	47.04±13.85	46.4±13.88	46.72±13.73	0.871
Weight	64.28±11.12	65.16±11.76	64.72±11.34	0.787
Height	167.84±6.43	165.8±6.73	165.82±6.83	0.061
BSA	1.73±0.16	1.72±0.16	1.72±0.16	0.854

P>0.05 not significant

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Table 4: ASA Grade-Frequency distribution in two groups of patients studied

Grade	Group P	Group C	Total
Grade I	15(60%)	22(88%)	37(74%)
Grade II	10(40%)	3(12%)	13(26%)
Total	25(100%)	25(100%)	50(100%)

p>0.05 not significant

Both the groups were also comparable in terms of pre-existing comorbidities (Table 5).

Table 5: Co-Morbidities-Frequency distribution in two groups of patients studied

Co-Morbidities	Group P	Group C	Total
No	14(56%)	16(64%)	30(60%)
Yes	11(44%)	9(36%)	20(40%)
▪ HTN	10(40%)	7(28%)	17(34%)
▪ DM	7(28%)	5(20%)	12(25%)
▪ CAD	0(0%)	1(4%)	1(2%)
▪ CKD	1(4%)	0(0%)	1(2%)
Total	25(100%)	25(100%)	50(100%)

HTN= Essential Hypertension, DM= Noninsulin dependent Diabetes Mellitus, CAD= Coronary artery Disease, CKD=Chronic Kidney Disease.
P>0.05 not significant.

Airway assessment parameters were also comparable in both the groups Table 6: MPG- Frequency distribution in two groups of patients studied.

MPG	Group P	Group C	Total
Grade I	3(12%)	2(8%)	5(10%)
Grade II	22(88%)	23(92%)	45(90%)
Total	25(100%)	25(100%)	50(100%)

MPG= Mallampatti Grade, (Grade 3 and 4 were excluded from the study) p>0.05 not significant.

Table 7: Comparison of Outcome Variables in two Groups of Patients Studied

Variables	Group P	Group C	Total	P Value
Total surgical time (min)	172.4±68.02	176.2±59.18	174.3±63.13	0.834
Emergence time (min)	10.16±3.1	16.4±2.96	13.28±4.35	<0.001**
Extubation time(min)	14.96±4.23	20.48±3.43	17.72±4.72	<0.001**

The mean total duration of surgery in both the groups was found to be comparable; however mean emergence time was seen to be statistically significantly higher in the control group as compared to the propofol group. Similarly, Mean extubation time was also significantly higher in the control group.

Table 8: Mental Status-Frequency distribution in two groups of patients studied

Mental Status	Group P	Group C	Total
Calm	25(100%)	13(52%)	38(76%)
Confused	0(0%)	6(24%)	6(12%)
Agitated	0(0%)	6(24%)	6(12%)
Total	25(100%)	25(100%)	50(100%)

P<0.001**, Significant

Immediate postoperative mental status was seen to have higher number of confused and agitated patients in the control group. This difference was seen to be statistically significant as compared to the propofol group. (p<0.001).

Table 9: SOMCT Score-Frequency distribution in two groups of patients studied

SOMCT Score	Group P	Group C	P Value
5MIN			
▪ Good	22(88%)	4(16%)	<0.001**
▪ Fair	3(12%)	21(84%)	
▪ Poor	0(0%)	0(0%)	
10MIN			
▪ Good	22(88%)	0(0%)	<0.001**

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▪ Fair	3(12%)	25(100%)	
▪ Poor	0(0%)	0(0%)	
15MIN			
▪ Good	25(100%)	21(84%)	
▪ Fair	0(0%)	4(16%)	<0.001**
▪ Poor	0(0%)	0(0%)	
Total	25(100%)	25(100%)	

Out of the 5 questions answered in the postoperative period by the patients the scoring of good, fair and poor was done as follows, if < 3 mistakes were performed: good, 3-5 mistakes: Fair and unable to perform: Poor.

It was observed that at 5 minutes postoperatively, performance of more number of patients in the propofol group was good (22: 4) and more number of performances in the control group were Fair (21:3). This difference was statistically significant. The same trend continued at 10 minutes and 15 minutes, with the patients in propofol group performing better than the control group with respect to short orientation memory concentration test results.

Table 10: Comparison of Aldrete Score in Two Groups of Patients Studied

ALDRETE Score	Group P	Group C	Total	P Value
5min	9.4±0.71	9.36±0.7	9.38±0.7	0.842
10min	9.96±0.2	10±0	9.98±0.14	0.322
15min	10±0	10±0	10±0	1.0
30min	10±0	10±0	10±0	1.0
60min	10±0	10±0	10±0	1.0
120min	10±0	10±0	10±0	1.0

The Aldrete scores were comparable in both the groups at all-time intervals in the immediate postoperative period (p>0.05).

Incidence of nausea and vomiting were comparable in both the groups.

