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COMPARISON OF INDUCTION, MAINTENANCE AND RECOVERY CHARACTERISTICS OF SEVOFLURANE-N₂O AND PROPOFOL-SEVOFLURANE-N₂O WITH PROPOFOL-ISOFLURANE-N₂O

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ABSTRACT: BACKGROUND: Rapid redistribution of the intravenous induction agent could lead to lightening of the plane of anesthesia before adequate depth is attained with the inhalational agent. This has promoted the rediscovery of single agent anesthesia, which avoids problems associated with transition phase. The aim of the study was to compare induction, maintenance and recovery with sevoflurane anesthesia from propofol and isoflurane anesthesia when administered with nitrous oxide to patients undergoing laparoscopic surgeries. **METHODS:** Sixty consenting patients of ASA physical status I or II aged between 20-55yrs of either sex scheduled for elective laparoscopic surgeries were randomly assigned to receive either I propofol for induction of anesthesia and isoflurane-nitrous oxide for maintenance (control), II propofol for induction and sevoflurane-nitrous oxide for maintenance, or III sevoflurane-nitrous oxide for induction and maintenance of anesthesia. Induction, maintenance and recovery characteristics were noted and compared between groups. **RESULTS:** Inhalational induction with sevoflurane-nitrous oxide was relatively prolonged (106±14s) and smooth without any episodes of coughing or laryngospasm. There were no untoward hemodynamic changes. Post induction mean arterial pressure (MAP) values were less in the groups where propofol was used (77.83±5.29mmHg and 78.96±5.58mm Hg in groups I and II respectively) as compared to the group in which sevoflurane-nitrous oxide was used for induction (83.16±4.70mmHg). Recovery time in the isoflurane-nitrous oxide group was much longer (7:47±0:47minutes) compared to the sevoflurane-nitrous oxide groups (4:41±0:26minutes and 4:37±0:26minutes in groups II and III respectively). **STATISTICAL ANALYSIS:** Data are expressed as mean ± standard deviation. Data were analyzed using analysis of variance and chi-square test. **CONCLUSION:** Induction of anesthesia with sevoflurane-nitrous oxide was relatively prolonged without any side effects. Patients were hemodynamically stable throughout in all groups. Emergence and recovery after maintenance with sevoflurane-nitrous oxide was significantly faster than after isoflurane-nitrous oxide anesthesia.

KEYWORDS: sevoflurane, propofol, inhalational induction.

INTRODUCTION: Although current day practices for establishing the anesthetic state consists of initial administration of an intravenous sedative-hypnotic followed by inhalational agents for maintenance, there is an increasing interest in the use of volatile anesthetics for both induction and maintenance in adults. One of the concerns with the present technique is the transition phase from induction to maintenance.

One of the major objections in performing inhalational induction of anesthesia used to be patients dislike for the black rubber face mask. Widespread availability of modern clear plastic masks

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along with non-pungent and rapidly acting volatile anesthetic has made inhalational induction an option even in adults.

The kinetics of propofol allow for fast induction of anesthesia and rapid recovery of consciousness. Studies comparing propofol with older inhaled anesthetics generally have found propofol to be superior in both recovery features and other postoperative outcomes like postoperative nausea and vomiting (PONV) etc.

Sevoflurane, having low blood-gas solubility provides both rapid induction and recovery.^{1,2} There have been many randomized controlled studies comparing sevoflurane and propofol for anesthetic induction.^{3,4,5} Individually, many studies have not shown any definite advantage of one technique over the other. In addition, the hemodynamic effects of sevoflurane in adults during induction, and maintenance in comparison with other agents needs to be studied.

Hence, we conducted a study to compare the induction, maintenance and recovery profiles after general anesthesia with sevoflurane-nitrous oxide alone or propofol-sevoflurane-nitrous oxide to an anesthetic technique consisting of propofol-isoflurane-nitrous oxide. Secondary objectives included comparison of PONV between groups.

MATERIALS AND METHODS: Sixty patients of ASA physical status I or II aged between 20-55 yrs, of either sex scheduled for laparoscopic abdominal surgeries of less than about 2 hours duration were studied after prior approval of ethics committee of the institute. Patients with clinically significant cardiovascular, pulmonary, renal or hepatic disease or with history of hypersensitivity to halogenated anesthetic agents were excluded.

