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# Nitrous Oxide Influence on Induction of Anaesthesia with Sevoflurane

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## ABSTRACT

***Objective:*** To find out if the addition of Nitrous Oxide to Sevoflurane significantly reduces induction time and to study the effect of Nitrous Oxide on the frequency of adverse events during induction.

***Study Design:*** Quasi-experimental study

***Place and Duration of Study:*** Operation Theatre Complex, PAF Hospital Mushaf Sargodha Pakistan from Jul to Sep 2018.

***Methodology:*** One hundred adult indoor patients undergoing elective surgeries were included in the study. Their ages were from 18 to 34yrs, and all fell in ASA I and II category. In Group-A, 43 and Group- B, 57 patients were enrolled. Sevoflurane at a high concentration of 8% was given to all patients for induction. In Group-A, 100% oxygen was used as a vehicle, while in Group-B, 70% Nitrous Oxide and 30% oxygen were used as vehicles. Induction time was measured from switching Sevoflurane to when the patients' arms fell horizontal. We documented adverse effects, including coughing, laryngospasm, bronchospasm, fall in SpO2 <94%, apnea, excitation (head or limb movements), bradycardia and arrhythmias were documented.

***Results:*** Mean induction time was 59.00±13.00s and 58.00±8.00s in Groups A and B, respectively. The difference was statistically insignificant (*p*-value=0.874). Similarly, there was no significant difference in adverse events between the two groups.

***Conclusion:*** We concluded that adding Nitrous Oxide has no clinically significant advantage in the induction of anaesthesia with Sevoflurane in adults.

**Keywords:** Adult inhalational induction, Nitrous oxide, Sevoflurane.

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## INTRODUCTION

Sevoflurane, an inhalational anaesthetic agent, is considered the best choice for inhalational induction, especially in children.[1,2] It has a pleasant odour and non-irritant nature to the airway. Because of a low blood-gas partition coefficient, alveolar to inspiratory (FA/FI ratio) fraction equilibrium occurs swiftly, resulting in rapid induction,[3,4] and early change in depth of anaesthesia.[5] Therefore, Sevoflurane mask induction is considered a good alternative for the induction of anaesthesia in adults, especially where there is a fear of losing the airway after IV induction or in patients who are phobic of needles.[6] Furthermore, Sevoflurane has minimal effects on the cardiovascular system.[3] That is why it can be used at a higher concentration safely. In addition, Nitrous Oxide is cheaper than volatile anaesthetic gas.[7]

Nitrous Oxide (N2O) also has a low anaesthetic potency and has a MAC of 105. Therefore, it has a low blood-gas partition coefficient. It is usually added to the carrier gas mixture to hasten the speed of induction. This is due to concentration and the second gas effect. The MAC is additive.[8] Thus, adding Nitrous Oxide to carrier gas will result in a higher MAC value. Nitrous Oxide increases the sympathetic nervous system activity that increases the peripheral vascular tone and heart rate so counterbalancing the hypotensive effects of volatile anaesthetic agents.[9] There is minimal respiratory depression with nitrous oxide. However, mask induction may be complicated with coughing, laryngospasm, bronchospasm, breath holding, apnea, hemodynamic instability and bradycardia.[10] We conducted this study to investigate the effects of Nitrous Oxide added to the gas mixture on induction time with Sevoflurane, and the frequency of common complications during induction was recorded. The tidal volume induction technique at a high concentration was selected as it requires minimum patient cooperation.

## METHODOLOGY

The study was carried out at the Operation Theatre complex, PAF Hospital Mushaf Sargodha Pakistan from July to September 2018. We inducted 100 indoor patients into our study after obtaining the approval of the Ethics Committee.

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**Inclusion Criteria:** All patients of either gender, aged 18 to 35 years booked for elective surgeries with ASA I and II class were inducted into the study

**Exclusion Criteria:** Patients with a BMI of greater than 30kg/m2; those with risk of difficult mask ventilation or intubation, having hypertension, pulmonary or cardiovascular disease, a contraindication to succinylcholine or N2O and patients with a risk of malignant hyperthermia were excluded from the study.

Eight hours of fasting was ensured in all patients before surgery. Patients were randomly assigned to one of the two Groups, A and B, by flipping a coin technique. The patient had yet to be briefed about this allocation. Group-A: consisted of 43 adult patients. 8% Sevoflurane in 100% oxygen was used for induction. Group-B: consisted of 57 adult patients. Sevoflurane, 70% Nitrous Oxide and 30% oxygen, has been given to induce anaesthesia.

Before initiating the induction of anaesthesia, informed and written consent was obtained from each patient. Any premedication was avoided. Standard monitoring, that is, pulse oximeter, ECG (lead II), and non-invasive blood pressure, were attached before initiation of anaesthesia. Baseline readings were vital signs were recorded. The patient was put in a supine position and was asked to keep one hand raised, about 90 degrees from the horizontal at the elbow, during induction for as long as possible. A disposable Bain Breathing Anaesthesia Circuit with a well-fitted face mask with minimal leaks was applied. To ensure that no leakage is present, the circuit has been carefully tested before starting the procedure. A 6 litre/min fresh gas flow rate was used in all patients.

All patients were pre-oxygenated with three satisfactory breaths in 100% oxygen. After preoxygenation, 8% Sevoflurane was added to both groups. Group- A continued to receive 100% oxygen at 6 litres/min, while in Group- B, Oxygen was reduced to 1.8 L/Min, and nitrous was added at 4.2 L/min. Patients' dropping of hands was recorded as induction end time. Maintenance of anaesthesia was done, whatever was suitable for the patient. Adverse effects include cough, laryngospasm, bronchospasm, apnea (i.e. stopping of respiratory movements for more than 10s), fall in SpO2 <94%, bradycardia or arrhythmias and excitation (vocalization or movement of head and neck or limbs) were registered.

