Journal of Anesthesiology
2014; 2(5): 32-39
Published online November 17, 2014 (http://www.sciencepublishinggroup.com/j/ja)
doi: 10.11648/j.ja.20140205.11

Does inhalational nitrous oxide affect induction dose of propofol and haemodynamic?

Sanjeev Singh[1, 2, 3]

[1]Department of Anaesthesia and Intensive care, School of Medical Sciences, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana, West Africa
[2]Department of Anaesthesia and Intensive care, Satyabhama Academy Of Medical Sciences & Research Institute, Lucknow, India
[3]Department of Cardiac Anaesthesia, Artemis Health Institute, Gurgaon, India

Email address:
drsanjeev73@rediffmail.com

To cite this article:
Sanjeev Singh. Does Inhalational Nitrous Oxide Affect Induction Dose of Propofol and Haemodynamic? *Journal of Anesthesiology.* Vol. 2, No. 5, 2014, pp. 32-39. doi: 10.11648/j.ja.20140205.11

Abstract: Background: Propofol is a commonly used induction agent. Propofol does not possess any strong analgesic effect, when used alone for induction of anaesthesia. In dose of more than 2 mg/kg bolus known to cause hypotension even requiring vasopressors. Nitrous oxide (N_2O) has been in use for more than 150 years. Although N_2O reduces the requirement of propofol for induction and maintenance, the effects of both the drugs on overall haemodynamic remain controversial. The aim of this study was to evaluate the efficacy and safety of induction dose of propofol when N_2O was concurrently administered and haemodynamic alteration with addition of N_2O to therapeutic dose of propofol. Materials and Methods: This was a prospective, randomized and double blinded comparison study that was conducted after obtaining institutional ethical approval. The study population consisted of eighty patients aged between 18 to 60 years from either sex and classified as American Society of Anaesthesiologists (ASA) physical status I or II which were scheduled for various elective surgical procedures under general anaesthesias. Participants were randomly allocated into two groups comprising 40 subjects each. Group PN received breathed 67% N_2O (4 L/min) + 33% O2 (2L/min) and propofol. Group PO: breathed 100 % O_2 (6L/min) and propofol. Changes in heart rate (HR), systolic blood pressure (SBP), mean arterial pressure (MAP) and Oxygen saturation (SpO_2) were measured Preoperatively (baseline T0), After 3minutes of premedication (T1), After 1minute of inhalation of 100% O_2 before induction of anesthesia (T2), After induction (T3), At 2, 5 and 10 minutes after induction (T4), (T5), and (T6). Results: Induction time and dose of propofol in PN group were significantly less. As 42.5% of the patients were induced in less than 100 sec, 57.5% in less than 200 sec and none of the patients required more than 200 sec for induction as compare to group PO where 77.5% required more than 200 sec, 22.5% in less than 200 sec and none of the patients were induced in less than 100 sec. The mean ± SD of induction time in groups PN and PO were 113.38±35.93 and 258.00±59.43 seconds respectively with $p < 0.001$. In group PN, 57.5% required 0.5-1.0mg/kg, 40% required less than 0.5mg/kg unlike group PO where 77.5% required 1-2mg/kg. The mean ± SD induction dose required for induction of anesthesia were 0.58±0.19 mg/kg and 1.43±0.40 mg/kg with and without 67% N_2O in O_2. Increase in HR in groups PN and PO 16.38% and 6.42% respectively. Conclusions: Co-administration of N_2O during induction of anaesthesia achieves significant reduction in induction dose as well as induction time of propofol. It provides significant stability in SBP, and MAP, without affecting arterial oxygen saturation. N_2O causes significant increase in HR.

Keywords: Blood Pressure, Heart Rate, Nitrous Oxide, Propofol (Source: Mesh, NLM)

1. Introduction

Propofol an intravenous (IV) anaesthetic agent, is widely used for induction of anaesthesia due to rapid onset, recovery and low degree of excitatory activity.[1] However, as propofol alone possesses no strong analgesic effect, it is often administered in combination with additional analgesics. Addition of analgesics and volatile anaesthetic agents augments induction characteristics and reduces the dose of propofol.[2] Propofol commonly produces decrease in systemic vascular resistance (SVR- 15-25%), Stroke volume (SV- 20%), cardiac Index (CI-15%), left ventricular stroke work index (30%), myocardial contractility as well as It causes transient apnea mostly in a dose and rate dependent

manner.[3] At higher doses it causes significant decrease in arterial blood pressure and heart rate by 37% and 24%, respectively [4], which is particularly undesirable in elderly, and high risk group of patients as may cause hypotension.

N_2O has been a cornerstone of anaesthetic practice since its first use because of its analgesic, anxiolytic and anaesthetic properties. It is good analgesic but a weak anaesthetic agent. It is used commonly as an adjunct to balanced general anaesthesia (GA) and a gaseous vehicle for the administration of more potent volatile anaesthetics. When used as an adjunct, the resulting minimum alveolar concentration (MAC) reduction for the other volatile anaesthetic agent. Potential side effects like acute and chronic pain, neurological, cardiovascular outcomes, and wound infection remain controversial. Certain characteristics of nitrous oxide as its propensity to postoperative nausea and vomiting, expansion of gas-filled cavities, the second-gas effect, and diffusion hypoxia are very well known.[5] It remains incumbent upon the practitioner to utilize the patient history and data to evaluate the risk–benefit profile for the use of nitrous oxide.