Written and informed consent was obtained from all patients. The surgeries included laparoscopic appendectomy, laparoscopic cholecystectomy, laparoscopic hernia repair etc. Patients were randomly assigned to one of the three groups. In group I (control group), anesthesia was induced with propofol and maintained with isoflurane-nitrous oxide. In group II, anesthesia was induced with propofol and maintained with sevoflurane-nitrous oxide. In group III, anesthesia was induced and maintained with sevoflurane-nitrous oxide.

On the operating table, baseline parameters (ECG, heart rate, blood pressure, oxygen saturation) were noted. Premedication in the form of glycopyrrrolate 4 micrograms/kg i.v. was given after placement of intravenous cannula. After administering fentanyl (1.5 micrograms/kg i.v.) and lidocaine (1.5 mg/kg i.v.), and after adequate preoxygenation with 100% oxygen for two to three minutes, anesthesia was induced with either propofol or sevoflurane-nitrous oxide.

In groups I and II, anesthesia was induced with propofol (2mg/kg) administered over 10-15 seconds. In group III, anesthesia was induced by inhalation of sevoflurane using Ohmeda Tec 7 vaporizer with nitrous oxide, 50% in oxygen with a total gas flow of 6 litre per minute using semiclosed circuit. Sevoflurane was delivered at an inspired concentration of 4% with nitrous oxide, 50% in oxygen from the start of anesthetic induction.

The induction time was noted in all patients from the time of start of drug administration (either propofol or sevoflurane) to the time of loss of consciousness (failure to respond to eyelash stimulation). The occurrence of pain from injection of intravenous propofol, excitatory phenomenon (moving), respiratory problems (coughing, breath holding, apnea, laryngospasm, bronchospasm) and other adverse effects were noted. In all three groups, vecuronium was used to facilitate intubation (0.1mg/kg) and also for maintenance.

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In group I, anesthesia was maintained with isoflurane and nitrous oxide, 50% in oxygen, and in groups II and III with sevoflurane and nitrous oxide, 50% in oxygen.

Heart rate and blood pressure were maintained within 15% of the pre-incision values by adjusting the inspired concentration of the volatile anesthetic. Anesthesia was maintained with a total gas flow of 3 litre per minute using a semiclosed circuit (circle absorber system). ECG, heart rate, non-invasive blood pressure, SpO_2 , EtCO_2 were monitored throughout. These vitals were recorded every minute from induction of anesthesia for 5 minutes and subsequently at 15 minutes intervals. Diclofenac (1.5mg/kg) as slow i.v. infusion immediately after induction and fentanyl (1 microgram/kg) about 45 minutes after induction was given to all patients.

At the end of surgery, residual neuromuscular blockade was reversed with neostigmine (50 micrograms/kg) i.v. and glycopyrrolate (8 micrograms/kg) i.v. Administration of the volatile anesthetic and nitrous oxide was discontinued after the onset of spontaneous breathing, just before reversal of neuromuscular blockade.

During recovery, emergence was assessed at 15 second intervals after discontinuation of the volatile anesthetic. Time at which patients opened their eyes and responded to verbal commands were recorded. Extubation of trachea was done when patients were breathing regularly and able to respond to verbal commands. Extubation time and time at which patients were able to state their name was also recorded. Postoperatively, patients were monitored for 48 hours. Complications like nausea and vomiting were recorded.

Data are expressed as mean $\pm$ standard deviation. Continuous variables were analysed using analysis of variance and categorical variables were analysed using chi-square test. P value < 5% was considered as statistically significant. Analyses were carried out using SPSS version 16. The study had adequate power (above 90%) in order to have a difference in recovery time (seconds) of at least 100 between groups (I and II, and I and III).

RESULTS: There were no significant differences in the age, weight or sex distribution in between the groups. The surgeries performed were laparoscopic abdominal surgeries. The average operating time in all groups were similar and was between 66 and 71 minutes. The details are mentioned in Table 1. Induction of anesthesia in groups I and II was smooth with no side effects. Ninety percent of patients in group I and eighty five percent of patients in group II went into apnea after induction with propofol.

Induction time in groups I and II were comparable (42.5 ± 8.29 s in group I and 40.9 ± 5.64 s in II), whereas it was significantly longer in group III (106.2 ± 14.81 ; p value < 0.001). In group III as induction proceeded, spontaneous ventilation became progressively more shallow, and manual assistance of ventilation was required. There was no incidence of cough, laryngospasm or excessive oral secretions. However, in four patients, breath-holding was noticed. In other four patients, movement was seen during induction. Both of these subsided spontaneously. There was a single case of bradycardia which had to be treated with anticholinergic agent. Induction details are mentioned in Table 2.

