(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 4, Issue 3, Page No: 22-29
May-June 2021

Effect of Inhalation of Nitrous Oxide on the Induction Dose and Time Requirement of Propofol for Induction of General Anaesthesia

Dr Aparna Abhijit Bagle Dr Shivani Shrirang Phansalkar* Dr Reema Jawale
[1]Professor, [2]Postgraduate Third Year Resident, [3]Postgraduate First Year Resident
Dept of anaesthesiology Dr. D. Y. Patil Medical College, Hospital & Research Centre,Pimpri, Pune Maharashtra, India-411018

***Corresponding Author:**
Dr Shivani Shrirang Phansalkar
Dept of anaesthesiology Dr. D. Y. Patil Medical College, Hospital & Research Centre,Pimpri, Pune Maharashtra, India-411018

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

Background: Induction of anaesthesia can be accomplished by inhalation of anaesthetic gases or by use of intravenous agents, or both. Nitrous oxide is used as an adjuvant analgesic and as a vehicle for administration of more potent volatile agents. It enhances the anaesthetic effect of other intravenous as well as inhalational agents and helps in potentiating their action.

Aim: To study the efficacy and safety of concurrent administration of Nitrous oxide with propofol for induction of general anaesthesia.

Methods: A total of 60 patients were included in the study with patients divided in to PN and P group after obtaining due consent. In Group P – patients given 100% oxygen(6L/min) and in Group PN– patients given 67% nitrous oxide(4L/min) and 33%oxygen(2L/min).

Results: The mean requirement of Propofol for induction in PN group was 43.50 ± 6.18 mg whereas in P group was 92.1 ± 9.35mg. The mean time for induction was 130.50 ±18.54 seconds in PN group whereas this was 276.50 ± 28.04 seconds in P group. The duration of laryngoscopy and haemodynamic changes was comparable in both the groups. Significantly lesser number of patients experienced pain in PN group while injecting propofol.

Conclusion: Nitrous oxide can be used as an effective adjunctive anaesthetic drug in reducing propofol requirement and reducing the induction time with desirable hemodynamic stability.

Keywords: general anaesthesia, nitrous oxide, propofol, induction dose, induction time.

INTRODUCTION

General anaesthesia is an induced state of unconsciousness, amnesia and analgesia with or without reversible muscle paralysis. Induction of anaesthesia can be accomplished by inhalation of anaesthetic gases or by use of intravenous agents, or both. For the duration of the procedure, a plane of anaesthesia is maintained using either continuous inhalation or intravenous agents, either alone or in combination.

Propofol has been accepted in recent years as most commonly used agent for intravenous induction of anaesthesia. Induction, with propofol is smooth, rapid, has rapid awakening and orientation times, better intubating conditions, and upper airway integrity.[1]The major disadvantage with propofol is a substantial decrease in arterial blood pressure . Induction dose of Propofol 2mg/kg body weight results in nearly 30% decrease in systolic blood pressure [2.] The hypotensive action of Propofol is

attributed to the reduction in sympathetic activity, vasodilatation and myocardial depression. This fall in blood pressure is of little significance in healthy patients but is of great significance in patients having coronary artery disease etc. because it can lead to myocardial ischemia.[3]

During use of propofol in general anaesthesia, a number of methods were tried to reduce the induction requirements of dose of propofol and hemodynamic changes associated with it which include a priming dose of propofol, use of Intravenous opioids, benzodiazepines, barbiturates, local anesthetics and concomitant use of nitrous oxide (N_2O) as inhalational agent.[4-9]

Nitrous oxide is an odorless, colorless, non-flammable gas. Nitrous oxide is used during general anaesthesia, procedural sedation, anaesthesia for dental surgeries and to treat severe pain.