Many authors have studied the reduction in effective concentration (EC_{50}), plasma concentration (CP_{50}) for noxious stimulus, $CP_{50\,LOR}$ (loss of response) of propofol with N_2O.[6, 7] Although N_2O reduces the requirement of propofol for induction and maintenance, the effects of both drugs on overall haemodynamic remain controversial.[7] However use of N_2O as an inhaled additional drug for the induction of propofol anaesthesia has not been studied extensively.[8] The present study was designed primarily to determine the efficacy and safety of minimum induction dose of propofol, when N_2O was concurrently administered and haemodynamic variations.

1.1. Material and Methods

This study was undertaken after an institutional approval by the Committee on Human Research Publications and Ethics was obtained. The study was conducted at Satyabhama Academy Of Medical Sciences & Research Institute in 2008-2009. Informed consent was obtained from 80 patients. The study population consisted of ASA physical status I (normal healthy patients) or II (patients with mild systemic disease), male and female adults between the ages of 18‑60 years scheduled for various elective surgical procedures.

1.2. Study Design

This study was a prospective, randomized, and double blinded clinical comparison study. The Sample size for the study was 80 generated using a sample size calculator. The study participants were randomly divided into two groups by a computer generated randomization table. A study nurse (Person A) who was not involved in the randomization process of N_2O to enhance blinding. Person B monitored the heart rate (HR), systolic blood pressure (SBP), mean arterial pressure (MAP) and oxygen saturation (SpO_2) with respect to time, whilst Person C was responsible for intubation of the patients. Person A and C were kept constant throughout the study. Person B, C, and the patient were kept unaware of the N_2O to enable double blinding.

Inclusion criteria: for the study were ASA class I or II, age range 18‑60, oropharyngeal anatomy of Mallampati class I and any operation other than cardiac surgery performed under general anesthesia with endotracheal intubation.

Exclusion criteria: for the study included patients who were pregnant, morbidly obese, with risk of aspiration of gastric contents, cardiovascular disease, heart rate <60 beats per minute (bpm), basal SBP < 100 mm Hg, and other conditions such as bronchial asthma, diabetes mellitus, drug allergies. Duration of laryngoscopy was noted and in case where duration exceeded 15 sec was excluded from this study. Patients with relative contraindication to the use of halothane as well as N_2O during induction of anesthesia such as intestinal obstruction, middle ear disease, pneumothorax, air embolism, sinus or middle ear surgery**.**

2. Pre-Surgical Protocol

Prior to surgery all patients underwent pre-anaesthetic evaluation for systemic diseases and routine laboratory investigations such as haemoglobin (Hb), total lymphocyte count, differential lymphocyte count, urine analysis and other investigations were done as necessary. Information collected also included weight, nutritional status, airway assessment by the Mallampatti scoring system, a detailed examination of the respiratory, cardiovascular, central nervous system. Patients looked for hypotension (basal SBP < 100 mm Hg, or a decrease in the initial systolic arterial pressure of 20% from baseline, or both),[9] and hypoxemia (SpO_2 < 90 that correlates with a PaO_2 of < 60 mmHg).[10] The procedure of general anaesthesia was explained to the patient. Patients were explained about the purpose and procedure. Informed consent was obtained. All patients were kept fasting overnight. Premedication included tablet alprazolam 0.25 mg and tablet ranitidine 150 mg orally, night prior and on the morning of the surgery.

2.1. Anaesthetic Technique

On arrival to the operation theatre (OT), patients were identified, a short preoperative history was taken, clinical examination and routine investigations were rechecked in all patients. Monitors were attached to patient and baseline HR, MAP, SBP and SpO_2 were recorded. The procedure was again explained to the patients. An intravenous (IV) line was established and all patients were premedicated with IV glycopyrrolate 0.2 mg, IV ondansetron 4 mg and IV fentanyl 1 mcg/kg.

After 3 minutes of pre-oxygenation patients were made to breathe respective gases (67% N_2O +33% O_2 in group PN and 100% O_2 in group PO) via a tight fitting face mask using a closed circuit breathing system with CO_2 absorber for 1 minute. Lidocaine 10 mg was given followed by IV propofol at a rate of 20 mg/min to maintain uniformity in all patients

(as titrated doses of 10 mg every 30 seconds). Propofol was stopped when there was loss of response to verbal command (ie, to open eyes). Onset of anaesthesia was confirmed with disappearance of the eyelash reflex. The induction time was taken as time from the start of propofol to loss of response and induction dose as the amount of propofol administered in that time. The study drug N_2O was randomly allocated to patients in a double blinded manner. Patients were ventilated with oxygen and 1% halothane using IPPV. About 2 min after IV vecuronium, laryngoscopy was performed with a Macintosh laryngoscope blade and trachea intubated with an appropriate size cuffed endotracheal tube. After confirmation of correct placement of ET tube, anaesthesia was then maintained with O_2 and halothane. During the study HR , MAP , SBP and SpO_2 were monitored at preoperatively (baseline T0), After 3 minutes of premedication (T1), After 1 minute of inhalation of 100% O_2 before induction of anaesthesia (T2), After induction (T3), At 2, 5 and 10 minutes after induction (T4), (T5), and (T6) respectively. Any complications like hypoxia, respiratory depression, allergic reactions etc were noted.

