The effect of Nitrous Oxide on post-operative gastric pain in Cataract Surgery under general anesthesia with laryngeal mask airway

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Abstract

Background: Gastric distension is one of the troublesome complications of laryngeal mask airway (LMA) use in anesthesia practice. On the other hand, we know that Nitrous Oxide (N2O) can distend the closed gas spaces including in the stomach. We aimed to determine whether N2O can aggravate LMA induced gastric distension and pain.

Method: One hundred and sixty four patients aged between 50-65 years, American Society of Anesthesiologists (ASA) status I, and scheduled for cataract surgery under general anesthesia, were randomly allocated in two groups.

After induction of anesthesia, it was maintained with propofol and nitrous-oxide oxygen (60%-40%) in group "A" versus propofol and oxygen 100% in group "B". Quality of mask ventilation before inserting LMA, heart rate and blood pressure were monitored and recorded. Using the Visual Analogue Scale (VAS) pain and also the incidence of nausea and vomiting after the surgery were recorded at 10, 20, 30 and 45 minutes after the operation. Data were analyzed using SPSS software, version 16, and P value less than 0.05 was considered as statistically significant in all instances.

Results: In group "A", 60 patients (72.3%) did not report any pain after operation and 23 patients (27.7%) reported epigastric pain. In group B, 70 patients (86.4%) did not have any pain, and 11 (13.6%) had epigastric pain. Statistical analysis of the results showed that the incidence of epigastric pain in the two groups was significantly different and those who received N2O suffered more postoperative epigastric pain.

Conclusion: According to the results of this study, when we use LMA and we are afraid of postoperative epigastric pain, we can eliminate N2O from our anesthetic drugs.

Key words: General anesthesia, nitrous oxide, laryngeal mask airway

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Introduction

Nowadays, using laryngeal mask airway (LMA) for short duration surgery is common, due to a decrease in the complications (1) related to endotracheal intubation. In this regard, many anesthesiologists prefer it to endotracheal intubation. In general anesthesia, laryngeal mask airway (LMA) is the best known supraglottic airway device (SGA) when intubation using laryngoscopy is difficult or when one wants to reduce hemodynamic changes.(2)

In spite of all advantages, gastric distension (3) is one of the troublesome complications of LMA use in anesthesia practice and epigastric pain may be even more troublesome than the surgical site pain for the patient; also, the LMA cuff can cause pressure on the neuropraxia of the lingual nerve, hypoglossal nerve, and recurrent laryngeal nerve.(4)

Nitrous oxide is one of the weakest anesthetic gases with minimum alveolar concentration (MAC) of 104%. It means that even with the maximum permitted prescription (70% concentration), it cannot be used as a sole anesthetic. Therefore, it should be used in combination with other anesthetics (inhaled or intravenous) to induce or maintain anesthesia (Masjedi 5).

The use of nitrous oxide, in the absence of special circumstances indicating its lack of use, is desirable(6). Although nitrous oxide is known as a weak anesthetic, a strong analgesic facilitates reduction of the required dose of other patent anesthetic drugs (7, 8, 9). Nitrous oxide has a low blood solubility (blood/Gas partition coefficient of 0.47) with rapid increase of its relative pressure in blood after prescription (7).

Although few studies have evaluated the effect of this gas on epigastric pain, we know that nitrous oxide which is one of the most common inhaled anesthetics can distend the closed spaces including gastro-intestinal tract (10). We hypothesized that nitrous oxide can aggravate LMA induced gastric distension and accordingly increase epigastric abdominal pain.

Method

Sample size was estimated on the basis of a pilot study on 50 cases. Then, the sample volume was calculated and determined using Med-Calc statistical software with 5% error rate and 80% statistical power (attrition of 20%) as 190 cases. α=0.05, β=0.10, μ1=1.1, μ2=2.35,SD1=2.95, SD2=2.8, Z1-a/2=1.96, Z1-b/2=0.85.

$$n_1 = n_2 = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 \times (s_1^2 + s_2^2)}{(\mu_2 - \mu_1)^2}$$

This randomized, double-blind clinical trial was performed on 164 patients 55-65 years of age, who were scheduled for Cataract Surgery at Khalili hospital from 2015–2017. After obtaining permission from the ethics committee of Shiraz University of Medical Sciences (2014,246,IRCT20 15010420542) and receiving written informed consent, a table of random numbers was used to divide patients into two groups of 82 through a process of computer-generated block randomization.