N_2O is a frequently used along with propofol in general anaesthesia. Although it reduces the requirement of propofol for induction and for maintenance, effect of both drugs combined is controversial on overall hemodynamics. In healthy humans, the addition of 70% N_2O to bolus propofol at a dose of 2 mg/kg did not alter hemodynamic variables. [8-10]Nitrous oxide is used as a complementary analgesic and as a carrier for more potent volatile agents. It enhances the anaesthetic effect of other intravenous as well as inhalational agents and helps in potentiating their action.[11]

Hence, the objective of this study was to find out whether induction dose of propofol could be reduced with administration of nitrous oxide prior to intravenous induction. The secondary objectives included assessment of induction time, vital parameters and response to laryngoscopy and intubation.

MATERIALS AND METHODS:

After approval from institutional ethics committee,this prospective randomised,comparative study was conducted on 60ASA grade I & II patients with age between 18 to 60 years of either gender posted for elective surgery under general anaesthesia.

Patients not willing to be a part of the study, patients with ASA status 3 or more, patients on pain perception modifying drugs, patients with known sensitivity to any of the drugs used for general anaesthesia, pregnant, morbidly obese patients, patients with risk of aspiration of gastric contents, patients with cardiovascular or hepatic or renal disease, bronchial asthma or diabetesmellitus, relative contraindications to the use of nitrous oxide and laryngoscopic duration>15 sec were excluded from study.

We used software win-pepin for sample size calculation.Taking confidence interval of 95% and power of study 80%, to get at least difference in induction dose of 20mg we need sample size of 24 in each group, and total of 48. Considering dropouts and exclusions during study, we took sample size of 30 in each group and total of 60 patients.

60 patients were randomly divided into two equal groups: Group P and Group PN by computer generated random number table. Group P- 30 cases (administration of Propofol without N2O), group PN-30 cases (concurrent administration of N2O with Propofol).

A detailed pre anaesthetic evaluation was carried out a day prior to the surgery, patients were fasted for 6 to 8 hours. On arrival to the operation theatre (OT) baseline HR, SBP, DBP, MAP and SpO2 were noted. Patients were pre-medicated with Inj. Midazolam 1mg and Inj.Fentanyl 2mcg / kg prior to the induction.

After 3 minutes of pre-oxygenation patients were made to breathe respective gases via a tight fitting face mask using a bain's circuit for 1 minute. In Group P – patients given 100% oxygen(6L/min) and in Group PN– patients given 67% nitrous oxide(4L/min) and 33%oxygen(2L/min) Then propofol infusion was started at 10mg/30s. Pain on injection of Propofol was noted by the behavioural scale (facial expressions) of the patient. Propofol was stopped when there was a loss of response to verbal commands (i.e to open eyes). Onset of anaesthesia was confirmed by loss of response to verbal command. The induction time was measured from start of propofol infusion to loss of response to verbal command and induction dose as the amount of propofol administered in that time. After induction inj.succinyl choline (2mg / kg) was given and all patients were ventilated for 1min within respective group. After confirmation of correct placement of ET tube, anaesthesia was then maintained with O2,

Volume 4, Issue 3; May-June 2021; Page No 22-29

nitrous oxide and isofluorane and intermittent doses of inj.vecuronium. During the study HR, SBP, DBP, MAP and SpO2 were monitored at preoperatively (baseline t0), After 3 minutes of premedication (t1), After 1 minute of inhalation of 100% O2 or (67%N2O) and (33%)O2 before induction of anaesthesia (t2), After induction At 2, 5 and 10 minutes after induction (t3), (t4), and (t5) respectively. At the end of the surgery all the patients were reversed with inj Neostigmine (0.005mg/kg) and inj.glycopyrrolate (0.008mg/kg) and patients were extubated after gaining consciousness, adequate power and were shifted to recovery room. In recovery all the patients will be monitored for vital parameters and any side effects like nausea, vomiting etc.

RESULTS:

A total of 60 patients were included in the study with patients divided in to PN and P group. Baseline characteristics, hemodynamic parameters and other study parameters were as follows.