Statistical Package for Social Sciences (SPSS) version 20.0 was used for the data analysis. Mean and standard deviation were calculated for quantitative data. Frequency and percentage were used to express qualitative data, including adverse effects and gender. Comparison between the two groups was made by student t-test and Chi-square test. The *p*-value of ≤ 0.05 was considered statistically significant.

## RESULTS

One hundred adult indoor patients undergoing elective surgeries were included in the study. Fifty-seven patients were included in Group- B. These patients received Nitrous Oxide alongside oxygen and Sevoflurane for induction of anaesthesia. Group-A had 43 patients enrolled who did not receive Nitrous Oxide alongside oxygen and Sevoflurane for induction of anaesthesia. The mean induction time wasfound it to be 59.00±13.00 seconds in Group- A and 58.00±7.00 seconds in Group- B (*p*=0.652) (Table-I). The frequency of adverse events during induction was almost similar in both groups (Table-II). During induction, the cough was similar in either group (*p*=0.83). The difference in excitation in both groups was also insignificant (*p*=-0.87). There was no hypoxemia, apnea, bronchospasm, laryngospasm, bradycardia or arrhythmia.

**Table-I: Induction Time Comparison (In Seconds) (n=100)**

| Induction Time (Seconds) (Mean±SD) | Group- A (n=43) | Group- B (n=57) | *p*-value |
|---|---|---|---|
| | 59.00±13.00 | 58.00±7.00 | 0.652 |

**Table-II: Adverse Events During Induction (n=100)**

| Adverse Events | Group-A (n=43) | Group-B (n=57) | *p*-value |
|---|---|---|---|
| Fall in SpO2 <94% | 0 | 0 | - |
| Cough | 9(20.93%) | 13(22.81%) | 0.83 |
| Apnea | 0 | 0 | - |
| Laryngospasm | 0 | 0 | - |
| Bronchospasm | 0 | 0 | - |
| Patients with bradycardia | 0 | 0 | - |
| Patient with arrhythmias | 0 | 0 | - |
| Excitation | 7(16.28%) | 10(17.54%) | 0.87 |

## DISCUSSION

Nitrous Oxide has been used in anaesthetic practices for more than a century. It is considered that Nitrous Oxide and Sevoflurane act in an additive manner, i.e., their MAC (Minimum Alveolar concentration) is additive.[11,12] MAC is the measure of the potency of a volatile anaesthetic. Thus, reduce the concentration of volatile anaesthetic required to produce the same effect.[13]

Many studies have shown the interaction between Sevoflurane and nitrous oxide. Some studies supported the use, while others failed to find any advantage of using nitrous oxide.[14,15] Hall *et al*.[16] used

8% Sevoflurane and studied the effect by adding 67% nitrous oxide. They found that the addition of Nitrous Oxide made induction rapid and safer. Single breath vital capacity induction technique was employed in their study. Another study by O'Shea *et al*.[17] found that Nitrous Oxide addition to Sevoflurane has no advantage during the induction of anaesthesia. They used the tidal volume gradual induction method and added 50% Nitrous Oxide to the gas mixture in their study.

The induction time in their study was more than a minute, which is higher than in other studies, probably because they gradually increased the concentration of Sevoflurane. Similarly, Fernandes *et al*. found no decrease in induction time, assessed by BIS, using 5% Sevoflurane in 50% N2O.7 Likewise, Yurino *et al*.[18] concluded that the addition of Nitrous Oxide does not increase the speed of induction. On one side, Nitrous Oxide presence increases the uptake of volatile anaesthetic agents because of concentration, and the second gas effect will decrease the induction time.

We found that Sevoflurane, even at such a high concentration, has no significant respiratory complication as present in induction with other volatile. This demonstrates the non-irritant nature of Sevoflurane. There was no bronchospasm, laryngospasm, apnea (breath holding >10s) and hypoxia. Induction was only complicated by coughing that too in a few patients. The coughing was about 21% in both groups (A: 9/43; B 13/57).

Different studies used different measures to define the induction of anaesthesia endpoint.[15,18] In our study, the endpoint used to describe the induction of anaesthesia was when the arm dropped horizontally. It is consistent with any other measure, such as loss of eyelash reflex or loss of voluntary finger tapping or fall of weight held in hand. Arm position is an easily visible endpoint which does not require intermittent stimulation like finger tapping or loss of eyelash reflex. Nevertheless, it can be affected by excitation. Excitation lowered the arm in two patients and made the endpoint equivocal. However, his exclusion from the study did not affect the statistical analysis. We have studied a sufficient number of patients in our research and concluded that Nitrous Oxide did not affect the time for induction of anaesthesia.

## CONCLUSION

We concluded that the administration of Nitrous Oxide during induction of anaesthesia with Sevoflurane does not give any added advantage in terms of induction time reduction or reduction in adverse effects that occur during inhalational induction. Hence, not adding Nitrous Oxide during inhalational induction can increase the oxygen reserves that will increase the time to act during serve respiratory complications and failure to intubate. However, Sevoflurane is an agent that is ideal for inhalational induction. It provided a smooth induction at a high concentration with a very low cardio-pulmonary complication.

**Conflict of Interest:** None.

**Author's Contribution**

Following authors have made substantial contributions to the manuscript as under:

IUH: Conception, study design, drafting the manuscript, approval of the final version to be published.

MUZ & FAJ**:** Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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