

# To determine and compare the incidence of PONV with intra-operative use of Medical Air and Nitrous Oxide for General Anesthesia in patients undergoing Breast Surgery: A prospective randomized study

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## Abstract

**Background:** Post operative Nausea Vomiting (PONV) is one of the feared and incapacitating side effect of surgery that is associated with significant morbidity that leads to delayed recovery and prolonged hospital stay. Nitrous Oxide (N<sub>2</sub>O) widely used as an anaesthetic carrier gas. It has analgesic and sedative properties but it potentiates the incidence of PONV. Whereas Medical Air (MA) is an inert, environment friendly and can safely be used as an alternate vehicle for anaesthesia.

**Methods :** 60 female patients of ASA I & II posted for Breast Surgery between March-September were randomly allocated in to two groups of 30 each. Group A received oxygen & Medical Air (Fio<sub>2</sub> 0.4), while Group B received oxygen & Nitrous oxide (Fio<sub>2</sub> 0.4) All the patients were induced with iv propofol (1- 2 mg/kg) & fentanyl (2 microgram/kg) and maintained with 40% oxygen with air/N<sub>2</sub>O & sevoflurane and vecuronium bromide (0.08mg/kg). All the patients were reversed with Neostigmine (0.05mg/kg) and glycopyrrolate (0.02mg/kg). As per recent PONV guideline all the patients received PONV prophylaxis as injection dexamethasone 4mg iv at the start of surgery and injection ondansetron 4mg iv at the end of surgery. At the end of surgery all of them received injection diclofenac in the dose of 1.5mg/kg iv which was repeated 8hrly in the post operative period. Paracetamol 15mg/kg was given iv on patient demand or when pain score goes above 4 on NRS, as rescue analgesia. PONV was recorded at 1st hr, 6hr and 12hr post operatively.

**Results:** Incidence of PONV at 1st hr in MA group was only 3.3%, where as in Nitrous Oxide group it was 26.4% with a p value of <0.023. At 6hrs, in MA group incidence was zero, where as in nitrous oxide group it was 20% with a p value of <0.023. The total incidence of PONV within 12 hrs was 1 patient in MA group where as 14 patients in N<sub>2</sub>O Group with a p value <0.0002. Total dose of paracetamol required in both the groups were comparable. Conclusion : MA group has significantly less incidence of PONV than Nitrous oxide group.

**Keywords:** PONV, Medical Air, Nitrous Oxide, Rescue analgesia.

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## I. Introduction

Post Operative Nausea vomiting (PONV) is one of the feared and most distressing symptoms associated with significant morbidity that leads to delayed discharge and prolonged hospital stay. [1] It is seen in 30-40% of normal population, which rises up to 75-80% in certain high risk group. [2] Women are 2-3 times more susceptible to PONV than man. [3] Breast surgery which is primarily done in an out patient setting is associated with high incidence of PONV increases upto 80% in absence of prophylactic treatment [4]. Nitrous oxide widely used anaesthetic carrier gas, modulates pain perception and consciousness. The dominant mechanism of its analgesic action is central inhibition of NMDA receptors. [5] Nitrous oxide has analgesic and sedative properties but may potentially increased the incidence of PONV by several potential mechanisms like increase in middle ear pressure, bowel distension, activation of the dopaminergic system in the chemoreceptor trigger zone, interaction opioid receptors [6]. Whereas medical air is an inert gas, environment friendly, doesn't have green house effect, can safely be used as an alternative vehicle for anaesthesia. The present study is

designed to determine and compare incidence of PONV with intra-operative use of MA and Nitrous Oxide for general anesthesia in patients undergoing Breast Surgery and to know the total dose of rescue analgesics in the post operative period in both groups. ( within 24 hrs.)