Parameter	PN group	P group	P value	Statistical Significance
Mean age(in years)	35.26±12.53	39.63±6.72	0.09	Not significant
Male	16	18	0.602	Not significant
Female	14	12		
Mean weight(in Kgs)	53.77±5.62	53.8±5.02	0.98	Not significant
Mean height (in cms)	167.77±2.64	168.27±3.22	0.51	Not significant
Pain during propofol injection-Yes	5 (16.67%)	22 (73.33%)	<0.001	Significant
Pain during propofol injection-No	25 (83.33%)	8 (26.67%)	<0.001	Significant
Induction dose of propofol	43.5±6.18	92.17±9.35	<0.0001	Highly Significant
Mean Induction time	130.5±18.54	276.5±28.04	<0.0001	Highly Significant
Duration of laryngoscopy	50.33±5.86	49.83±5.94	0.74	Not significant

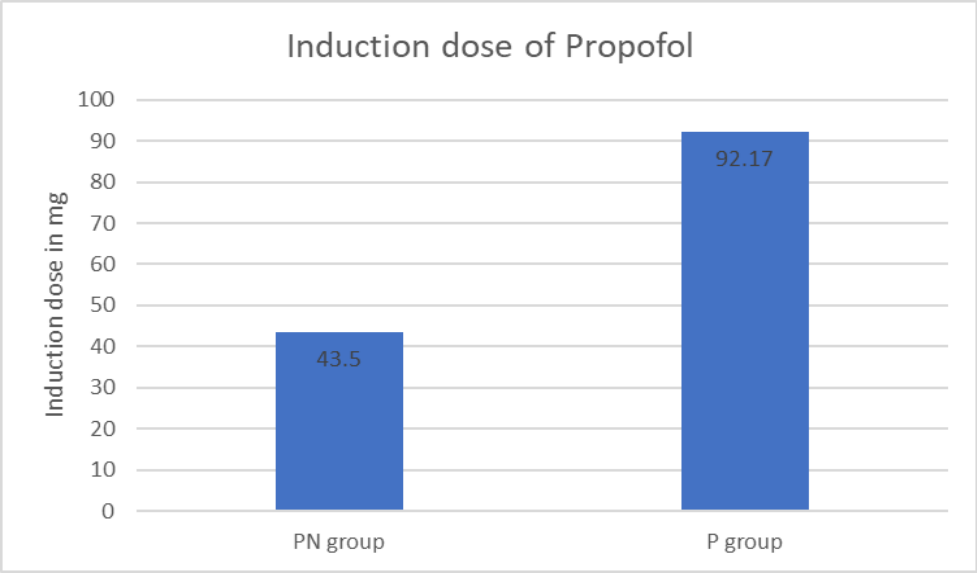

Figure 1

Volume 4, Issue 3; May-June 2021; Page No 22-29

The mean requirement of Propofol in PN group was 43.50 ± 6.18 mg whereas in P group was 92.17 ± 9.35 mg. The difference was significant with P<0.0001. There was significantly lesser propofol dose requirement in PN group.