3. Parameters and Statistical Analysis

Summary statistics of patient gender, age, and weight for all three groups were reported as means±standard deviation (SD). HR, SBP, MAP, $Sp0_2$ were recorded using Infinity Delta XL Drager, Draeger Medical Systems, Inc. Telford, PA 18969, USA.

Patients were also observed for complications like hypotension, hypertension, arrhythmias, and hypoxaemia. Statistical analysis was done by student *t*-test, Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups and *P* values were calculated. Levenes test has been performed to assess the homogeneity of variance. Haemodynamic variables were represented by mean±SD. In all analyses, $p<0.05$ was considered statistically significant. The Statistical software package SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data.

4. Results

Table 1. *Age distribution of patients.*

Age in years	Group PN		Group PO	
	No	%	No	%
18-20	2	5.0	2	5.0
21-30	11	27.5	12	30.0
31-40	13	32.5	10	25.0
41-50	9	22.5	11	27.5
51-60	5	12.5	5	12.5
Total	40	100.0	40	100.0
Mean ± SD	37.05±10.70		37.90±11.35	

Samples are age matched with p=0.731

All the demographic profiles in the PN and PO groups were comparable [Table 1]. The age range was 18-60 years for both PN and PO group. The mean values of the age with standard deviations are 37.05±10.70 and 37.90 ±11.35 for PN and PO groups respectively. There was no significant difference between the two groups ($p>0.05$).

In groups PN and PO 45% patients were males and 55% were females respectively. No significant difference was observed in sex wise distribution of the cases between the two groups ($p>0.05$) [Table 2] The Male: Female ratio is maintained in both the groups of the study.

Table 2. *Gender distribution of patients.*

Gender	Group PN		Group PO	
	No	%	No	%
Male	18	45.0	18	45.0
Female	22	55.0	22	55.0
Total	40	100.0	40	100.0
M: F Ratio	1:1.2		1:1.2	

Samples are gender matched with p=1.000

Table 3. *Weight (kg) distribution of patients.*

Weight (kg)	Group PN		Group PO	
	No	%	No	%
41-50	7	17.5	11	27.5
51-60	14	35.0	14	35.0
61-70	12	30.0	9	22.5
71-80	7	17.5	5	12.5
81-90	0	0.0	1	2.5
Total	40	100.0	40	100.0
Mean ± SD	60.22±9.28		58.67±11.41	

Samples are weight matched with p=0.507

As shown above (Table 3), the weights of the patients were between 41-90 kgs with a mean and standard deviation of 60.22±9.28 and 58.67±11.41 for PN and PO groups respectively. No significant difference was observed in the weight distribution in the two groups ($p>0.05$). In majority of the patients of both the groups, the body weight range between 41-80 kg. The mean body weight is comparable in both the study groups.

Table 4. *ASA Physical status distribution of patients.*

ASA	Group PN		Group PO	
	No	%	No	%
ASA I	28	70.0	26	65.0
ASA II	12	30.0	14	35.0
Total	40	100.0	40	100.0

Distribution ASA is statistically similar in two groups with p=0.633

Table 5. *Operative procedure of the patients.*

Operative procedures	Group PN (n=40)		Group PO (n=40)	
	No	%	No	%
General surgery procedures	7	17.5	18	45.0
ENT procedures	8	20.0	4	10.0
Urological procedures	1	2.5	3	7.5
Gynaecological procedures	3	7.5	2	5.0
Neurosurgical procedures	4	10.0	1	2.5
Others	17	42.5	12	30.0

Table 6. *Distribution of Induction time (sec) in patients.*

Induction time (sec)	Group PN (n=40)		Group PO (n=40)	
	No	%	No	%
<100	17	42.5	0	0.0
101-200	23	57.5	9	22.5
>200	0	0.0	31	77.5
Mean ± SD	111.38±35.93		258.00±59.43	
Inference	Induction time (sec) is significantly less in Group PN (111.38 ±35.93sec) when compared to Group PO (258.00sec±59.43) with p<0.001**			

In group PN, 42.5% patients were induced in less than 100 sec and 57.5% required less than 200 sec for induction of anaesthesia. None of the patients required more than 200 sec. Where as in group PO, (77.5%) required more than 200 sec for induction of anaesthesia. None of the patients were induced in less than 100 sec as compared to 42.5% in group PN. The mean induction time was significantly less in group PN (111.38 ± 35.93) as compared to group PO (258.00± 59.43) ($p < 0.001$)

Table 7. *Distribution of Induction dose (mg/kg) in patients.*

Induction dose (mg/kg)	Group PN (n=40)		Group PO (n=40)	
	No	%	No	%
<0.5	16	40.0	0	0.0
0.5-1.0	23	57.5	3	7.5
1.0-2.0	1	2.5	31	77.5
>2.0	0	0.0	6	15.0
Mean ± SD	0.58±0.19		1.43±0.40	
Inference	Induction dose is significantly less in Group PN (0.58±0.19 mg/kg) when compared to Group PO (1.43±0.40 mg/kg) with p<0.001**			

