



## ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

# Dexasone and metoclopramide vs. granisetron in the prevention of postoperative nausea and vomiting

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## SUMMARY

**Introduction** Postoperative nausea and vomiting (PONV) is one of the most common postoperative complications. The incidence in adult population is 20–30%, and it can be up to 80% in high-risk population such as gynecological and laparoscopic surgeries.

The objective of this study is to compare the efficiency of the combination therapy in comparison with monotherapy in the prevention of PONV in gynecological and laparoscopic surgeries.

**Methods** An observational prospective cohort study was conducted on a sample of 64 patients (32 patients per group) treated postoperatively at the Gynecology and Obstetrics Ward of GH Subotica, in the period from January–March 2017. The anesthesiologist in charge administered the combination of dexasone and metoclopramide or granisetron in monotherapy according to protocol to patients for prevention of PONV.

**Results** The demographic characteristics of patients are homogenous and show a statistically significant difference only in the characteristics of length of smoker status and maximum intra-abdominal pressure during surgery. The total incidence of postoperative nausea in the fifth, 15th and 60th minute was 15.6%, 17.2% and 18.7% respectively, and in the fourth, eighth, 12th, and 24th postoperative hour it was 12.5%, 7.8%, 10.9%, and 6.2%, respectively. The incidence of postoperative vomiting in the fifth, 15th, and 60th minute was 1.6%, 4.7%, and 4.7%, respectively, and in the fourth, eighth, 12th, and 24th postoperative hour it was 1.6%, 3.2%, 1.6%, and 1.6%, respectively.

**Conclusion** The study proved that the combination effect of dexasone and metoclopramide is not inferior compared to monotherapy with granisetron.

**Keywords:** postoperative; nausea; vomiting

## INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most frequent postoperative complications, occurring after surgery under general, regional, or local anesthesia. Previous studies have shown that patients regard vomiting as the most undesirable complication of anesthesia and qualify it as a more unpleasant sensation than pain [1, 2]. The incidence of PONV in adult population is 30% [3], and in high-risk population such as gynecologic and laparoscopic surgery, it can be up to 80% [4, 5].

The potential risk factors for PONV can be classified into four groups:

1. patient related factors (female sex, age, positive anamnesis for PONV, kinetosis, non-smoker status, the patient's American Society of Anesthesiologists (ASA) status, positive anamnesis for migraine, menstrual cycle phase);
2. surgery related factors (length of surgery, type of surgery);
3. anesthesia related factors (inhalation anesthetics, intravenous anesthetics, opioids, muscle block reversal, anesthetic technique and N<sub>2</sub>O);

4. early postoperative period related factor (pain, opioid administration, postoperative movement of patients, early fluid and food ingestion and hypotension) [6].

The most used antiemetic drugs used in PONV prevention and therapy include dopamine receptor antagonists, serotonin 5-HT<sub>3</sub> receptor antagonists, and corticosteroids [7, 8].

In the therapy and prevention of PONV, anesthesiologists have the most experience in the application of dopamine antagonist metoclopramide. Due to its short-term action, it should always be administered towards the end of the surgery. At the dosage of 0.1–0.2 mg/kg, it very rarely causes adverse effects in adult patients [7, 8].

From the group of corticosteroids, antiemetic effect has been shown in the administration of dexasone. Its exact mechanism of action is unknown, but it is assumed to be based on inhibition of prostaglandin synthesis, decrease of serotonin levels in the brain, local anti-inflammatory action, and reduction of brain-blood barrier permeability [7, 8]. Dexasone potentiates the action of other antiemetics through the stabilization of receptors on which they act [9]. The recommended dose of 2.5–5 mg is administered at the beginning of the surgery.

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One of the most potent selective 5-HT<sub>3</sub> antagonists is granisetron, which can provide a 24-hour antiemetic effect at the dose of 1 mg after anesthesia induction. The main factor limiting the clinical use of granisetron is its price, rendering the routine prophylaxis with this drug being extremely costly [7, 8].

There are over 60 randomized controlled studies comparing the effects of antiemetics in comparison with monotherapy, and most showed better results when using two or more agents with different location of receptor action, which is also in compliance with the multifactorial origin of PONV [10, 11]. A rational approach when combining antiemetics implies that combined administration of drugs potentiates their positive sides, and reduces adverse effects.

A prospective randomised study by Wallenborn et al. [12] proved dosage dependent antiemetic effect of metoclopramide, as well as the efficiency of combination of PONV.