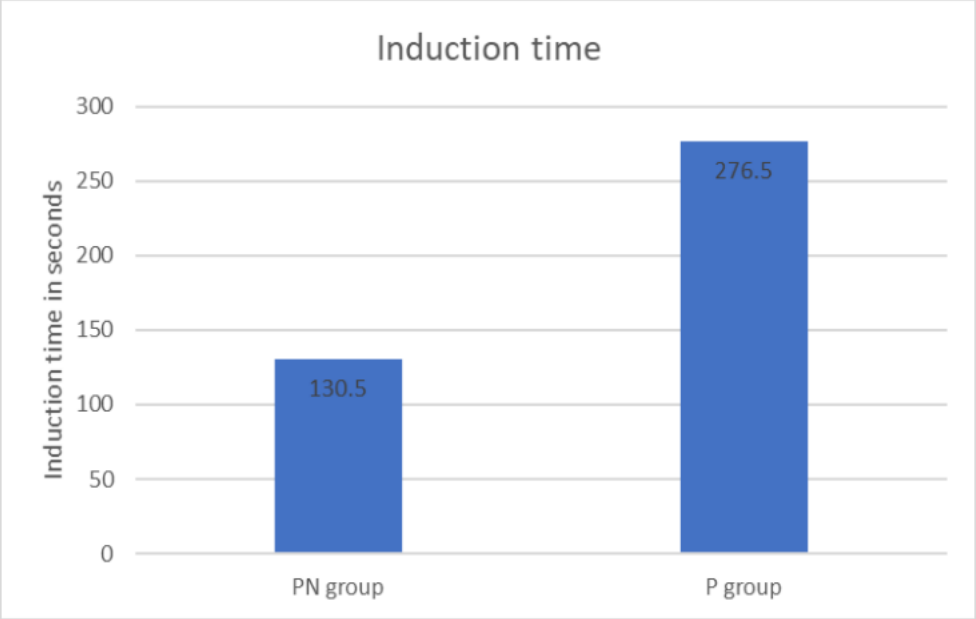

Figure 2

The mean time for induction was 130.50 ± 18.54 seconds in PN group whereas this was 276.50 ± 28.04 seconds in P group. The P value was significant with value of <0.0001. There was significantly early induction in PN group.

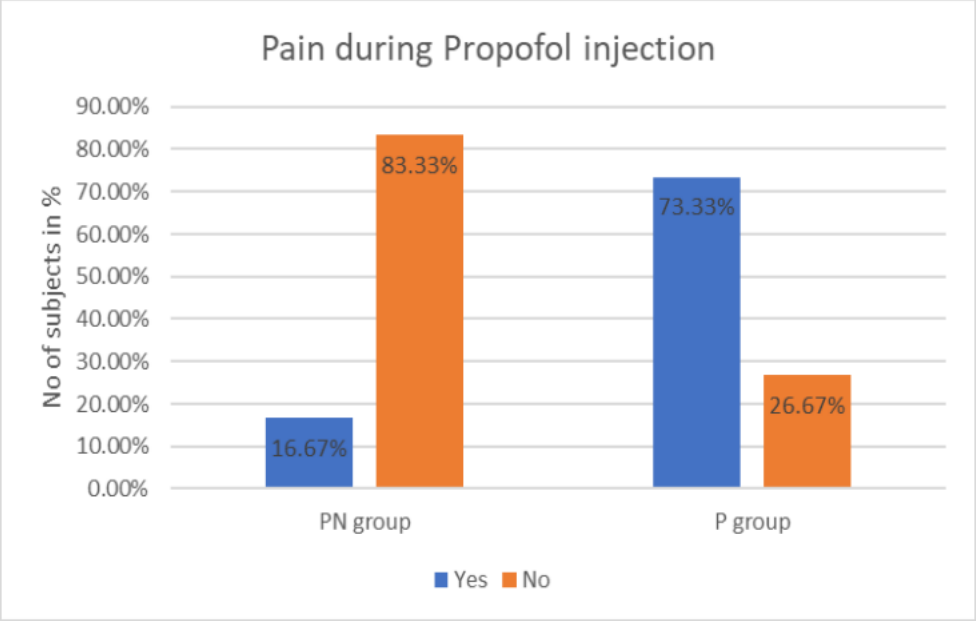

Figure 3

Significantly less number of patients experienced pain in PN group. There were only 5 (16.67%) in PN group who experienced pain while injecting propofol whereas 22 (73.33%) experienced pain in P group.

Volume 4, Issue 3; May-June 2021; Page No 22-29

The duration of laryngoscopy was alike in both the groups. The heart rate, SBP, DBP and oxygen saturation were measured at multiple time intervals from T0 to T5.They were comparable statistically as well as clinically in both the groups at all the time intervals.