In group PN, about 40% patients required induction dose less than 0.5 mg/kg and 57.5% patients were induced with 0.5- 1.0 mg/kg. None of the patients required more than 2mg/kg for the induction of anaesthesia. In group PO, 77.5% of the patients were induced with 1 – 2 mg/kg induction dose. But none of the patients were induced with less than 0.5 mg/kg as compared to 40% in group PN. The induction dose was significantly less in group PN (0.58± 0.19), as compared to group PO (1.43±0.40) with p<0.001.

Table 8. *Comparison of heart rate (bpm) in the two study groups of patients.*

HR (bpm)	Group PN (n=40)	Group PO (n=40)	p value
T0	80.75±12.45	82.50±7.34	0.446
T1	87.15±13.55	91.55±11.18	0.117
T2	88.30±15.01	91.97±12.48	0.226
T3	93.98±11.27	87.80±12.61	0.024*
T4	98.25±10.59	87.70±13.36	<0.001**
T5	99.35±8.82	86.25±12.17	<0.001**
T6	97.15±10.60	91.20±12.59	0.025*

The baseline mean heart rate and standard deviation were 80.75± 12.45 and 82.50± 7.34 in groups PN and PO respectively, which were statistically comparable (p= 0.446). In group PN, there was significant increase in mean heart rate after induction of anaesthesia (93.98± 11.27). There was continuous increase in heart rate till 10 mins after induction. Heart rates were 98.25±10.59, 99.35±8.82 and 97.15±10.60 at 2, 5 and 10 min respectively.

In group PO, no significant change in mean heart rate was observed immediately after induction of anaesthesia (87.80±12.61). The mean heart rate was stable at 2 and 5min 87.70±13.36 and 86.25±12.17 respectively. The inter group PN had statistically significant increase in heart rate as compared to group PO (p<0.001).