## II. Methodology

It is a prospective randomized control trial study. After getting approval from Ethics committee and written informed consent from all the patients the study was carried out in operation theater of AHRCC , Cuttack between March to September 2017. ASA III, IV,V Female patients, age less than 18 years , patients with contraindications to fentanyl, diclofenac, paracetamol, vecuronium, chronic pain patients in long term opioid medication, use of regional anesthetic technique (e.g Paravertibral Block) were excluded from the study. A total no.of 60 female patients posted for Breast Surgery were randomly divided into two groups of 30 each. Group A received Medical Air with oxygen , group B received Nitrous Oxide with oxygen . All the patients were premedicated with glycopyrrolate (0.005 mg/kg ) midazolam (0.05 mg/kg) and fentanyl 2µgm / Kg. General Anaesthesia was induced with propofol 2mg/kg, suxamethonium 2mg/kg IV and patients were intubated with CETT of size 7mm. Anaesthesia was maintained with vecuronium (0.08 mg/kg) and sevoflurane. Group A received Medical Air with O<sub>2</sub> and group B received nitrous oxide with O<sub>2</sub> to maintain Fio<sub>2</sub> of 0.4 and MAC of 1. Patients were reversed with Neostigmine (0.05mg/kg) and Glycopyrrolate (0.02 mg/kg) . As per recent PONV guideline all the patients received PONV prophylaxis, inj Dexamethasone 4mg IV at the start of surgery and inj.Ondansetron 4mg at the end of surgery. At the end of surgery all of them received inj. diclofenac (1.5 mg/kg) IV which was repeated 8 hrly in the post operative period. Paracetamol (15 mg/Kg) IV was given on patients demand or if pain score  $\geq$  4/10 on NRS as Rescue analgesic. After tracheal extubation, all the patients were shifted to post anesthesia care unit and followed up till 24 hrs in post surgery ward or discharge from the hospital which ever was earlier.

Data Analysis Demographic clinic and disease related variable were taken as frequency ( percentage ) and mean ( S.D); median as appropriate. Catagorial variable were analysed by using chi square test or fisher exact test (for binary variable) . Change in score in the group and between the groups were analysed by using paired 't' test and unpaired 't' test respectively . P value <0.05 was considered statistically significant

## III. Results :-

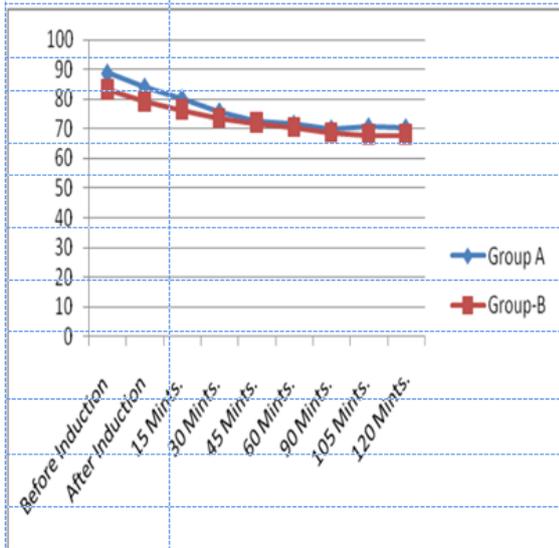
### Patients' Demography

Parameters	Group - A	Group - B
Age(years)Mean SD	36.40±9.03	41.63±9.16
Weight(kgs)Mean SD	52.40±6.2	53.25±7.05
Duration of surgery(mins)Mean SD	110.33±9.04	112.34±9.04

Table-1

Sixty patients, thirty in each group were included in the study and observations were analysed. The groups were comparable with respect to demographic characteristics like age, weight and duration of surgery (Table -1).