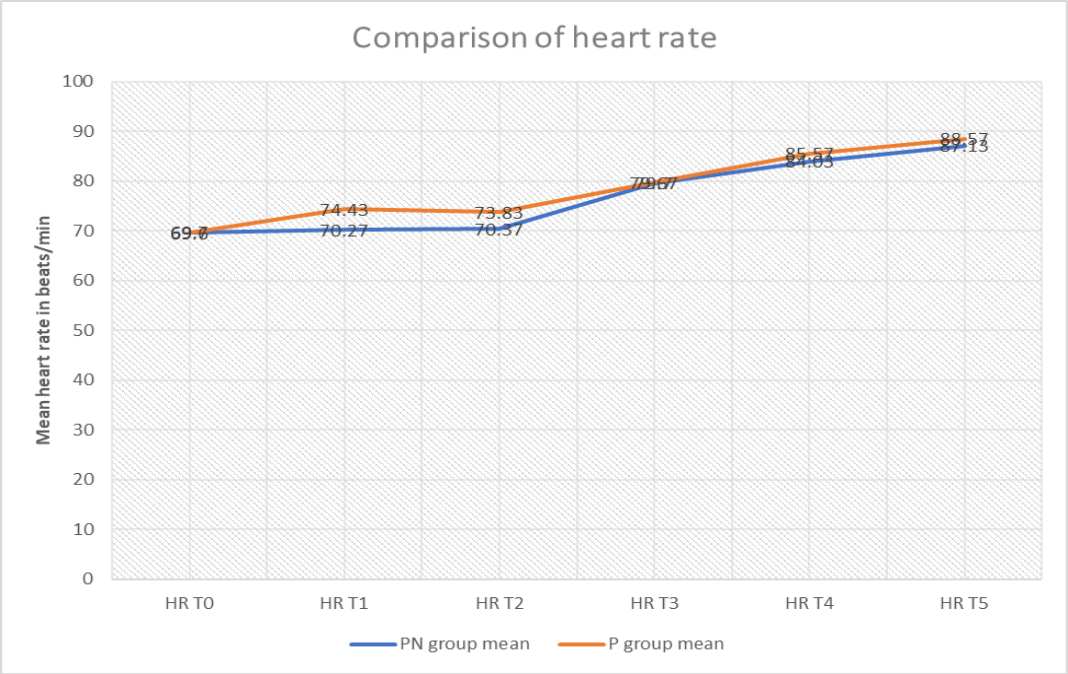

Figure 4

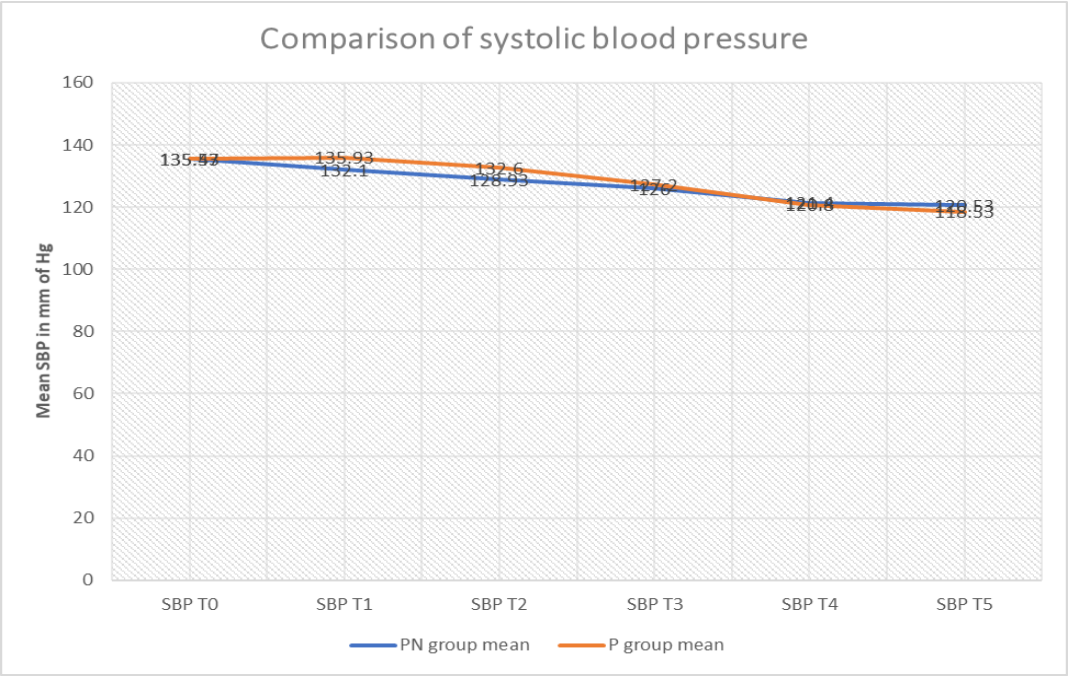

Figure 5

Volume 4, Issue 3; May-June 2021; Page No 22-29

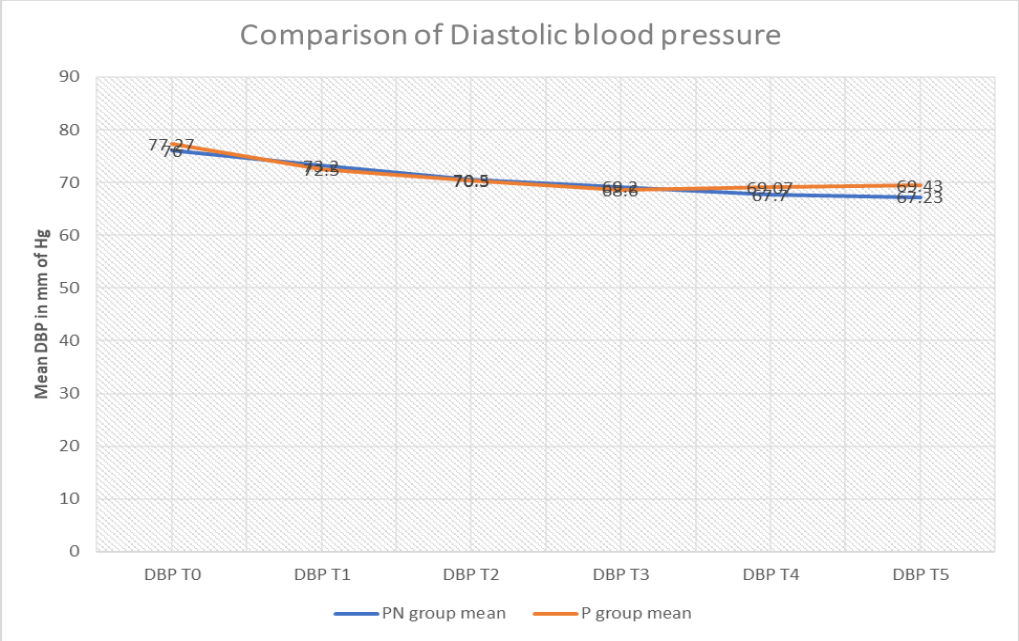

Figure 6

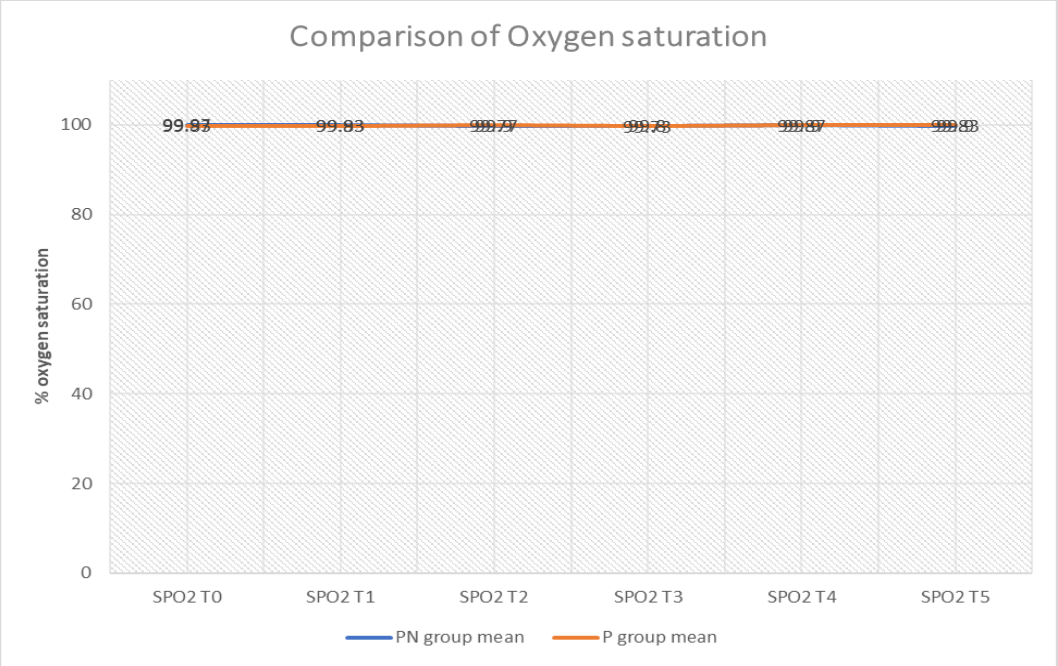

Figure 7

In our study 3 patients in PN group whereas 2 patients in P group experienced nausea and vomiting post operatively. The difference was non significant when compared in both the groups.

DISCUSSION:

The current study evaluated the efficacy and safety of concurrent administration of Nitrous oxide with propofol for induction of general anaesthesia. Age, weight, height and gender distribution in both the groups were comparable in our study. There were only 5 (16.67%) in PN group who experienced pain while injecting propofol whereas 22 (73.33%) experienced pain in P group. Reduction in pain is explained by analgesic property of nitrous oxide. **Sinha PK et al. (2005)**[12] also observed that more number of patients in Lignocaine group experienced pain on propofol injection compared to Nitrous oxide group, however the difference was statistically non significant.

Volume 4, Issue 3; May-June 2021; Page No 22-29