Table 11: Incidence of Nausea-Frequency distribution in two groups of patients studied

NAUSEA	Group P	Group C	Total	P Value
5min				
No	22(88%)	22(88%)	44(88%)	1.000
Yes	3(12%)	3(12%)	6(12%)	
10min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
15min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
30min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
60min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
120min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
Total	25(100%)	25(100%)	50(100%)	

The incidence of nausea were comparable in both the groups at all-time intervals in the immediate postoperative period (p>0.05).

Table 12: Incidence of Vomiting- Frequency distribution in two groups of patients studied

VOMITING	Group P	Group C	Total	P Value
5min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
10min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
15min				

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No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
30min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
60min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
120min				
No	25(100%)	25(100%)	50(100%)	1.000
Yes	0(0%)	0(0%)	0(0%)	
Total	25(100%)	25(100%)	50(100%)	

The incidence of vomiting were comparable in both the groups at all-time intervals in the immediate postoperative period (p>0.05).

Discussion

Propofol in subhypnotic doses is known to attenuate airway reflexes, reduces anxiety, has antiemetic effect, and weak analgesic properties [5]. General anaesthesia with sevoflurane as the inhalational maintenance agent for longer duration surgeries is known to be associated with a turbulent emergence [3, 4]. This study was thus designed to use the benefits of subhypnotic doses of propofol on recovery from sevoflurane anaesthesia as there are very few published articles in this area.

In this prospective randomized single-blinded controlled study, we evaluated the effectiveness of a sub hypnotic dose of propofol (0.5mg/kg) given at the time of surgical closure, on the time required for emergence and extubation, the quality of emergence from anaesthesia seen by short orientation memory concentration test (SOMCT), modified Aldrete's score and also on reducing the incidence of PONV in patients receiving general anaesthesia with sevoflurane as maintenance agent.

50 adult (18-60) patients, of either gender, posted for elective surgeries under general anaesthesia with sevoflurane were divided into two groups.

Group P: 25 patients receiving 0.5 mg/kg Propofol IV bolus after discontinuing sevoflurane at the time of skin closure (but no antiemetic).

Group C: 25 patients receiving 0.15 mg/kg ondansetron +0.08 mg/kg Dexamethasone IV bolus at the time of skin closure.

The parameters observed were Emergence time (min), extubation time (min), mental status, SOMCT score, Aldrete score and incidence of nausea and vomiting at different time intervals in the immediate postoperative period.

Both the groups were comparable in terms of demographic variables and frequency distribution of pre-existing co morbidities.

It was seen that patients who received sub-hypnotic dose of propofol (Group P) showed less emergence time and extubation time which was statistically significant ($p<0.05$) when compared with the control group. Our results were similiar to the results of some other authors [1]. This can be explained by the short elimination half-life of propofol. Propofol given at the end of inhalational anaesthesia is also known to act as a sedative during the clearing process of sevoflurane to suppress the excitation synapses and prevent agitation during emergence.

It was observed that postoperative mental status was seen to have higher number of confused and agitated patients in the control group. This difference was seen to be statistically significant as compared to the propofol group. ($p<0.001$). Earlier studies have shown similar results with the use of propofol [1], and the finding can again be attributed to the property of propofol to prove itself superior in terms of recovery spee and anxiolysis in comparison to other maintenance agents [3].

A short orientation memory concentration test was carried out at different time intervals in the postoperative period. It was observed that at 5 minutes postoperatively, performance of more number of patients in the propofol group was good (22: 4) and more number of performances in the control group were Fair (21:3). This difference was statistically significant. The same trend continued at 10 minutes and 15 minutes, with the patients in propofol group performing better than the control group with respect to short orientation memory concentration test results. This finding was also on similar lines with studies published by other authors [1].

The results of modified aldretes score assessed at different time intervals were found to be comparable in both the groups at different time intervals. Similiarly the incidence of Nausea and Vomiting in both the groups was also found to be comparable in both the groups. In group P, no antiemetic was administered at the time of skin closure, while group C received a combination of dexamethasone and ondansetron as per institutional protocol. It can be thus re- instated from these results that propofol itself can be relied

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upon for its anti- emetic properties at the time of closure. Our findings were similar to some more studies [8]. Propofol has also been shown to possess weak anti-serotonin (5HT3) properties, suggesting a possible effect on the CTZ, but not enough to fully explain the efficacy of the drug in emetic syndromes refractory to 5-HT3 antagonist therapy. The exact mechanisms by which propofol acts remain subject to speculation and await further studies.

Conclusion

A subhypnotic dose of propofol (0.5mg/kg), given at skin closure in patients receiving sevoflurane as maintenance agent under general anaesthesia, significantly reduces emergence time, extubation time, and also gives a calm, oriented, and clear headed recovery with lesser incidence of postoperative nausea and vomiting, in the absence of an antiemetic.

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Conflict of interest: None.

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