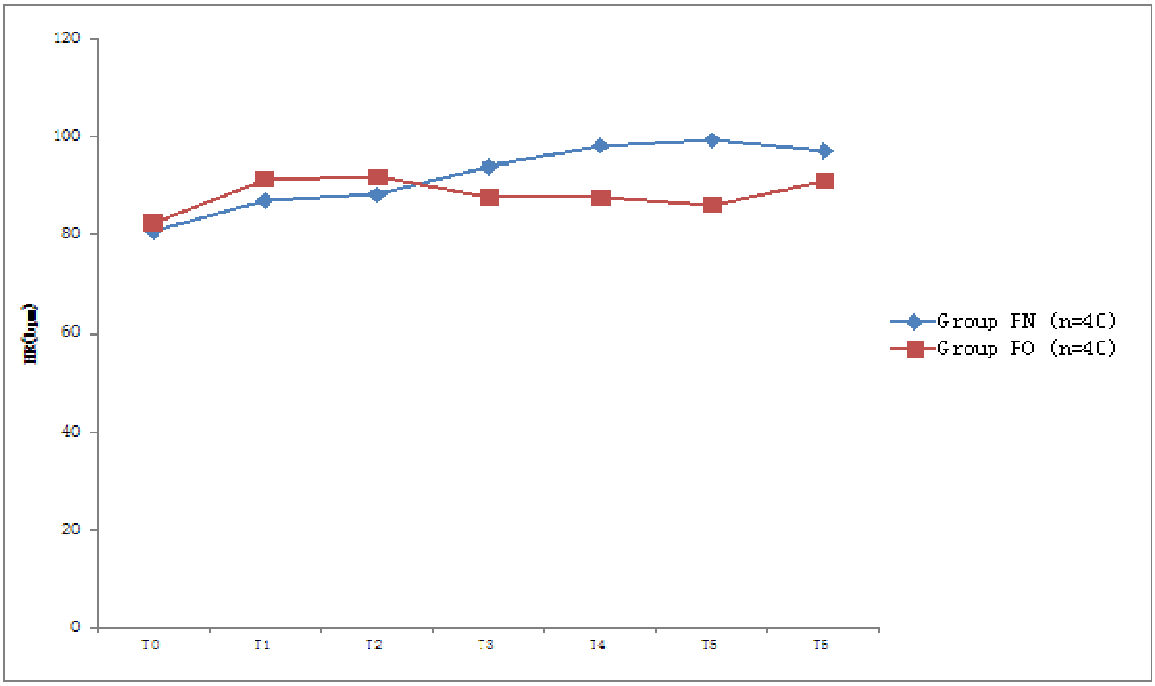

Fig 1. *Line diagram changes in heart rate in each group.*

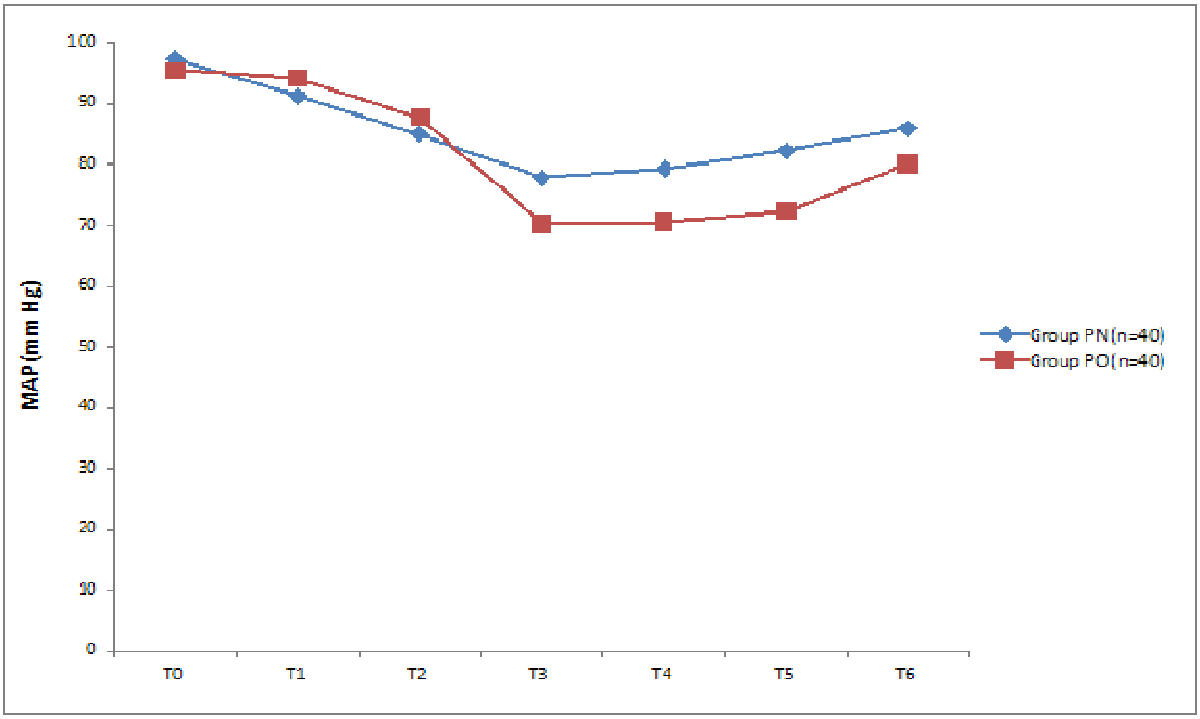

Fig 2. *Changes in mean arterial pressure in each group.*

In group PN, the baseline mean arterial pressure and standard deviation were 97.40±13.15. Immediately after induction there was reduction in mean arterial pressure 77.80±8.53 and mean arterial pressure returns to baseline value at about 10 min after induction of anaesthesia 85.93±11.75. Whereas, in group PO, the baseline mean arterial pressure and standard deviation were 95.50±17.65, immediately after induction of anaesthesia there was statistically significant reduction in mean arterial pressure to 70.28±16.65 and the reduction were observed even at 5 min after induction (72.33±15.25). The inter group analysis shows that the reduction in mean arterial pressure in group PO was highly significant when compared to group PN ($p<0.001$).

Table 9. *Comparison of mean arterial pressure in the two study groups of patients.*

MAP (mm Hg)	Group PN (n=40)	Group PO (n=40)	P value
T0	97.40±13.15	95.50±17.65	0.587
T1	91.25±12.27	94.28±14.41	0.315
T2	85.00±9.83	87.83±12.81	0.272
T3	77.80±8.53	70.28±16.65	0.013*
T4	79.25±10.42	70.58±15.72	0.005**
T5	82.30±10.00	72.33±15.25	0.001**
T6	85.93±11.75	80.15±18.24	0.096+

The baseline systolic blood pressure and standard deviation were 131.83±17.95 and 127.88±22.42 in groups PN and group PO respectively, which were comparable in both the groups. In group PO there was fall in systolic blood pressure immediately after induction of anaesthesia to 94.78±15.74. The fall in systolic blood pressure was observed even at 10 min after induction (103.88±16.22). In group PN the systolic blood pressure immediately after induction was 108.60±9.9, but it remained stable thereafter 107.83±12.00, 111.05±12.86, and 113.95±10.46 at 2, 5, and 10 min respectively. Inter group analysis shows group PN had stable systolic blood pressure after induction of anaesthesia as compared to group PO.

