DOI: 10.4149/BLL_2012_108

Bratisl Lek Listy 2012; 113 (8)
490 – 494

CLINICAL STUDY

Effect of N_2O on nausea and vomiting via intraabdominal pressure

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Abstract: *Background and objective:* In this study we aimed to investigate whether there is an effect of N_2O on postoperative nausea and vomiting (PONV) via intraabdominal pressure (IAP).
Methods: A total of 40 patients with risk class ASA I-II and age ranging between 20 and 50 years were enrolled in the study. The patients were monitored for electrocardiography (ECG), peripheral oxygen saturation (SpO_2), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), end-tidal carbon dioxide ($ETCO_2$) and body temperature. IAP was measured by a central venous pressure manometer placed in the urine catheter. Heart rate (HR), SpO_2, SBP, DBP, MBP, $ETCO_2$, body temperature and IAP were measured before the induction of anesthesia and every 10 minutes throughout the operation. Nausea and vomiting were questioned at the first and second postoperative hours. The patients were randomly grouped into two groups. Induction in both groups was provided using 2 mg/kg propofol, 2 μg/kg fentanyl and 0.1 mg/kg vecuronium, and endotracheal intubation was performed. The maintenance of anesthesia was provided by 40 % O_2 + 60 % N_2O, 1–2 % sevoflurane and 50 μg fentanyl + 2 mg vecuronium every 45 minutes in the first group. In the second group, 60 % dry air was used instead of 60 % N_2O.
Results: There was no significant difference in terms of HR, SpO_2, SBP, MBP, $ETCO_2$, body temperature, nausea-vomiting and IAP.
Conclusions: In conclusion, we think that N_2O usage during the general anesthesia in patients without intraabdominal problems may increase IAP level for some degree whereas it does not increase PONV. In addition, N_2O usage does not change $ETCO_2$ values *(Tab. 3, Fig. 3, Ref. 32)*. Full Text in PDF *www.elis.sk*.
Key words: intraabdominal pressure, nitrous oxide, PONV.

Implication: In this study we aimed to investigate whether there is an effect of N_2O on postoperative nausea and vomiting (PONV) via intraabdominal pressure (IAP).

It is known that N_2O during general anesthesia is diffused to closed spaces and causes an increase in pressure. Its solubility is 35 times higher than nitrogen. It is contraindicated in conditions where the air is trapped in tissues and spaces of the body such as in ileus, pneumoencephaly, pneumothorax, Eustachian tube obstruction and air embolism. The diffusion of N_2O into gas-containing spaces during long abdominal operations leads to intestinal distention, negative effects on surgical conditions and delay in return of intestinal functions (1). Postoperative nausea and vomiting is an adverse clinical condition hindering patient comfort and is hence unwanted for patients and physicians. The incidence of postoperative nausea and vomiting in cases undergoing general anesthesia is 30–80 % (2). Divatia et al reported, there is evidence to suggest that use of nitrous oxide during anesthesia contributes significantly to PONV. Nitrous oxide has been shown to activate several receptor systems to produce vomiting. These include the medullary dopaminergic system, the sympathetic nervous system, and the opioid receptors in the brain. Changes in middle ear pressure, as well as bowel distension after diffusion of nitrous oxide into closed cavities, also may contribute to PONV (3).

It is not clear whether the N_2O causes nausea and vomiting via central pathways or increased IAP. In this study we aimed to investigation whether there is an effect of N2O on postoperative nausea and vomiting (PONV) via intraabdominal pressure (IAP).

Methods

Following approval of the study by the Ethics Committee and after written and oral consents were obtained from the patients, a total of 40 patients with risk class ASA (American Society of Anesthesiologists) I-II and age ranging from 20 years to 50 years who were to undergo elective surgery were enrolled in the study. The patients had no endocrine, hepatic, renal or cardiac problems. The patients were randomly grouped into two groups. They were monitored for electrocardiography (ECG), peripheral oxygen saturation (SpO_2), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), end-tidal carbon dioxide ($ETCO_2$) and body temperature (Petas® KMA 800). End-tidal CO_2 ($ETCO_2$) (Drager® Primus anesthesia apparatus) was also monitored. Intraabdominal pressure (IAP) was measured using

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a central venous pressure (CVP) manometer placed in the urine catheter. Intravenous access was established using a 20 G catheter and fluid maintenance was provided by 0.9 % saline. The patients were not given any sedatives or antiemetics. Heart rate (HR), SpO_2, SBP, DBP, MBP, $ETCO_2$, body temperature and IAP were measured before the anesthesia induction and every 10 minutes throughout the operation. Induction in both groups were provided using 2 mg/kg propofol and 2 µg/kg fentanyl, and endotracheal intubation was performed using 0.1 mg/kg vecuronium. The maintenance of anesthesia was provided by sevoflurane (1–2 %) and 50 µg fentanyl + 2 mg vecuronium + 40 % O_2 + 60 % N_2O every 45 minutes in the first group. In the second group, dry air was used instead of N_2O. At the end of the surgical procedure, extubation was performed after standard decurarization with atropine and neostigmine. Patients were questioned in terms of postoperative nausea (0: None, 1: mild, 2: moderate, 3: severe) and vomiting (yes–no) at first and second hours.