Exclusion criteria were emergency operations, full stomach patients, history of abdominal surgery, gastric pain and post-operative nausea and vomiting, patients with uncontrolled medical diseases such as blood pressure above 160/90 mmHg, patients with any contraindication for N2O use, toothless patients, upper respiratory infection, certain co-morbidities (heart failure, congenital heart disease and asthma), use of drugs that have an effect on blood pressure or heart rate, and a long duration of surgery (more than 45 minutes), and finally patients who needed extra doses of muscle relaxation were excluded from this study.

The patients were taken to the operating room and standard monitoring (non-invasive blood pressure, electrocardiogram, pulse oxymetry and Capnography) were applied. Induction of anesthesia was similar in both groups and performed by one anesthesiologist. Premedication, 0.03 mg/kg intravenous midazolam and 2 μ/kg of fentanyl were given to all patients; then, 5 mg/kg Pentothal and 0.6 mg/kg atracurium was administered respectively for induction of anesthesia and muscle relaxation. Mask ventilation before inserting LMA was done by 2 expert anesthesia nurses in 3 minutes and then LMA inserted and fixed in the supraglotic area by the corresponding anesthetist. In the two groups, LMA size 3 was used for patients weighing below 50 kg, size 4 for those weighing 50-70 kg, and size 5 for those over 70 kg. After insertion, the cuff pressure was maintained at 60 cmH2O with a hand pressure gauge (VBM, Germany).

Ventilation continued with tidal volume of 10 ml/kg, respiratory rate of 12/min and the inspiratory:expiratory ratio was 1/2. Anesthesia was maintained with propofol 100 μg/kg/min and O2 (40%) and N2O (60%) in the first group and 100% oxygen in the second group with preservation of normocapnia and normoxia.

Cataract surgery was done and the blood pressure and heart rate were recorded each time. At the end of surgery, all anesthetic drugs were closed and the patient allowed to breath spontaneously and then reversed by 0.03 mg/kg atropine with 0.06 mg/kg neostigmine. All the patients were extubated without exerting any force and so quietly they were transported from the operating room to the Post Anesthesia Care Unit (PACU). Immediately after normal awakening of the patient in recovery the assistant nurse, without any information about group allocations, asked the patients to report epigastric pain according to VAS pain scale and observation.

Furthermore, nausea-vomiting and hemodynamic condition according to blood pressure and heart rate were recorded and registered. (VAS) Visual Analogue Scale is a standard method to measure the severity of pain and the patient's

pain intensity ranging from 0 points (no pain) to 10 points (worst pain). These scores are dependent on the patient's expression; a score of 0 was assigned to no pain, 1-3 light pain, 4-6 moderate pain, and 7-10 worst pain.

Patients were also evaluated as to the received intravenous ranitidine and also in terms of possible side effects such as nausea and vomiting. If there was a pain score more than 0 the patient was given intravenous ranitidine (50mg/2ml) and the data were recorded.

Statistical analysis

All statistical analyses were performed using SPSS, version 16 (SPSS Inc., Chicago, IL, USA). The Kolmogorov Smirnov test was used for normal data distribution; to compare the quantitative variables between the two groups, independent t-test was used, and if the data distribution was abnormal parameters the Mann Whitney U-test was used. The significance level of 0.05 was used in this study

Results and Discussion

There were no significant differences observed in the patient's age, gender, weight, duration of ventilation, duration of anesthesia and quality of ventilation in both groups. (Table 1).

Quality of ventilation			Duration of anesthesia (min)	Duration of Ventilation (min)	Weight (kg)	Sex (M/F)	Age (years)	variable Groups
poor	moderate	good						
3	16	64	32.6 ± 4.4	29 ± 3.5	62.10±5.09	51/32	58± 5.31	Group A
0	9	72	33.5± 4.5	31 ± 3	63.92±4.42	55/26	57±6.01	Group B
P=0.117	P=0.144	P=0.212	P=0.565	P=0.65	P=0.69	P=0.375	P=0.93	Significance

No significant difference was seen in the hemodynamic features of the patients (systolic blood pressure, diastolic blood pressure, and heart rate) between the two groups, both in the period before the operation and in 5, 10, 15, 20, 30 and 35 minutes under the operation.[Table 2 - page 80].

