Original Research Article

Haemodynamic Response to Laryngoscopy and Intubation After Preoxygenation with Nitrous Oxide: Randomized Clinical Trial

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Abstract

Background: Nitrous oxide inhalation significantly reduces the induction dose of propofol and also can prevent the hypotension and bradycardia accompanying propofol induction. **Aim:** To study the effect of pre-induction inhalation of nitrous oxide on haemodynamic parameters during laryngoscopy and intubation. **Material and Methods:** Patients were randomly divided into two equal groups by closed envelope technique to Group A and group B. Group A: received incremental doses of propofol following nitrous oxide inhalation for 3 minutes, pre-oxygenated with 4 litres/minute nitrous oxide and 2 litres/minute of oxygen. Group B: received only propofol as induction agent, inhaled with pre-oxygenated with 6 litres/minute of oxygen for 3 minutes with a tight fitting face mask. Pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure of each patient were measured at pre-inducstion and different intervals. **Results:** Mean systolic blood pressure at pre-induction in Group A was 133.39±13.734 and in Group B was 125.14±20.526. The diastolic pressures decreased in both Groups post induction, but the fall in these pressures was more in Group B than in Group A. The decrease in MAP was more in Group B than in group A and showed a significant difference when compared. **Conclusion:** Inhaling 66% nitrous oxide for 3 minutes before induction prevented a precipitous fall in mean arterial pressure at induction and effectively attenuated stress response to laryngoscopy and intubation without desaturation.

Key Word: Laryngoscopy, Intubation, Nitrous oxide, pre-oxygenation, haemodynamic response

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INTRODUCTION

Nitrous oxide, one of the oldest and still popular anaesthetic gas has been a cornerstone in anaesthetic practice since its first use in 1840's. Though, a poor anaesthetic agent, it has good analgesic properties. It is usually used as an adjuvant and a vehicle for the administration of more potent volatile anaesthetics. Nitrous oxide decreases the minimum alveolar concentration (MAC)[1] required for volatile anaesthetics and also decreases the need for intravenous (IV) anaesthestics.[2-4] Propofol nowadays has become a commonly used intravenous anaesthetic agent as it provides faster onset of action, antiemesis, rapid recovery, potent attenuation of pharyngeal and laryngeal reflexes and adequate depth of anaesthesia during intubation. So, it is considered the newer age anaesthetic agent, which got rapidly accepted worldwide as an almost ideal induction agent. Hence, it is increasingly being used for induction and maintenance of anaesthesia and for sedation in and outside the operating room.[5]The major disadvantages of propofol induction are the considerable decrements in arterial blood pressures,[6-8] bradycardia[9,10] and its high cost. When propofol is used alone, it produces hypotension and bradycardia at a dose when gives a good plane of

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anaesthesia for intubation. A fact which is commonly practiced in anaesthesia is that, using different drugs with similar actions can be combined to achieve a desired action, without reaching a toxic concentration of any of the drug. So, if nitrous oxide inhalation significantly reduces the induction dose of propofol, it will be advantageous as nitrous oxide is relatively cheaper compared to propofol and also can prevent the hypotension[6-8] and bradycardia[9,10] accompanying propofol induction. Hence, the present randomized clinical trial was conducted to study the effect of pre-induction inhalation of nitrous oxide on haemodynamic parameters during laryngoscopy and intubation.

MATERIAL AND METHODS

The present randomized clinical trial was conducted in a tertiary care hospital over a period of two years after obtaining permission from Institutional Ethical Committee.

Sample size

Sample size was based on the results obtained on the dose of propofol and induction time from the earlier publications[11] and with 99% confidence and 99% power, minimum sample size came to 19 in each group. However, we recruited 152 patients in this randomized, prospective clinical trial.

Inclusion criteria

- Age 20-60 years of either sex
- Patients undergoing elective surgery under general anaesthesia with endotracheal intubation
- ASA physical status I and II.

Exclusion criteria

- Allergy to propofol.
- Pregnant and lactating women.
- Patients belonging to ASA III and above
- Obesity, COPD, Bronchial asthma, Interstitial lung diseases
- Uncontrolled hypertensives
- Patient refusal

Patient groups

Patients were randomly divided into two equal groups by closed envelope technique to Group A and group B.