Heart rate and MAP decreased in all three groups on induction. Decrease in MAP was significantly greater in groups I and II where anesthesia was induced with propofol. In all the groups, laryngoscopy and intubation produced a transient increase in heart rate and MAP which returned to preintubation values within 1-2 minutes. There was no significant variation in heart rate and MAP during maintenance period in all three groups.

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No significant difference in recovery characteristics were noted between groups II and III. In the isoflurane group (I), the emergence times from cessation of administration of anesthetic agent to spontaneous eye opening ($5:56 \pm 0:47$ s), response to simple commands ($6:28 \pm 0:40$ s), extubation ($6:45 \pm 0:41$ s), and to correctly stating the name ($7:47 \pm 0:47$ s) were significantly longer (p value < 0.001) when compared to the sevoflurane groups (II and III). Overall, recovery was faster in groups II and III.

No significant difference in the incidence of PONV was found between groups. There were no significant hemodynamic complications noted postoperatively.

DISCUSSION: Rapid emergence from anesthesia and postoperative recovery of cognitive function as well as hemodynamic stability are important requirements of modern anesthesia. Generally both propofol and sevoflurane meet these criteria. Sevoflurane is widely used in clinical anesthesia because of its relative lack of airway irritation^{1,2} or myocardial depressant effect. Sevoflurane has a low blood-gas partition coefficient of 0.69. This low solubility contributes to a rapid induction of and emergence from anesthesia than is possible with other volatile anesthetics in current use.

Fentanyl was used in our study before induction of anesthesia to minimize the hemodynamic response to tracheal intubation in all groups. Induction of anesthesia with sevoflurane was rapid and notable for the lack of respiratory irritation (cough, laryngospasm, bronchospasm etc) from the outset, but a few instances of breath-holding, apnea and movement were noted which subsided spontaneously. Thus, there was only a transient phase of excitation which was observed in our patients. This phase might have been masked by the use of fentanyl before induction.

However, patients induced with propofol had higher incidence of apnea. Propofol was used in two groups because its short elimination half time would be less likely to interfere with the assessment of emergence and recovery times. Although induction time was comparatively longer (106.2s) with sevoflurane compared to propofol (group I-42.5s; group II-40.9s) with $p < 0.001$, it was not apparent to the observer. Lidocaine was administered in our study as a prophylaxis against pain associated with propofol administration.

As lidocaine can produce hemodynamic and central nervous system effects, an identical dose was administered to patients in all three treatment groups. K. R. Watson and M. V. Shah et al⁶ conducted a study of clinical comparison of single agent anesthesia with sevoflurane versus target controlled infusion of propofol. They found that propofol had a significantly faster mean induction time (67s) than sevoflurane (97s). The administration of up to 8% sevoflurane has allowed for a more rapid induction in this study as compared to our study where we used 4% concentration of sevoflurane for induction.

MAP was better maintained during sevoflurane induction compared with propofol and while the hypotension associated with propofol may be of limited significance for healthy patients, it may be disadvantageous in the elderly and those with coronary artery disease. There are many studies which have found that sevoflurane preserves myocardial function perioperatively better than propofol.^{7,8,9} Overall sevoflurane induction in adults is as efficacious as with propofol or better.

Similar results were found in a study conducted by Ian smith et al¹⁰ and A Thwaites et al.¹¹ A Thwaites et al found that inhalation induction with 8% sevoflurane would appear to offer several objective advantages like better maintenance of MAP as found in our study and cost-effectiveness when compared to propofol induction.

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Significant minority of patients in their study found this technique unpleasant and were unwilling to undergo further inhalation induction. Cost factors and patient preference were not noted in our study. They found that sevoflurane induction was not associated with excitatory activity. The lower concentration of sevoflurane used in our study could account for excitatory effects seen in few of our patients.

Matsuyuki et al¹² found that sevoflurane was least irritant when compared to halothane, isoflurane and enflurane and was most suitable for inhalational induction. Hwan S. Joo et al⁷ conducted a metaanalysis of sevoflurane versus propofol for anesthetic induction. They also found that sevoflurane and propofol had similar efficacy for anesthetic induction. However, because of the more frequent incidence of PONV and trend toward patient dissatisfaction in the sevoflurane induction group, they concluded that propofol still seems to have advantages as an ideal drug to induce anesthesia.