**Pulse Rate**

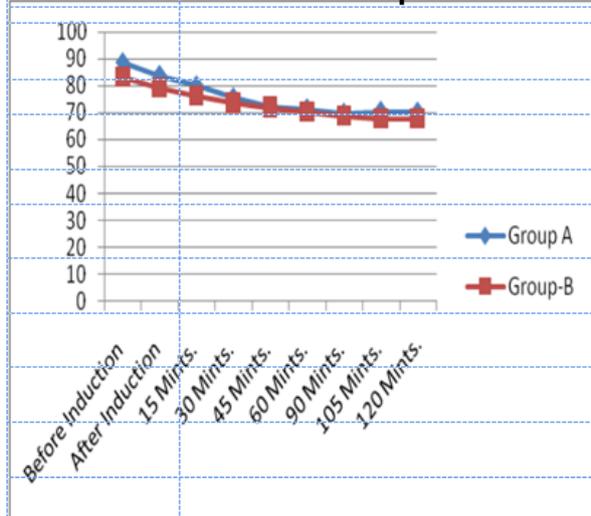


**Fig-1**

	Group A	Group B
<b>Before induction</b>	84.42 ± 8.3	83.42 ± 7.6
<b>After Induction</b>	86.43 ± 7.6	86.58 ± 6.2
<b>15 min</b>	82.26 ± 6.4	83.58 ± 6.8
<b>30min</b>	84.26 ± 7.2	82.58 ± 7.2
<b>45min</b>	82.52 ± 5.8	84.62 ± 5.8
<b>60min</b>	84.52 ± 6.2	82.62 ± 7.2
<b>90min</b>	86.40 ± 7.2	83.58 ± 6.8
<b>105min</b>	79.80 ± 4.8	78.70 ± 5.2
<b>120min</b>	80.76 ± 6.2	82.26 ± 8.2

**Table-2**

**Mean arterial pressure**



**Fig- 2**

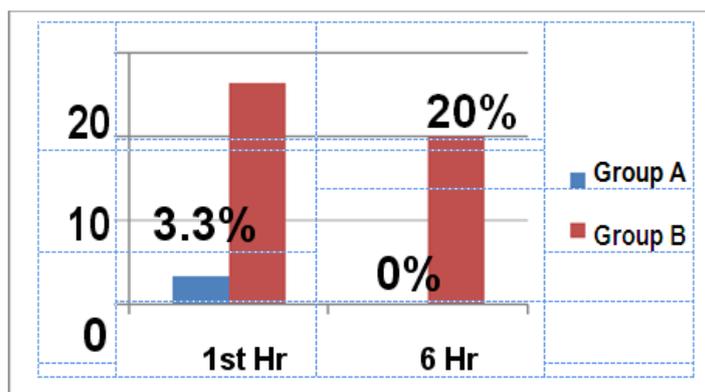
	Group A	Group B
<b>Before induction</b>	88.77 ± 12.9	83.23 ± 11.1
<b>After Induction</b>	84.00 ± 12.5	79.23 ± 10.75
<b>15 min</b>	80.13 ± 12.07	76.33 ± 9.85
<b>30min</b>	75.67 ± 11.1	73.57 ± 8.9
<b>45min</b>	72.33 ± 9.1	72.00 ± 7.6
<b>60min</b>	71.50 ± 6.5	70.37 ± 6.6
<b>90min</b>	69.87 ± 5.7	68.63 ± 5.4
<b>105min</b>	70.60 ± 5.4	67.87 ± 5.6
<b>120min</b>	70.27 ± 5.1	67.87 ± 5.6

**Table-3**

Pulse rate and man arterial pressure were recorded from pre-induction, every 15 mints till 120 min. Both the group were comparable (Table 2 and 3).

PONV recorded as Nausea & vomiting at 1 hr, 6 hrs and 12 hrs post operatively. Pain scores recorded 1 hr, 2 hrs, 3 hrs., 4hrs, 12 hrs and 24 hrs post operatively by NRS. Our primary outcome measures was to know incidence of PONV. Secondary outcome measure was to know the total dose of rescue analgesics required within 24 hrs post operatively

**Incidence of PONV**



**Fig 3**

Incidence of PONV at 1st hr in MA group was only 3.3%, where as in Nitrous Oxide group it was 26.4% (p< 0.02). At 6 hrs, in MA group incidence of PONV was ‘0’ where, as in nitrous oxide group it was 20% with ‘p’ value of < 0.02.(Fig 3) Total Incidence of PONV within 12 hrs, only 1 patient in medical air group where as there were 14 patients in nitrous oxide group with a ‘p’ value of < 0.0002

Total Dose Rescue analgesia in 24 hours(paracetamol 15 mg/kg)

<b>Group A</b>	<b>1100mg ±780</b>
<b>Group B</b>	<b>1200mg ± 730</b>

**Table4**

P<0.61

Total dose of paracetamol required in both the groups were comparable.(Table 4)