- Group A: received incremental doses of propofol following nitrous oxide inhalation for 3 minutes, pre-oxygenated with 4 litres/minute nitrous oxide and 2 litres/minute of oxygen
- Group B: received only propofol as induction agent, inhaled with pre-oxygenated with 6 litres/minute of oxygen for 3 minutes with a tight fitting face mask.

Methodology

In this study, all the patients were examined during the pre-operative visit. A detailed history was taken and a complete general physical examination performed. Routine investigations, as per the clinical scenario demands, were carried out and recorded. In the operation room a large bore IV access was started under local anaesthesia and patients were pre-medicated with intravenous glycoyrrolate 0.2mg and fentanyl 2mcg/kg. Patients in group A were asked to inhale 4 litres/minute nitrous oxide and 2 litres/minute of oxygen while patients in group B were pre-oxygenated with 6 litres/minute of oxygen for 3 minutes with a tight fitting face mask. Loss of response to verbal command (taking deep breaths/opening eyes) and no response to jaw thrust were taken as the end point of induction. Starting at the end of three minutes, after assessing response to verbal command and jaw thrust, both the groups were given propofol bolus 20 mg every minute intravenously. Induction time was calculated as time from start of propofol injection to loss of response to verbal command and jaw thrust, and induction dose as total amount of propofol administered till that time. After confirming the ability to mask ventilate, patients were given suxamethonium 2mg/kg and midazolam 1 mg intravenously and ventilated with same gas mixture plus isoflurane 1%. After one minute a quick and gentle laryngoscopy was done and patients were intubated with an appropriate sized endotracheal tube. Pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure of each patient were measured at preinduction, at induction,1, 3, 5, 10 and 15 min after induction. Desaturation was defined as SpO2<90% and if any patient developed desaturation during nitrous oxide inhalation, the patient was ventilated with 100% oxygen and the data was not used for statistical analysis.

Statistical analysis

Data analyzed using IBM SPSS statistics 20 software. All the continuous variables are presented are presented are presented as mean+/-SD and categorized variables are presented as percentage. To compare the averages of continuous variables between two groups (Group A and Group B) those following normal distribution, independent sample 't' test was used. The variables not following normal distribution Mann Whitney U test was used. Paired Sample T test was used for comparing the average parameters at different time periods (within groups). For comparing the categorical variables (Gender, ASA) between groups, Chi-square test was used. The p-value less than 0.05 was considered as statistically significant.

RESULTS

The mean age in group A was 44.57±12.90 years while in Group B it was 43.04±12.85 years. The age comparison showed no significant difference in distribution among two groups. Thirty-nine males and thirty-six female patients were enrolled in group A, whereas thirty-four males and forty-three female patients were enrolled in group B. Mean weight in group A was 62.47±8.96 kgs while in Group B was 61.22±9.907kgs. The weight comparison showed no significant difference in distribution among two groups as the p-values was 0.417. Group A had forty-four ASA1 patients and thirty-one ASA 2 patients, while Group B had forty-three ASA 1 and thirty-four ASA 2 patients. The group comparison revealed no significant difference among two groups with regard to distribution of gender and ASA physical status as the p-values for gender comparison was 0.333 and for ASA comparison was 0.726, both >0.05.

Table 1: Patient characteristics in two groups

Characteristics	Group A	Group B	P value
Age (Mean± SD)	44.57±12.90	43.04±12.85	0.464
Sex (Male/Female)	39/36	34/43	0.333
Weight (Mean± SD)	62.47±8.961	61.22±9.907	0.417
ASA (I/II)	44/31	43/34	0.726

Group comparison of heart rates during various time intervals revealed no significant difference in its distribution as the p-values were more than 0.05.