But at the recovery room, systolic blood pressure at 15, 20, 25 and 30 minutes and diastolic blood pressure at 30 minutes, there was a statistically significant difference between the two groups.[Table 3 - page 81]

The severity of pain score at 10-20 minutes and 20-30 minutes after arrival to recovery was significantly different in the two groups.[Table 4]

At the 30-45 minutes (mean±SD)	At the 20-30 minutes (mean±SD)	At the 10-20 minutes (mean±SD)	At the 0-10 minutes (mean±SD)	Pain in RR Groups
1.05 ± 0.30	3.80 ± 0.36	2.38 ± 0.48	2.04 ± 0.35	Group A
0.75± 0.13	0.98 ± 0.33	1.11 ± 0.40	0.86 ± 0.37	Group B
0.10	0.042*	0.048*	0.052	p-value

The patients in both groups did not have post-operative nausea and vomiting.

The results of this study showed that a significant difference was not seen among demographic parameters (age, sex, weight), duration and quality of ventilation, and time of anesthesia.

Gastric insufflation, of course, may happen during mask ventilation before inserting LMA, so we excluded the patients who had poor mask ventilation. Also, quality and time of mask ventilation was not meaningfully different in the two groups; therefore, we cannot relate the increase of pain to poor ventilation or difference between duration of operations.
Ho-Tai L. and colleagues compared gastric distension between LMA and mask ventilation and concluded that in LMA anesthesia less gastric distension happened in comparison with mask ventilation (3).

No significant difference was observed between the two groups in terms of hemodynamic characteristics including heart rate, systolic, and diastolic blood pressure, in 5, 10, 15,20,25,30 and 35 minutes under anesthesia; it means that N2O causes stable cardiovascular status; also, Chizuko's study confirms this matter in Sedation dose of N2O inhalation (11).
In the recovery room, we had a statistically significant difference at 20, 25, 30 and 45 minutes in systolic blood pressure and at 30 minutes in diastolic blood pressure.

A significant difference was shown between the two groups in VAS scale pain at the recovery room at 10-20 and 20-30 minutes. The significance level in systolic and diastolic blood pressure parameters in the recovery was closely related to the amount of pain at times asked. For example, at the time of 30 minutes of recovery, we registered the highest severity of pain, increased in systolic and diastolic blood pressure at the same time between the two groups.

In the operating room

Table 2

variable Groups	Pre-operative Systolic blood pressure	Systolic blood pressure 5 min	Systolic blood pressure 10 min	Systolic blood pressure 15 min	Systolic blood pressure 20 min	Systolic blood pressure 25 min	Systolic blood pressure 30 min	Systolic blood pressure 35 min
Group A	136.52 ± 19.80	142.52 ± 18.85	140.82 ± 19.40	138.70 ± 18.30	136.42 ± 17.90	133.30 ± 17.60	130.20 ± 17.50	139.65 ± 18.35
Group B	134.10 ± 19.55	138.52 ± 18.60	135.32 ± 19.35	134.52 ± 18.35	132.52 ± 17.85	129.42 ± 17.70	125.52 ± 16.85	133.50 ± 18.45
Significant	P=0.31	P=0.29	P=0.27	P=0.30	P=0.29	P=0.28	P=0.25	P=0.22
	Pre-operative Diastolic blood pressure	Diastolic blood Pressure 5 min	Diastolic blood Pressure 10 min	Diastolic blood Pressure 15 min	Diastolic blood Pressure 20 min	Diastolic blood Pressure 25 min	Diastolic blood Pressure 30 min	Diastolic blood Pressure 35 min
Group A	77.90 ± 18.85	80.75 ± 18.89	79.65 ± 18.40	77.80 ± 18.50	76.75 ± 18.45	76.70 ± 18.63	75.90 ± 17.90	79.81 ± 18.73
Group B	73.80 ± 18.92	76.81 ± 18.84	75.81 ± 18.55	73.63 ± 18.43	72.81 ± 18.33	72.72 ± 18.22	70.65 ± 17.83	75.81 ± 18.53
Significant	P=0.31	P=0.30	P=0.29	P=0.28	P=0.29	P=0.28	P=0.28	P=0.31
	Pre-operative Heart rate	Heart rate 5 min	Heart rate 10 min	Heart rate 15 min	Heart rate 20 min	Heart rate 25 min	Heart rate 30 min	Heart rate 35 min
Group A	89.60 ± 15.43	90.80 ± 16.85	90.89 ± 18.88	88.60 ± 17.75	88.11 ± 17.93	86.81 ± 17.65	84.81 ± 18.53	91.81 ± 18.85
Group B	85.53 ± 15.33	86.91 ± 16.83	85.80 ± 18.49	84.61 ± 17.83	83.81 ± 17.33	82.50 ± 17.63	79.81 ± 18.49	88.81 ± 18.75
Significant	P=0.33	P=0.34	P=0.30	P=0.30	P=0.27	P=0.29	P=0.27	P=0.42