**IV. Discussion**

The history of nitrous oxide is more than 200 years old and its clinical use as anaesthetic is more than 150 years old. However it is not the ideal anaesthetic. It can not be used effectively without decreasing the concentration of oxygen that may be delivered. Although widely used for many decades, there are certain clinical situations where nitrous oxide should be avoided. Due to the increase of cerebral blood flow the use of nitrous oxide is a contraindication in all cases with raised intracranial pressure.[7] In patients with significant vitamin B12 deficiency even a short exposure of only 1–3 hours may lead to severe neurological impairments and shall be avoided in such cases especially in children.[8] Several recent reviews of the effects of nitrous oxide have come up with the conclusions regarding the appropriate role of this drug in modern practice and there is currently a large clinical trial in adults looking at the clinical outcomes with the use of nitrous oxide in general anaesthesia[9] which has questioned the routine use of nitrous oxide in patients undergoing surgical procedures in general anaesthesia. This prompted the authors to undertake this study to find an answer to this question and to see if the continued traditional use of nitrous oxide as a carrier gas in general anaesthesia could be avoided in our hospital where the new anaesthesia machines allow the combination of oxygen and air as carrier gas and there are inhalational agents (e.g., Sevoflurane, ) as controllable as nitrous oxide and new I/V agents. The authors in this study used the mixture of oxygen with Medical Air as a substitute for nitrous oxide. The anaesthetist can freely choose the oxygen concentration and adapt it to the needs of an individual patient or the respective surgical procedure. In the present study the authors used 40% oxygen in air/N<sub>2</sub>O for all the cases as carrier gas during the surgical procedure . Aggarwal et al [10] have proved that in young healthy patients undergoing general anaesthesia ventilation with nitrogen/ oxygen mixture (FiO<sub>2</sub> 0.4) improved pulmonary gas

exchange if compared with the use of nitrous oxide/oxygen or pure oxygen. In our study there was a marked reduction in the incidence of nausea and vomiting after surgery in MA and oxygen group. It was only 3.3%, in MA and oxygen group and nitrous oxide group it was 26.4% at 1st hour. At 6 hrs, in MA group it was absolutely '0' and in nitrous oxide group it was 20%. As per the study conducted by Syed Mushtaq Gilani et al by omitting Nitrous oxide from anesthetic regimen had a substantial impact on patient comfort after surgery by reducing incidence of PONV. There was a marked reduction in incidence of PONV, 11% in Nitrous oxide group and 5% in nitrous oxide free group.

Nitrous oxide (N<sub>2</sub>O), a widely used anesthetic gas, modulates pain perception and consciousness. The dominant mechanism of its analgesic action is central inhibition of NMDA receptors.[11] Based on a similar mechanism of action, the intraoperative use of N<sub>2</sub>O may also exert a similar effect on acute postoperative pain and analgesic drug requirements. However, the effects of N<sub>2</sub>O on early postoperative pain are not well understood, and studies have provided inconclusive evidence. [12,13] While some found a reduced duration of patient controlled analgesia use or reduced opioid-induced hyperalgesia, others found increased early postsurgical pain after N<sub>2</sub>O anesthesia. [14] Most recently Chan and others showed a reduction of chronic, but not acute postoperative pain after N<sub>2</sub>O anesthesia. The main finding of the study conducted by Andrease Duma et al was that N<sub>2</sub>O was not associated with intra- and early postoperative opioid consumption and pain, an observation that was also present among patients taking chronic opioid medication. The totality of evidence suggests that N<sub>2</sub>O has a negligible, or even absent, association with intra- and early postoperative pain and opioid consumption. In a recent well conducted and powered ancillary study of the ENIGMA trial, Chan and others[15] also found no evidence that N<sub>2</sub>O had an effect on pain during the first 3 days after surgery. However, they observed that the use of N<sub>2</sub>O during anesthesia may reduce the risk of chronic postoperative pain by a factor of 2. This result raises the possibility that the use of N<sub>2</sub>O may be beneficial for patients at risk of developing chronic postoperative pain, but perhaps not acute pain. In our study we found out that total rescue analgesia in both the groups (medical air group and nitrous oxide group) were comparable. The question of whether N<sub>2</sub>O should be used or omitted clearly depends upon several factors, that in general revolve around the benefits of the drug vs its detrimental effects.

## V. Results:

In our study we found out that MA group has significantly less incidence of PONV than Nitrous oxide group. Total dose of rescue analgesia required in 24 hrs was comparable in both the groups. Efficacy MA group in preventing PONV in patients undergoing Breast Surgery under General Anaesthesia is better than Nitrous Oxide group. Future studies should try and determine that patients in whom Medical Air may be most beneficial in prevention of PONV.

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