Table 10. *Comparison of systolic blood pressure in the two study groups of patients.*

SBP (mm Hg)	Group PN (n=40)	Group PO (n=40)	p value
T0	131.83±17.95	127.88±22.42	0.387
T1	125.93±17.37	124.70±18.67	0.762
T2	116.53±11.00	117.43±15.74	0.768
T3	108.60±9.99	94.78±15.74	<0.001**
T4	107.83±12.00	94.78±15.81	<0.001**
T5	111.05±12.86	95.55±14.78	<0.001**
T6	113.95±10.46	103.88±16.22	0.001**

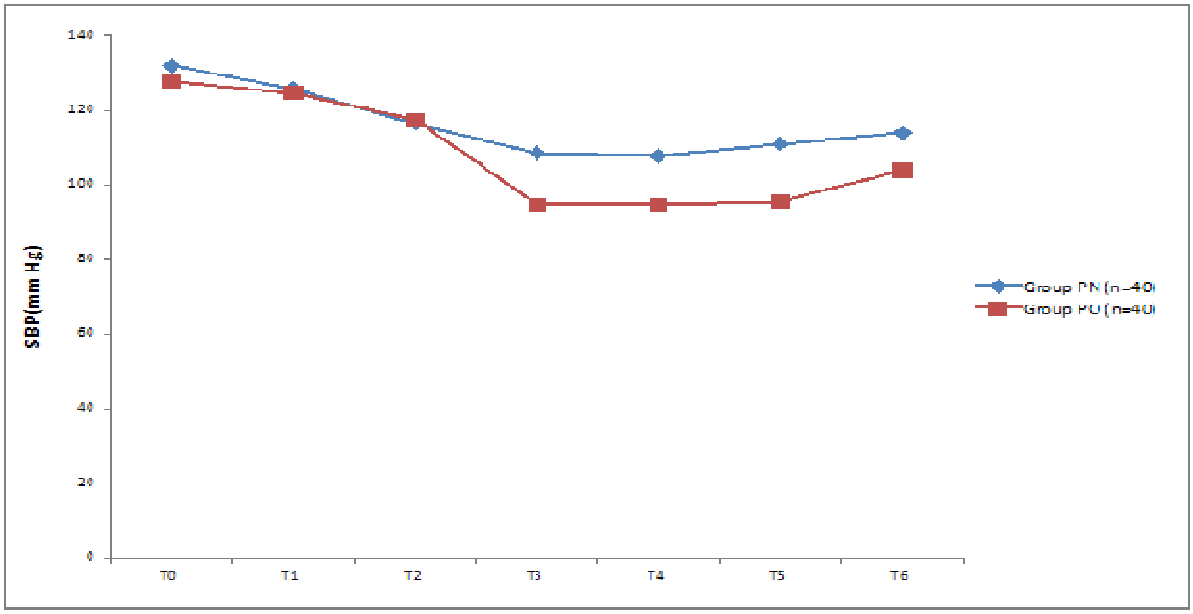

Fig 3. *Changes in systolic blood pressure in each group.*

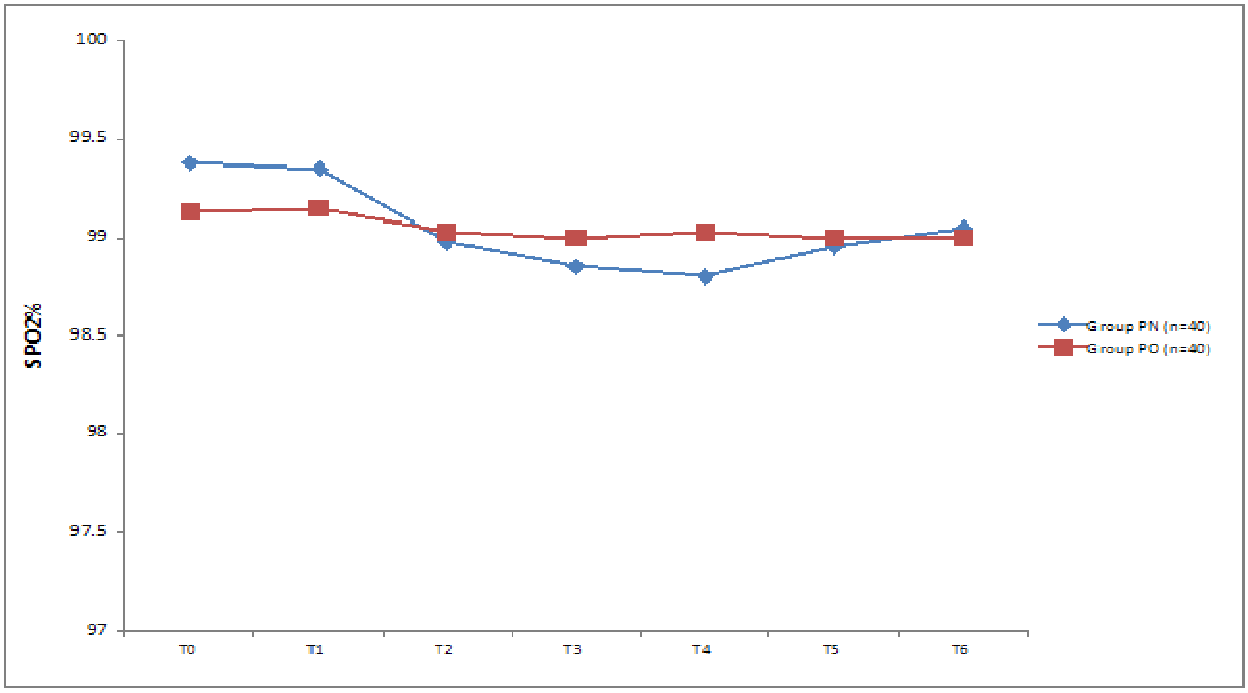

Fig 4. *Changes in arterial oxygen saturation in each group.*

Table 11. *Comparison of Oxygen saturation (SpO_2) in the two study groups.*

S_PO_2%	Group PN (n=40)	Group PO (n=40)	p value
T0	99.38±0.59	99.13±0.53	0.1
T1	99.35±0.53	99.15±0.36	0.053+
T2	98.98±0.58	99.03±0.16	0.598
T3	98.85±0.66	99.00±0.00	0.156
T4	98.80±0.61	99.03±0.16	0.026*
T5	98.95±0.50	99.00±0.00	0.532
T6	99.05±0.45	99.00±0.00	0.484