During the course of surgery, there were no significant differences in mean heart rate values between three groups. MAP values in group III were slightly greater when compared to other groups throughout the surgery. The incidence of tachycardia could be controlled with rise in inspired concentration of volatile anesthetic agent. There were no episodes of bradycardia in any of the groups. W. Scott Jellish et al¹³ compared the effects of sevoflurane versus propofol in the induction and maintenance of anesthesia in adult patients and found that both groups were hemodynamically stable throughout the study period.

In our study, use of sevoflurane resulted in faster emergence from anesthesia than after isoflurane. There was no significant difference in recovery times between groups II (propofol induction) and III (sevoflurane induction). No complications like excitement or delirium were noted during emergence in any of the groups. Faster emergence was noted in sevoflurane group in similar studies.¹⁴⁻¹⁷ Beverly K. Philip et al¹⁴ who conducted a study in ambulatory surgeries found that the incidence of postoperative nausea was low with sevoflurane group.

Elina R. J. Seitsonen et al¹⁵ who conducted a study on recovery from isoflurane and sevoflurane anesthesia after out-patient gynecological surgery, concluded that isoflurane and sevoflurane are equally acceptable maintenance anesthetics. Ian Smith et al and Robinson et al¹⁷ found that emergence and early recovery after maintenance with sevoflurane-nitrous oxide was faster than after an isoflurane-nitrous combination.

We found no significant difference in the incidence of PONV between groups. This was similar to the findings of W. Scott Jellish et al. Jacob Wallden et al¹⁸ who conducted a study on comparison of propofol-remifentanyl and opioid free sevoflurane on early postoperative gastric emptying concluded that there were no major differences in early postoperative gastric emptying between the groups. Jan Wallenborn et al¹⁹ who conducted a study on the impact of isoflurane, desflurane or sevoflurane on the PONV concluded that type of inhaled agent had no influence of PONV frequency or severity.

Factors influencing postoperative nausea and vomiting include young age, female sex, obesity, diabetes, type and site of surgery etc. In our study these factors were nullified by the fact that the patient population had similar average ages, similar sex distribution, no large differences in the type of surgery and none were diabetic or obese. Also, no significant hemodynamic complications or clinical signs of nephrotoxicity were noted in any of the groups postoperatively. The findings need corroboration by further studies for extrapolation into general practice, especially for patients with higher risks of anesthesia because of smaller sample size.

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Further studies are also needed to understand patient preference and cost effectiveness for inhalational induction with sevoflurane in adults.

To conclude, induction of anesthesia with propofol was rapid, with sevoflurane-nitrous oxide, it was relatively prolonged but without significant side effects. Patients were hemodynamically stable throughout the surgery in all the groups. Decrease in MAP values were slightly more in groups with propofol induction. Emergence and recovery after maintenance with sevoflurane-nitrous oxide was significantly faster than after isoflurane-nitrous oxide combination. Thus, sevoflurane may be useful as an alternative to propofol for induction of anesthesia even in adults, especially in patients where hypotension after induction is detrimental, and in patients where rapid emergence and recovery of cognitive function is very much desired.

OBSERVATION AND RESULTS:

	Group I	Group II	Group III
Mean age(yrs)	30.6	33.7	30.95
Mean weight(kgs)	52.5	55.95	52.4
No. of males	07	10	09
No. of females	13	10	11
Operating time(min)	71.25	66.50	68
Anesthesia time(min)	90.25	86.75	88.25

Table 1: Demography of patients

	Group I	Group II	Group III
Induction time(s)	42.5±8.29	40.9±5.64	106.2±14.81 (p value<0.001)
Pain on injection	0	0	-
Cough	0	0	0
Apnea(no. of patients)	90% (18)	85% (17)	15%(3)
Movement (no. of Patients)	0	0	20%(4)
Other side effects			Bradycardia - 1 Breath holding – 4

Table 2: Induction of anesthesia characteristics

Reported as mean ± SD else number and %.

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	Mean recovery times (seconds±SD)		
	Group I	Group II	Group III
Spontaneous eye opening	356±47	206±20 (p<0.001)	201±18 (p<0.001)
Response to simple commands	388±40	214±17 (p<0.001)	208±16 (p<0.001)
Extubation	405±41	231±17 (p<0.001)	225±18 (p<0.001)
Stating the name	467±47	281±26 (p<0.001)	277±26 (p<0.001)

Table 3: Recovery characteristics

Reported as mean±SD

Graph 1: Heart rates at various intervals

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Graph 2: Mean arterial pressure at various intervals

Graph 3: Recovery characteristics

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