Statistical Analysis

The Repeated Measurement Variance Analysis and Duncan multi-comparison test were used for the statistical analysis. The level of significance was set as $p<0.05$ and the level of advanced significance was set as $p<0.01$.

Results

The groups were similar for demographic data (Tab. 1). There was no significant difference between the groups in terms of SBP and MBP ($p>0.05$). There was no significant difference within the groups in terms of preoperative and intraoperative SBP ($p=0.256$) (Tab. 2). There was a decrease in intraoperative values compared to preoperative values when Group 1 and Group 2 were compared for MBP within their groups ($p<0.01$) (Tab. 3).

There was a significant decrease in DBP at 110 and 120 minutes intraoperatively compared to the preoperative values in Group 2 compared to Group 1 ($p<0.05$). There was no significant difference in other values at different times.

There was a decrease in the intraoperative DBP values compared to the preoperative values within Group 1 and Group 2 ($p<0.01$) (Fig. 1).

There was no significant difference in IAP between the groups and within the groups compared to the preoperative period ($p>0.05$). The mean IAP was 7.6 cmH_2O (5.58 mmHg) in the N_2O group and it was 5.36 cmH_2O (3.94 mmHg) in the dry air group ($p>0.05$) (Fig. 2).

There was no difference in the HR, SpO_2, $ETCO_2$ (Fig. 3) and body temperature between the groups and in-group comparison in the preoperative period ($p>0.05$). Nausea was observed only one case in each group at the first hour, at other times as well as nausea and vomiting was not observed in any patient.

Tab. 1. Demographic data of the cases (Mean±SD).

	Group 1 (n=20)	Group 2 (n=20)
Age (year)	37.5±9.28	30.65±10.16
Gender M/F	17/3	14/6
ASA I/II	20/0	20/0

F – Female, M – Male, ASA – American Society of Anesthesiologists

Tab. 2. Systolic blood pressure values of the groups (Mean±SD).

	Group 1 (n=20)	Group 2 (n=20)
Preoperative	127.45±11.45	126.35±10.95
Minute 10	105.35±10.26	105.30±9.97
Minute 20	102.10±11.89	105.75±13.01
Minute 30	103.25±9.30	114.50±16.61
Minute 40	104.30±8.84	114.35±10.99
Minute 50	107.80±12.77	112.95±11.98
Minute 60	106.30±13.17	114.90±12.42
Minute 70	107.67±13.38	117.87±13.94
Minute 80	108.07±17.10	118.00±9.70
Minute 90	109.70±16.55	115.22±11.32
Minute 100	102.11±13.88	115.00±15.82
Minute 110	109.86±14.94	106.67±15.89
Minute 120	104.67±17.17	105.00±17.78
Minute 130	95.50±7.78	104.00±16.46
Minute 140	99.50±9.19	110.00±26.87

Tab. 3. The mean arterial pressure values of the groups (Mean±SD).

	Group 1 (n=20)	Group 2 (n=20)
Preoperative	96.05±11.36	94.50±12.07
Minute 10	76.75±12.69 Δ	75.35±10.78▼
Minute 20	76.25±11.56 Δ	77.95±11.63▼
Minute 30	79.00±9.64 Δ	87.30±11.87▼
Minute 40	81.75±9.62 Δ	85.60±12.56▼
Minute 50	82.30±10.12 Δ	84.80±10.85▼
Minute 60	82.40±10.49 Δ	86.80±11.37▼
Minute 70	81.06±10.34 Δ	86.40±11.15▼
Minute 80	81.29±13.69 Δ	85.86±9.16 ▼
Minute 90	82.00±13.07 Δ	87.11±11.20▼
Minute 100	78.89±14.00 Δ	83.00±12.48▼
Minute 110	84.71±15.20 Δ	82.33±26.27▼
Minute 120	82.33±15.47 Δ	78.33±13.32▼
Minute 130	74.00±15.56 Δ	75.33±11.37▼
Minute 140	81.00±9.90 Δ	78.00±19.80▼

*$p<0.01$: inter group comparison, Δ $p<0.01$ in Group 1 comparison, ▼ $p<0.01$ in Group 2 comparison

Discussion

Nitrous oxide is widely used in general anesthesia for analgesic purposes. The most important disadvantage is its diffusion to closed spaces causing a pressure increase. Its diffusion to spaces consisting gas leads to intestinal distension, negative effects on surgery and delay in return of intestinal functions postoperatively in long-duration abdominal operations (1).