The baseline arterial oxygen saturation and standard deviation were 99.38±0.59 and 99.13±0.53 in groups PN and PO respectively. In group PN reduction in arterial oxygen saturation was observed at 2 min 98.80±0.61. However it is statistically significant but did not resulted in hypoxia clinically. In group PO, there was no statistically significant reduction in arterial oxygen saturation 99.03±0.16, after induction 99.00±0.00 and thereafter.

None of the patients in PN and PO group had any complications during the study period.

5. Discussion

Propofol is a commonly used induction agent, often used in combination with benzodiazepines and opioids.[11] If not used carefully may cause hypotension and require vassopressors. Since last 150 years N_2O has been a cornerstone of anaesthetic practice and often used with intravenous anaesthetic induction agents. In our study propofol was administered in titrated doses. With a slower infusion rate of 10mg/30 sec, we found that the induction time prolonged as in study by Ju in control group, however co-administration of 67% N_2O in O_2 shortened the induction time.[12] In our study the induction time and dose of propofol in PN group were significantly less as compared to control group. In PN group 42.5% of the patients were induced in less than 100 sec, whereas in group PO 77.5 % required more than 200 sec for induction. The mean ± SD induction time was significantly less in group PN (113.38±35.93sec) as compared to group PO (258.00±59.43sec) with $p < 0.001$, which is highly significant.

We studied the induction dose of propofol with and without N_2O. Our analysis showed that in group PN, 57.5% required 0.5-1.0mg/kg, and 40% required less than 0.5mg/kg, where as in group PO 77.5% required 1-2mg/kg. The mean ± SD for induction of anaesthesia was 0.58±0.19 mg/kg and 1.43±0.40 mg/kg with and without N_2O. Our findings were similar to Ju that the induction dose of propofol was reduced by almost 40% with concurrent use of N_2O.[12]

In our study where induction time with N_2O was 111.38±35.93 sec as compared to 141.8±46.7 sec in the study by Ju. This may be was due to all our patients received fentanyl but in Ju study patients received N_2O were not given fentanyl.[12]

Infusion rates of propofol ranging from 20-500 mg/ min were compared in several studies. Reduction in total dose of propofol used with slower infusion rates with an increase in the induction time.[13] In the study by Kumar mean induction dose of propofol was 2mg/kg in control group. In study group propofol priming with 20% calculated dose 30 seconds before remaining dose of propofol until loss of eyelash reflex reduced requirement of propofol by 27.48%. In our study with addition of nitrous oxide 97.5% patients' induction with 50% reduced dose of propofol of 5- 1mg/kg. In his study in control and study groups 8% and 1% of patients had complications like hypotension which were not visible in our study.[14] It shows that cardiovascular changes occurring in response to the amount of drug administered and not the rate of administration.[15]

Target controlled infusion (TCI) is a recently developed system that aids rapid recovery from propofol anaesthesia. When the target concentration of propofol required to prevent movements in 50% (CP_{50}) and 95% (CP_{95}) of patients were studied with and without 50% N_2O, it was concluded that CP_{50} value was significantly higher in those who did not receive N_2O than in those who did. [16] Studies have shown reduction of CP_{50}, CP_{95} of propofol by 25-28% with 67% N_2O, 43% reduction of $CP_{50\ LOR}$ of propofol with 67% N_2O. [6, 7] Our study results are similar to these studies which showed that co-administration of N_2O not only achieves more acceptable induction time with slow propofol infusion, but also results in a reduction in the total dose of propofol required.[12-14]

Reports on the effect of nitrous oxide in combination with volatile anaesthetic agents on heart rate have been inconsistent.[13–15] In contrast to McKinney study, we observed an increase in HR to statistically significant value immediately after induction, at 2 min, and 5 min in group PN.[16] The circulatory effects of N_2O can be explained by its tendency to stimulate sympathetic nervous system (SNS). Though it directly depresses myocardial contractility but arterial blood pressure, CO and HR are essentially unchanged or slightly elevated because of its stimulation of catecholamines or SNS activation.[17,18] 40-70% N_2O causes modest increases in HR in healthy patients, however, decline in HR can occur with N_2O in patients with coronary artery disease (CAD).[18] In McKinney study average age was about 70 years as compare to our 37 years. This decrease in heart rate attributed to the limited responsiveness of the aged cardiovascular system to sympathomimetic effects, may explain the absence of an increase in heart rate in his study. An increase in HR to significant value with nitrous oxide compensate well with decrease in systolic blood pressure with propofol. As RPP (rate pressure product) was calculated by multiplying heart rate with systolic blood pressure. RPP is a good estimate of myocardial oxygen requirement.[19] The RPP levels close to 20,000 are normally associated with angina and myocardial ischemia, which is not noticed in our patients.