In the Recovery Room (RR)

Table 3

Systolic blood pressure 45 min	Systolic blood pressure 30 min	Systolic blood pressure 25 min	Systolic blood pressure 20 min	Systolic blood pressure 15 min	Systolic blood pressure 10 min	Systolic blood pressure 5 min	Pre-operative Systolic blood pressure	variable
140.95 ± 18.38	155.20 ± 17.50	155.30 ± 17.65	148.42 ± 17.60	147.70 ± 18.40	145.28 ± 18.44	142.95 ± 18.95	140.25 ± 16.60	Group A
118.50 ± 18.40	120.52 ± 17.59	120.42 ± 17.62	122.52 ± 17.58	125.72 ± 18.53	130.22 ± 18.38	133.22 ± 17.70	136.15 ± 16.65	Group B
P=0.055	P=0.033*	P=0.034*	P=0.047*	P=0.054	P=0.08	P=0.107	P=0.31	Significant
Diastolic blood Pressure 35 min	Diastolic blood Pressure 30 min	Diastolic blood Pressure 25 min	Diastolic blood Pressure 20 min	Diastolic blood Pressure 15 min	Diastolic blood Pressure 10 min	Diastolic blood Pressure 5 min	Pre-operative Diastolic blood pressure	
82.37 ± 18.72	87.90 ± 17.50	86.70 ± 18.36	86.75 ± 18.46	85.80 ± 18.50	82.65 ± 18.40	80.65 ± 18.90	80.80 ± 18.45	Group A
67.40 ± 18.59	67.65 ± 17.30	68.72 ± 18.32	70.81 ± 18.39	71.63 ± 18.53	73.81 ± 18.55	74.81 ± 18.85	75.60 ± 18.40	Group B
P=0.07	P=0.05*	P=0.06	P=0.07	P=0.08	P=0.13	P=0.20	P=0.28	Significant
Heart rate 35 min	Heart rate 30 min	Heart rate 25 min	Heart rate 20 min	Heart rate 15 min	Heart rate 10 min	Heart rate 5 min	Pre-operative Heart rate	
89.59 ± 17.85	96.47 ± 18.58	96.26 ± 17.65	95.44 ± 17.93	95.55 ± 17.55	94.98 ± 18.64	92.46 ± 17.85	90.60 ± 16.53	Group A
77.81 ± 17.75	79.81 ± 18.29	82.50 ± 17.71	83.81 ± 17.93	84.61 ± 17.53	85.80 ± 18.32	86.91 ± 17.65	86.53 ± 16.43	Group B
P=0.10	P=0.06	P=0.08	P=0.095	P=0.12	P=0.13	P=0.21	P=0.33	Significant

In the study of Rossi and colleague, it was shown that the stomach distension increased the sympathetic nerve activity and blood pressure in healthy humans, indicating the existence of a functional relationship between gastrointestinal distension and cardiovascular function (12). Hirota stated Nitrous oxide activated the sympathetic nervous system under specific experimental conditions indirectly (13).

At the end of the period of recovery, the patients who had gastric pain received a single dose of ranitidine 50mg/2ml as recommended, and then no significant difference was seen in the hemodynamic features of the patients (systolic blood pressure, diastolic blood pressure, and heart rate) between the two groups (at 45 minutes). None of these patients needed to stay in the hospital due to gastric pain afterwards.

Although not capable of inducing general anesthesia in humans, N2O is a good analgesic agent and commonly used in anesthesia practice in combination with other anesthetic agents (14) and it impacts the patient's comfort after surgery by reducing the incidence of PONV (15). In spite of all that, N2O can distend closed spaces of the body including gastrointestinal tract (10) and, therefore, may aggravate LMA induced gastric distension. We didn't find any study on the effect of N2O on gastric distension during LMA or mask ventilation.

Conclusion

According to the results of this study, whenever we use LMA and we are afraid of post-operative epigastric pain due to poor ventilation or past history of gastric problem, we can eliminate N2O from our anesthetic drugs and replace it with short acting opioids or NSAIDs for augmentation of analgesia.

Limitations

Although most cataract surgery is under topical or local anesthesia in many countries, in our country, it is vice versa. Khalili hospital where this study was conducted, is a referral, university affiliated center for ophthalmologic operations in the southwest of Iran, where more than 80% of ophthalmic operations, mostly cataract, are under general anesthesia due to high enthusiasm for such a procedure from both ophthalmologists and patients.

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