The mean requirement of Propofol for induction in PN group was 43.50 ± 6.18 mg whereas in P group it was 92.1 ± 9.35mg. The mean time for induction was 130.50 ±18.54 seconds in PN group whereas this was 276.50 ± 28.04 seconds in P group.

Ng JM, Hwang NC et al (2000)[8] investigated the efficacy of N_2O for induction of anaesthesia by randomizing 117 pre medicated patients for surgery into three groups. Group FN was given 1 µg/kg fentanyl and inhaled 4 L/min N_2O + 2 L/min O_2. Group PN was given placebo and inhaled 4 L/min N_2O + 2 L/min O_2. Group FO was given 1 µg/kg fentanyl and inhaled 6 L/min O_2. Propofol was given at 20 mg/min after inhalation of gas mixture for 1 min. Propofol infusion was stopped when there was no response to verbal commands. The mean dose of propofol was 0.75 (0.30) mg/kg for group FN, 0.84 (0.26) mg/kg for group PN, and 1.33 (0.51) mg/kg for group FO, with the induction time of 133 (57) s for group FN, 142 (47) s for group PN, and 226 (78) s for group FO. Their conclusion was that inhalation of 66% N_2O in O_2 1 min before induction of anaesthesia using propofol at the rate of 20 mg/min, decreases the induction dose requirement of propofol by 44% and decreases the time for the induction of anaesthesia ($P< 0.001$).

Similarly to our study **Yokoe C et al**[13]observed that Nitrous Oxide inhalation with Propofol sedation reduced pain associated with Propofol injection. They noted that total amount of propofol used was significantly lesser when used along with nitrous oxide (249.8 ± 121.7 mg) than propofol alone (310.3 ± 122.4 mg).

In our study duration of laryngoscopy was comparable in both the groups, this non significant differences prevents any bias in any of the measurables arising due to non homogenous study conditions. As duration of laryngoscopy has direct effect on hemodynamic parameters so short duration of laryngoscopy is essential.

Oxygen saturations were measured at multiple time intervals from T0 to T5. The values were not significantly different in both the groups. None of the patients had a fall in oxygen saturation in either of the group. Heart rates were measured at multiple time intervals from T0 to T5. The values were non significantly different in both the groups at all the time intervals. SBP was measured at multiple time intervals from T0 to T5. The values were not significantly different in both the groups at all the time intervals. DBP was measured at multiple time intervals from T0 to T5. The values were not considerably different in both the groups during all the time intervals.