The objective of this study is to compare the efficiency of the combination of metoclopramide and dexasone in comparison with monotherapy with granisetron in the prevention of PONV in gynecological laparoscopic surgeries. In case of proving the non-inferiority of the combination compared to monotherapy, the clinical use of the combination of metoclopramide and dexasone in comparison with monotherapy would be justified for economic reasons.

## METHODS

An observational prospective cohort study was conducted on a sample of 64 patients (32 patients per group) treated postoperatively at the Gynecology and Obstetrics Ward of Subotica General Hospital, in the period from January to March 2017.

The conduct of this study was approved by the Ethical Committee of Subotica General Hospital, and the patients were introduced into studies after giving written consent to participation.

The study included patients over 18 years of age, who had undergone laparoscopic gynecological surgery, with ASA classification of physical health condition I – III (the latest approved classification dated October 15, 2014, available at <https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system>).

The study excluded:

1. Patients with ASA classification > III;
2. Patients with BMI of 35.3;
3. Patients allergic to medication planned for the study;
4. Patients with acute surgical disease and urgent surgery;
5. Patients with conversion during surgery;
6. Patients with liver central nervous system diseases;
7. Pregnant and nursing women;
8. Patients on antiemetic and opioid therapy;
9. Patients with kidney failure, expressed creatinine clearance rate lower than 30 ml/min;
10. Patients suffering from malignant diseases and receiving chemotherapy.

In accordance with the normal procedure, all patients were examined by anesthesiologists in the preoperative outpatient examination units one day prior to the surgery. Special attention was paid to risk factors (kinesis, anamnesis for prior PONV, migraine, menstrual cycle period and smoker status length). The following data were taken for each patient: body mass (BM), height (H), body mass index (BMI), blood pressure (BP), heart rate (HR).

Apfel's postoperative nausea (PON) prediction model (available at <https://www.ncbi.nlm.nih.gov/pubmed/10485781>) will be used at the end of the examination (Tables 1 and 2).

**Table 1.** Simplified Apfel score for postoperative nausea with four predictors

| Predictors                      | Points        |
|---------------------------------|---------------|
| Female sex                      | 1             |
| Prior PONV or kinesis           | 1             |
| Non-smoker status               | 1             |
| Postoperative opioid analgesics | 1             |
| Score                           | 0, 1, 2, 3, 4 |

PONV – postoperative nausea and vomiting

**Table 2.** Approximate probability of occurrence of postoperative nausea according to Apfel

| Risk      | Number of predictors | Expected incidence (%) |
|-----------|----------------------|------------------------|
| Very low  | 0                    | 10                     |
| Low       | 1                    | 21                     |
| Moderate  | 2                    | 39                     |
| High      | 3                    | 61                     |
| Very high | 4                    | 79                     |

Ingestion of solid food is discontinued eight hours prior to the scheduled beginning of surgery, and ingestion of clear liquids is discontinued two hours prior to surgery.

Before entering the operating theatre, the patient is admitted for induction, where the vein route is opened and the patient is rehydrated with 10 ml/kg of Hartmann's solution. The patients receive premedication amp. dormicum 5 mg IM. To prevent stress peptic ulcer, proton pump inhibitors (PPIs) were administered to all the patients. 20 minutes before premedication, the patient is admitted into the operating theatre and preoxygenated with 100% oxygen for three minutes. Monitoring is continued in the meantime (Electrocardiography, non-invasive measurement of blood pressure, hemoglobin saturation, capnography).

At induction to general endotracheal anesthesia, the patients receive IM amp. atropine as needed, amp. midazolam 2 mg IV, amp. propofol 2 mg/kg, amp. succinylcholine 1 mg/kg. Upon orotracheal intubation, the patient receives amp. rocuronium at the dose of 0.15 mg/kg. Volatile anesthetic sevoflurane is used for maintaining anesthesia. The patients are ventilated during anesthesia with a mixture of oxygen and nitrogen oxide 1:1, and analgesia is provided with opioid analgesic fentanyl and alfentanil as needed. During the surgery, the patients are laid in the Trendelenburg position.

The anesthesia chart records the beginning and the end of the surgical intervention, the start and the end of

anesthesia, the duration of pneumoperitoneum, as well as the maximum reached intra-abdominal pressure, blood pressure, pulse, values of exhaled carbon monoxide in the fifth, 30th and 60th minute, and every subsequent hour of anesthesia, 0.5–1 mg atropine and 1.5–2.5 mg Prostigmin are used for reversal of muscular relaxation.