Direct measurement of IAP is an invasive procedure and is not a logical and practical method in clinical practice. Therefore, IAP is measured with indirect methods clinically (4).

Intraabdominal pressure can be measured using direct and indirect methods. In the direct method, a catheter is placed in the abdominal cavity and the pressure is measured; in the indirect method, measurement can be made by a catheter placed in the stomach, urinary bladder, vena cava inferior or the rectum (4–7). Clinical and experimental studies showed that IAB

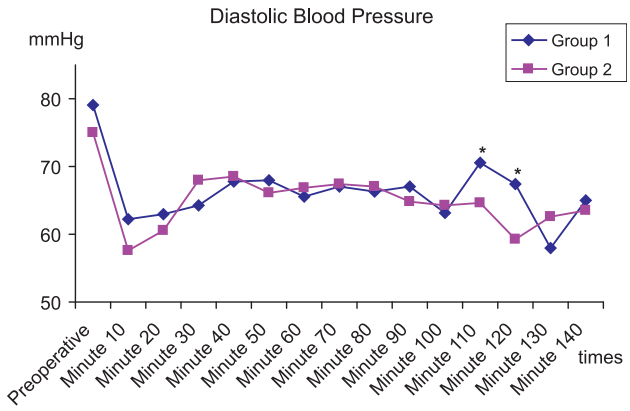

Fig. 1. Diastolic blood pressure values of the groups (*p<0.05).

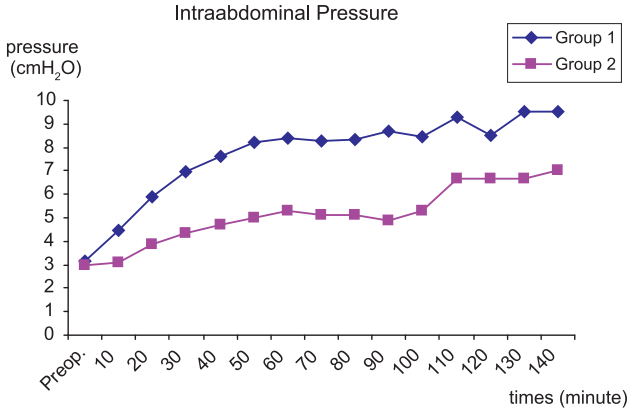

Fig. 2. Intraabdominal pressure values of the groups.

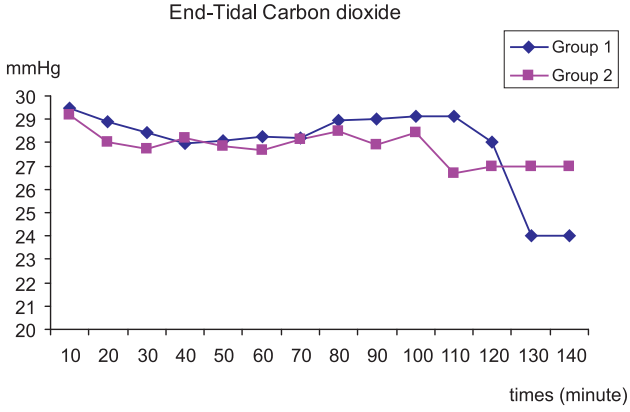

Fig. 3. ETCO2 values of the groups.

is correlated with stomach, bladder, rectum and in the inferior vena cava pressures (5). The advantage of direct measurement is continuous monitoring and the disadvantage is being more invasive, less rational and impractical (4, 7). The advantage of indirect measurement is being practical and the disadvantage is infection (femoral region) and venous thrombosis if measured from the vena cava inferior (5). In this study, indirect measurement of IAP was performed from the urinary bladder as it was practical and easily applicable. When IAP increases, visceral blood flow, renal blood flow, venous return, cardiac output, glomerular filtration rate, and brain perfusion are decreased, and pulmonary capillary wedge pressure, HR, airway pressure, CVP, thoracic and pleural pressure, vena cava inferior pressure, renal vein pressure, systemic vascular resistance and intra cranial pressure are increased (8,9).