Shiga T et. al[10]in 2003 studied that use of Nitrous oxide leads to minor hemodynamic changes in patients receiving a propofol-based anaesthetic. **Bhat KAet al.**[14] observed that blood pressure (before and after induction) were lessened as speed of injection increased from 50mg/min to 100mg/min to 200mg/min. So we injected propofol at the speed of 10 mg/30 s to minimise the hemodynamic alteration.

There were no serious adverse events noted on use of nitrous oxide.

Limitations:

This study did not evaluate use of other adjunctive agents to compare with nitrous oxide on propofol requirement. Study was not blinded. Sample size was small to extrapolate to regional levels trends. Study did not include patients above 60 years and below 18 years and patients with significant co-morbid conditions. Also cost-effective analysis was not done in the study.

CONCLUSION:

As observed from the results, use of nitrous oxide was related with significant reduction in dose of propofol for induction. Moreover, adjuvant use of nitrous oxide was associated with early induction when compared to other group. Moreover, hemodynamic stability was maintained at all the time points in nitrous oxide group. Nitrous oxide can be used as an effective adjunctive anaesthetic drug in reducing propofol requirement and reducing the induction time along with hemodynamic stability. We suggest conducting similar studies in future with a greater sample size and including varied population groups.

REFERENCES:

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

Volume 4, Issue 3; May-June 2021; Page No 22-29

2. Claeys MA, Gepts E, Camu F. Haemodynamic changes during anaesthesia induced and maintained with propofol. Br J Anaesth. 1988;60:3–9.

3. Dhungana Y, Bhattarai BK, Bhadani UK, Biswas BK, Tripathi M. Prevention of hypotension during propofol induction: a comparison of preloading with 3.5% polymers of degraded gelatin (Haemaccel) and intravenous ephedrine. Nepal Med Coll J 2008; 10:16-19.

4. M Kumar, N Saxena, AK Saxena. The effect of a colloid or crystalloid preload on hypotension caused by induction of anaesthesia with propofol and fentanyl. J Anaesth Clin Pharmacol 2008; 24:409-412.

5. Hosseinzadeh H, Eidy M, Golzari SEJ, Vasebi M. Hemodynamic stability during induction of anesthesia in elderly patients: propofol+ketamine versus propofol+etomidate. J Cardiovasc Thorac Res, 2013; 5:51-54.

6. El-Tahan MR. Preoperative ephedrine counters hypotension with propofolanesthesia during valve surgery: a dose dependent study. Ann Card Anaesth 2011; 14:30-40.

7. Ben-Shlomo I, Finger J, Bar-Av E, et al. Propofol and fentanyl act additively for induction of anaesthesia. Anaesthesia 1993; 48:111–3.

8. Ng JM, Hwang NC. Inhaling nitrous oxide reduces the induction dose requirements of propofol. AnesthAnalg. 2000;90:1213–6.

9. Carlier S, Van Aken H, Vandermeersch E, Thorniley A, Byttebier G. Does nitrous oxide affect the hemodynamic effects of anesthesia induction with propofol? Anesth Analg. 1989;68:728–33.

10. 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.

11. de Vasconcellos K, Sneyd JR. Nitrous oxide: Are we still in equipoise? A qualitative review of current controversies. Br J Anaesth. 2013;111:877–85.

12. Sinha PK, Neema PK, Rathod RC. Effect of nitrous oxide in reducing pain of propofol injection in adult patients. Anaesth Intensive Care. 2005;33:235–238.

13. Yokoe C, Hanamoto H, Sugimura M, Morimoto Y, Kudo C, Niwa H. A prospective, randomized controlled trial of conscious sedation using propofol combined with inhaled nitrous oxide for dental treatment. J Oral Maxillofac Surg. 2015 ;73:402–409.

14. Bhat JA, et al. Effect of Various Injection Speeds of Propofol on Blood Pressure, Time Taken and Dose Required for Induction of Anesthesia: A Prospective Observational Study. Adv Pharmacol Clin Trials 2018;3: 000133.

Volume 4, Issue 3; May-June 2021; Page No 22-29