After extubation and oxygenation, the patients are placed in a recovery room or an inpatient room, depending on the type of surgical intervention. Over the first 24 hours after surgery, vital signs are monitored postoperatively: blood pressure, heart rate, respiratory rate. Ketorolac is given every six hours (for pain on the visual analogue scale [VAS] up to 5), tramadol 50–100 mg (for pain VAS over 5), or combination of ketorolac and tramadol is used for postoperative analgesia. The anesthesiologist assessed PONV in the fifth minute, 15th minute, first hour, fourth hour, hour, 12th hour, and 24th hour. To assess nausea, which is a subjective category, VAS was used, on which each postoperative patient assessed individually the intensity of nausea on a scale of 0–100, where 0 stands for total absence of nausea, and 100 the most intensive possible nausea. The seriousness of postoperative vomiting, expressed as the number of emetic episodes was evaluated as follows: 0 – without vomiting; 1 – medium serious (up to four episodes) and 2 serious (more than four episodes).

According to the anesthesiologist's personal decision, for PONV prevention, the combination dexasone and metoclopramide was administered to patients. The patients received dexamethasone intravenously at the dose of 4 mg after induction to general anesthesia, and a 10 mg ampoule of metoclopramide 15 minutes before the end of the surgical intervention, or 1 mg IV granisetron in monotherapy 15 minutes before the end of the surgical intervention.

The sample size was calculated based on data obtained from earlier studies [13]. The study sample was calculated taking alpha as 0.05 and power of the study of 0.8 for Student's t-test (two independent samples), comparing the groups, according to statistical program G\*Power 3 (Heinrich Heine University, Düsseldorf, Germany). Based on the assumption requiring the largest sample, that is, the expected least difference in examined parameters between the two groups of patients, the total number of 32 patients per group was determined, or a total of 64 patients. Such a study sample assumes establishing a statistically significant difference (Student's t-test for two independent samples or Mann–Whitney test) between the two groups of patients with power of the study  $\geq 80\%$ .

## Variables

1. Independent variables: administration of dexamethasone and metoclopramide, or granisetron.
2. Dependent variables: PONV.
3. Confounding variables: the patient's age, ASA score, the patient's nutritive status, simultaneous administration of medications potentiating the effects of antiemetics, smoker status, migraine.

## Statistical analysis

Statistical data analysis encompassed methods of descriptive statistics. Absolute and relative numbers (%) were used, as well as central tendency measures (arithmetic mean, median) and dispersion measures (standard deviation, interquartile range). Parametric Student's t-test for two independent samples or its non-parametric alternative – Mann–Whitney test, was used for determining significance of difference in continuous variables, and difference between category features was examined by  $\chi^2$  test or Fisher's test of exact probability in situations where the frequency of individual categories is a linear trend. The probability level lower than 0.05 will be used for rejecting the null hypothesis. Commercial program package SPSS version 20 (IBM, Armonk, NY, USA) was used for processing the obtained results.

## RESULTS

Three patients were excluded during the study due to conversion. The mean value of patients' age with combined therapy and monotherapy does not show statistically significant difference. All the other patient's demographic characteristics are shown in Table 3. Both groups of patients are homogenous and show statistically significant difference only in the characteristics length of smoker status and maximum intra-abdominal pressure during the surgical intervention.

The total incidence of postoperative nausea in the fifth, 15th, and 60th postoperative minute was 15.6%, 18.7%, and 18.7%, respectively, and in the fourth, eighth, 12th, and 24th postoperative hour it was 12.5%, 7.8%, 10.9%, and 6.2%. Incidence of postoperative nausea across groups is shown in Table 4. The incidence of postoperative vomiting in the fifth, 15th, and 60th postoperative minute was 1.6%, 4.7%, and 4.7% and in the fourth, eighth, 12th, and 24th postoperative hour it was 1.6%, 3.2%, 1.6 and 1.6%. The incidence of postoperative vomiting across groups is shown in Table 5.

We found difference in the occurrence and degree of PON between two groups of patients, but it is not statistically significant (Figure 1). The degree of postoperative nausea has maximum value in the first hour, followed by a decline in the degree of postoperative nausea until the fourth hour, when recurring slight increase is observed (Figure 2). The patients who had had kinetosis in earlier anamnesis show statistical difference in the occurrence of PON in the first eight hours after the surgery (Figure 3).

The degree of postoperative analgesia was monitored by visual analogue scale (VAS). The strongest pain occurred in the 30<sup>th</sup> minute, and then the VAS value declined as the time passed (Figure 4).