Nausea and vomiting are one of the most important postoperative problems. The incidence of postoperative nausea and vomiting (PONV) due to general anesthesia has been reported as 30–80 % (2). The causes include non-anesthetic (patient-related and surgery-related) and anesthetic factors. Patient-related factors are age, gender, obesity, history of nausea and vomiting (motion sickness or postoperative nausea and vomiting), anxiety, and gastroparesis (10–12). Surgery-related factors are laparoscopic interventions, uterus dilatation, curettage, knee arthroscopy, lithotripsy, operations of the head-neck, stomach, duodenum, gall bladder, middle ear, in addition to strabismus and orchiopexy (10, 11). Anesthesia-related factors are pre-anesthetic medication, Ketamine, Neostigmine, gastric distention, aspiration, anesthetic method, postoperative factors, pain, dizziness, mobilization, oral intake and opioids (10–16). In our study, there were no non-anesthetic factors other than knee arthroscopy causing nausea and vomiting. The only anesthesia-related factors were opioid and Neostigmine. However, the number of cases undergoing knee arthroscopy was similar in both groups; opioid and neostigmine were administered to all cases in our study at doses according to their body weights.

The relationship between intraoperative N_2O use and the prevalence of PONV is still controversial in some references (17, 18). Some studies have reported that N_2O is a potential emetic factor and some others have reported the opposite (5, 19–21). In a meta-analysis, the risk of PONV when N_2O was not used decreased at a rate of 28 % (6). In this meta-analysis, in 20 studies of a total of 26, PONV was less prevalent in groups without N_2O; however, this decrease was significant only in five studies (6). In another study, in patients receiving PONV prophylaxis, the prevalence of PONV was decreased at a rate of 12 % in the group which received nitrogen instead of N_2O (7). N_2O causes an increase in the prevalence of postoperative vomiting when used with potent inhalation agents, especially in women undergoing laparoscopic interventions (22–24). It has been reported that N_2O causes a dose-dependent increase in the incidence of PONV after gynecological laparoscopic surgery. The rates of nausea and vomiting at the 24th postoperative hour in the group that was given dry air + O_2, 50 % N_2O + O_2 and 70 % N_2O + O_2, were 33 %, 46 % and 62 %, respectively (22). In another study, 65 % N_2O was not administered to the first group of patients who were to undergo colon resection, and N_2O was not administered to the second group. Although the rate of moderate-severe intestinal distention was 23 % in the first and 9 % in the second group, the incidence of postoperative nausea and vomiting was similar (20). Although there was no significant difference between the groups with and without N_2O in the prevalence of nausea and

vomiting at the postoperative 0-2 hours, there was a significant difference in the nausea at the postoperative 2–24 hours and the frequency of antiemetic use (20, 23–26). The mechanism of nausea and vomiting due to N_2O establishes via intraabdominal distension, besides via stimulation of CTZ or nausea center in medullae (3). Despite the fact that the mean IAP was 7.6 cm-H_2O in the group in which N_2O had been administered, and 5.36 cmH_2O in the group in which N_2O had not been administered in our study, the incidence of nausea and vomiting was found to be 5 % in both groups. The low incidence of nausea and vomiting may be due to our assessment of nausea and vomiting only in the early period and the low number of predisposing factors for nausea and vomiting.

N_2O directly depresses the myocardium in a dose-dependent manner. However, this effect is balanced with its effect causing sympathetic stimulation. Sometimes it may even be masked in an unfavorable way. When it is used with drugs depressing the sympathomimetic effect such as opioids, moderate circulatory depression occurs (27). The elevated intraabdominal pressure causes an increase in venous stasis, decrease in intraoperative portal vein blood flow and decrease in intraoperative urinary flow, and deteriorates the cardiac functions, and a 30 % decrease in cardiac output may be seen (28). In an experimental study, it was shown that capacitance veins were compressed when intraabdominal pressure was 10 mmHg but collapse did not occur. The capacitance veins collapsed when the intraabdominal pressure reached 20 mmHg and cardiac output decreased (29). It was reported in another study that when IAP was 14 mmHg during laparoscopic surgery, the rate of blood flow in the femoral vein was significantly decreased, venous return showed deterioration, and blood flow showed stagnance (30). Besides, the mean blood pressure shows an increase due to the increasing IAP during laparoscopic surgery (31, 32). We could not find a difference between the two groups in terms of systolic and mean blood pressures, and this may be due to the young age and the low ASA scores in our patients.

During laparoscopic surgery, the HR increases depending on the increase in IAP (31, 32). We could not find any difference of HR between the groups in our study.

Although there are studies in the literature on N_2O increasing the IAP, there is no study comparing its effects on $ETCO_2$ pressure. The IAP in our study was 5.58 mmHg in the N_2O group; it was 3.94 mmHg in the dry air group. There was no difference in the $ETCO_2$ in the ventilation modes. The $ETCO_2$ not being significantly different between the groups may be due to IAP values being within the physiological limits in both groups.

In conclusion, in patients without intraabdominal problems, while use of N_2O during the general anesthesia increases IAP levels, it does not increase the PONV, also does not change hemodynamics and $ETCO_2$ values.

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Received April 28, 2010.
Accepted April 15, 2012.