Table 2: Comparison of heart rates among two groups

Time	Group A	Group B	p value
	Mean ± SD	Mean ± SD	
Pre-induction	78.85 ± 14.865	79.96 ± 13.100	0.627
Loss of response	75.79 ±13.873	80.26 ±15.818	0.066
1 min	82.65 ± 15.641	84.78 ± 13.426	0.370
3 min	80.44 ± 15.740	84.82 ± 15.224	0.83
5 min	78.28 ± 12.905	81.47 ± 12.816	0.129
10 min	77.23 ± 13.590	78.55 ± 13.610	0.559
15 min	75.92 ± 12.595	75.61 ± 12.545	0.880

Mean SBP at pre-induction in Group A was 133.39±13.734 and in Group B was 125.14±20.526. As there is significant difference in distribution of systolic blood pressure at pre-induction, a percent difference in systolic blood pressure at pre-induction from various time intervals are used and the comparison showed insignificant difference in the distribution of pre-induction values among two groups.

Table 3: Comparison of percent difference of systolic blood pressure at various time intervals from baseline values

Time	Group A	Group B	P-Value
	Mean+/- SD	Mean+/-SD	
Loss of response	-6.2455±15.06033	-5.52 ± 23.95	0.82
1 min	-6.24 ± 16.14	7.17 ± 24.35	0
3 min	-1.62 ± 15.200	-1.07 ± 24.54	0
5 min	17.69 ± 12.96	-6.29 ± 18.01	0
10 min	-18.48 ± 12.93	-7.31 ± 19.60	0
15 min	-14.18 ± 14.39	-9.00 ± 18.01	0.05

Group comparison of systolic blood pressures among two groups in various time intervals showed significant difference in its distribution at the time of pre-induction values, at the time of loss of verbal response (LOVR), at 5 minutes post-induction and at 10 minutes post-induction.It was also seen that when the percent difference of systolic blood pressures at various time interval with the pre-induction values were made there was significant difference in its distribution at one minute, three minutes, five minutes and ten minutes. Statistical analysis shows that the systolic blood pressures decreased post induction and at various time intervals in both groups. But the decrease in systolic blood pressure was seen more in Group A when compared with Group B.

Table 4: Comparison of diastolic blood pressures among two groups

Time	Group A	Group B	P value
	Mean ± SD	Mean ± SD	
Preinduction	82.03 ± 11.320	78.43 ± 12.785	0.066
Loss of response	79.24 ± 13.616	73.58 ± 15.873	0.020
1 min	80.48 ± 18.246	81.92 ± 15.766	0.603
3 min	74.48 ± 15.384	76.55 ± 15.827	0.410
5 min	69.75 ± 11.761	73.96 ± 12.311	0.033
10 min	69.21 ± 11.271	74.22 ± 12.942	0.012
15 min	73.56 ± 12.660	72.14 ± 12.232	0.484

Group comparison of diastolic blood pressures revealed significant difference in its distribution at the time of loss of verbal response, at 5 minutes and at 10 minutes. The variable seems to have no significant variation in its distribution at pre-induction, at one minute, 3minute and 15 minutes post induction as the P-values obtained after comparison was more than 0.05.

Table 5: Comparison of mean arterial pressures among two groups

Time	Group A	Group B	p value
	Mean ± SD	Mean ± SD	
Preinduction	99.39 ± 14.927	96.31 ± 20.136	0.288
Loss of response	94.51 ± 16.208	86.57 ± 15.467	0.002
1 min	94.88 ± 20.718	99.69 ± 19.930	0.147
3 min	89.03 ± 17.578	91.50 ± 18.401	0.387
5 min	83.09 ± 12.935	88.42 ± 14.600	0.019
10 min	82.12 ± 12.013	87.21 ± 13.225	0.014
15 min	86.72 ± 12.903	85. 92 ± 13.485	0.710

Distribution of mean arterial pressures among two groups showed significant variation in its distribution at the time of loss of verbal response, at 5 minutes and at 10 minutes post induction. Comparison at rest of time period shows no significant variation in its distribution as the p-value is more than 0.05.