6. Conclusions

The present data suggests that Co-administration of N_2O during induction of anaesthesia achieves significant reduction in induction dose as well as induction time of propofol. It provides significant stability in SBP, and MAP, without affecting arterial oxygen saturation with increase in heart rate.

Comments

We accept the fact that there were few limitations to our study. We used end point for induction of anaesthesia as loss of verbal response and disappearance of eyelash reflex, which had its own limitations. End tidal N_2O monitoring would have been a better indicator of effective administration of N_2O than inspired N_2O used in our study. Further studies needs to be done in high-risk patients with BIS and end tidal N_2O monitoring.

References

[1] Perouansky M, Hemmings HC Jr. Intravenous anesthetic agents. In: HC Hemmings Jr, PM Hopkins, eds. Foundations of Anesthesia: Basic Science and Clinical Practice. 2nd ed. London: Mosby Elsevier; 2006:295-310.

[2] Krzych LJ ,Szurlej D, Bochenek A. Rationale for propofol use in cardiac surgery. Journal of Cardiothoracic and Vascular Anesthesia. 2009;23:878-85.

[3] Rasooli S, Parish M, Mahmoodpoor A, Moslemi F, Sanaie S, Faghfuri S. The effect of intramuscular ephedrine in prevention of hypotension due to propofol. Pak J Med Sci. 2007;23:893-897.

[4] Hashiba E, Hirota K, Suzuki K, Matsuki A. Effects of propofol on bronchoconstriction and bradycardia induced by vagal nerve stimulation. Acta Anaesthesiologica Scandinavica. 2003; 47:1059-63.

[5] Vasconcellos KD, Sneyd JR**.** Nitrous oxide: are we still in equipoise? A qualitative review of current controversies**.** BJA. 2013;111:877-85.

[6] Davidson JAH, Macleod AD, Howie JC, White M, Kenny GNC. Effective concentration 50 for propofol with and without 67% nitrous oxide. Acta Anesthesiol Scand 1993; 37: 458-64.

[7] Stuart PC, Stott SM, Millar A, Kenny GNC, Russell D. CP50 of propofol with and without nitrous oxide 67%. Br J Anaesth 2000; 84: 638-9.

[8] Shiga T, Wajima Z , Inoue T, Ogawa R. Nitrous oxide produces minimal hemodynamic changes in patients receiving a propofol-based anesthetic: an esophageal Doppler ultrasound study. Can J Anaesth. 2003; 50 :649-52.

[9] Annamalai A, Singh S, Singh A, Mahrous DE. Can Intravenous Dexmedetomidine Prolong Bupivacaine Intrathecal Spinal Anesthesia? J Anesth Clin Res. 2013; 12: 1-5.

[10] Ehrenfeld JM, Funk LM, Schalkwyk JV, Merry AF, Sandberg WS, Gawande A. The incidence of hypoxemia during surgery: evidence from two institutions. Can J Anaesth. 2010; 57:888-897.

[11] Tanaka M, Nishikawa T. Propofol requirement for insertion of cuffed oropharyngeal airway versus laryngeal mask airway with and without fentanyl: a dose finding study. Br J Anaesth 2003; 90: 14-20.

[12] Ju-Mei Ng and Nian-Chih Hwang. Inhaling nitrous oxide reduces the induction dose requirements of propofol. Anesth Analg 2000; 90: 1213-6.

[13] Uzun S, Ozkaya BA, Yilbaş SO, Ayhan B, Sahin A, Aypar U. Effects of different propofol injection speeds on blood pressure, dose, and time of induction. Turk J Med Sci 2011; 41: 397-401.

[14] Kumar AA, Sanikop CS, Kotur PF. Clinical investigation effect of priming principle on the induction dose requirements of propofol - a randomized clinical trial. Indian J. Anaesth. 2006; 50:283- 87.

[15] Peacock JE, Lewis RP, Reilly CS, Nimmo WS. Effect of different rates of propofol for induction of anaesthesia in elderly patients. Br J Anaesth. 1990; 65: 346-52.

[16] McKinney MS, Fee JPH. Cardiovascular effects of 50% nitrous oxide in older adult patients anaesthetized with isoflurane or halothane.BJA. 1998; 80: 169–173.

[17] Robert K. Stoelting. Inhaled Anesthetics. In: Pharmacology and Physiology in Anesthetic Practice. Stoelting RK, Hiller SC, 4th Edition. Philadelphia: Lippincott Williams and Wilkins; 2006: p .42-86.

[18] Edmond I. Eger II. Inhaled Anesthetics: Uptake and Distribution. In: Miller's Anaesthesia. Miller RD. 7th Edition. Philadelphia: Churchill Livingstone; 2010: p.539-60.

[19] Singh S, Laing EF, Owiredu WKBA, Singh A. Comparison of esmolol and lidocaine for attenuation of cardiovascular stress response to laryngoscopy and endotracheal intubation in a Ghanaian population. Anesthesia: Essays and Researches. 2013; 7: 83-88.