Table 6: Comparison of oxygen saturation among two groups

Time	Group A	Group B	p value
	Mean ± SD	Mean ± SD	
Preinduction	99.87 ± 0.475	99.92 ± 0.270	0.887
Loss of response	99.96 ± 0.257	99.81 ± 0.460	0.004
1 min	99.79 ± 0.890	99.82 ± 0.421	0.135
3 min	99.85 ± 0.485	99.81 ± 0.430	0.518
5 min	99.891 ± 0.452	99.83 ± 0.571	0.298
10 min	99.89 ± 0.388	99.94 ± 0.296	0.482
15 min	99.85 ± 0.425	99.90 ± 0.347	0.549

Group comparison of the oxygen saturation among two groups showed no significant difference at various time intervals as the p-value was more than 0.05.

DISCUSSION

In anaesthesia practice, multiple inhaled and intravenous agents are used which potentiate the anaesthetic effects and enable the usage of lesser amounts of drugs, which will subsequently reduce complications. It has been documented that when used in conjunction, nitrous oxide decreases requirement of intravenous anaesthetic agents like thiopentone and propofol.[2-4] Though in the west, there are moves to omit routine use of nitrous oxide, it still remains the most commonly used inhalation agent in developing countries. The future of nitrous oxide doesn't seem to be bleak, mainly because of its cost effectiveness. Hypotension[6-8] is invariably associated with propofol induction, more so in aged people. Preloading with colloid[12] or crystalloids is not very effective in preventing this hypotension, whereas, combining propofol with ketamine, or etomidate may prevent hypotension. Whether a reduction in induction dose of propofol, secondary to preinduction inhalation of nitrous oxide, could lead to an exaggerated stress response to laryngoscopy and intubation would be a natural concern. In the present study it was seen that nitrous oxide inhalation effectively suppressed the heart rate as well as the hypertensive responses, at the same time maintaining MAP at induction. Comparison of heart rates among two groups revealed no significant variation in its distribution among two groups. Heart rates remained same without much variation from the baseline in Group A than Group B. On comparing the systolic blood pressure among two groups the pre-induction or the baseline values showed significant variation among its distribution in two groups. Hence, to avoid error, a percent difference of systolic blood pressure from the baseline values was taken. The percent difference in systolic blood pressure from the baseline value when compared between the two groups showed significant difference. In both groups there were fall in systolic blood pressure post induction. Fall in blood pressure was more evident in Group A than in Group B. But during post intubation period the systolic blood pressure significantly rose in Group A while in Group B it was still below the pre-induction value. During rest of the time intervals systolic blood pressures remained below the pre-induction value. This is in agreement with the previous study done by Ng et al[2] where propofol infusion was used and also with the results obtained by Karalapillai et al.[3] It was seen that the mean arterial pressures decreased in both the groups at the time of loss of verbal response. The decrease in MAP was more in Group B than in group A and showed a significant difference when compared. Post intubation MAP rose in Group B while in Group A, MAP remained close to the value at the time of Loss of verbal response. Hence, with the use of nitrous oxide MAP was always maintained. In this aspect our method of using nitrous oxide prior to induction provided better haemodynamics response to laryngoscopy and intubation than in a study by Gore et al[13] where even with high doses of propofol (2,5mg/kg and 3mg/kg), there was rise in mean arterial pressures following intubation. The diastolic pressures decreased in both Groups post induction, but the fall in these pressures was more in Group B than in Group A. Administration of full dose of propofol could be the reason for this exaggerated fall in blood pressure in control group. Another concern while adopting this technique of pre-induction inhalation of nitrous oxide could be desaturation. There was no desaturation observed at induction during the present study and saturations in both groups remained well within clinically acceptable limits (99.81±0.46% vs 99.96±0.26%). So if patients are chosen carefully, avoiding those with anticipated difficult airway and low cardiorespiratory reserve, the technique seems quite safe in experienced hands. As cost containment is a growing concern in the heath sector nowadays, the observation in our study that inhaling nitrous oxide for 3 min leads to a 70% reduction in induction dose of propofol should be paid attention.

CONCLUSION

It can be concluded that inhaling 66% nitrous oxide for 3 minutes before induction prevented a precipitous fall in mean arterial pressure at induction and effectively attenuated stress response to laryngoscopy and intubation without desaturation.

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