When three groups of patients (non-steroidal anti-inflammatory drugs [NSAID], opioids, and NSAID with opioids) are compared depending on which type of analgesia they received postoperatively, there is a statistically significant difference in PON in the fourth hour after surgery. (Table 6) (Showing the degree of PON assessed

**Table 3.** Demographic characteristics of patients

| Parameters                    |                 | n [%]         | n [%]         | p            |
|-------------------------------|-----------------|---------------|---------------|--------------|
| Number of patients            |                 | 32 [50]       | 32 [50]       |              |
| Age structure                 |                 | 39.50 ± 12.1  | 36.38 ± 8.9   | 0.514        |
| ASA I                         |                 | 15 [46.9]     | 18 [56.2]     | 0.617        |
| ASA II                        |                 | 17 [53.19]    | 14 [43.8]     | 0.617        |
| BM [kg]                       |                 | 66.78 ± 9.78  | 63.13 ± 10.51 | 0.076        |
| BH [cm]                       |                 | 166.96 ± 4.64 | 166.53 ± 8.00 | 0.79         |
| BMI [kg/m <sup>2</sup> ]      |                 | 23.9 ± 3.24   | 22.7 ± 3.41   | 0.131        |
| Kinetosis                     | Yes             | 6 [18.8]      | 7 [21.9]      | > 0.05       |
|                               | No              | 26 [81.2]     | 25 [78.1]     |              |
| Migraine                      | Yes             | 8 [25]        | 5 [15.6]      | > 0.05       |
|                               | No              | 24 [75]       | 27 [84.4]     |              |
| Earlier PONV                  | Yes             | 4 [12.5]      | 6 [18.8]      | > 0.05       |
|                               | No              | 28 [87.5]     | 26 [81.3]     |              |
| Smoker status                 | Yes             | 9 [28.1]      | 18 [56.3]     | <b>0.043</b> |
|                               | No              | 23 [71.9]     | 14 [43.8]     |              |
| Earlier HT                    | Yes             | 5 [15.6]      | 3 [9.4]       | 0.708        |
|                               | No              | 27 [84.4]     | 29 [90.6]     |              |
| Thyroid gland disease         | Yes             | 4 [12.5]      | 2 [6.3]       | 0.668        |
|                               | No              | 28 [87.5]     | 30 [93.8]     |              |
| Apfel score                   |                 | 1.97 ± 0.822  | 2.25 ± 0.88   | 0.184        |
| The last dose of opioids      |                 | 26.78 ± 12.8  | 26.63 ± 13.61 | 0.908        |
| Total amount of fentanyl [µg] |                 | 226 ± 70.6    | 225 ± 71.1    | 0.908        |
| Total amount of esmeron       |                 | 39.5 ± 13.0   | 39.72 ± 15.76 | 0.902        |
| Duration of pneumoperitoneum  |                 | 36.7 ± 24.5   | 36.9 ± 26.0   | 0.861        |
| Maximum IAP (mmHG)            |                 | 13.25 ± 1.6   | 14.03 ± 1.6   | <b>0.049</b> |
| Postoperative analgesia       | NSAID           | 21 [65.6]     | 23 [71.9]     | 0.565        |
|                               | Opioids         | 1 [3.1]       | 0 [0]         | 0.465        |
|                               | NSAID + opioids | 10 [31.3]     | 9 [28.1]      | 0.683        |

n – number of patients; ASA – asa classification for assessment of risk of surgical intervention; BM – body mass; BH – height; BMI – body mass index; PONV – postoperative nausea and vomiting; HT – hypertension; Apfel score – score for preoperative assessment of risk of PON; IAP – intra abdominal pressure; NSAID – non-steroidal anti-inflammatory drugs; OPIOIDS – opioid analgesics

**Table 4.** Incidence of nausea across groups

| Groups      | PON 5  | PON 15 | PON 60 | PON 4 | PON 8 | PON 12 | PON 24 |
|-------------|--------|--------|--------|-------|-------|--------|--------|
| Combination | 12.5%  | 15.7%  | 12.5%  | 9.4%  | 6.3%  | 9.4%   | 9.4%   |
| Monotherapy | 18.75% | 18.75% | 25%    | 15.7% | 9.4%  | 12.5%  | 3.2%   |

PON – postoperative nausea

**Table 5.** Incidence of vomiting across groups

| Groups      | POV 5 | POV 15 | POV 60 | POV 4 | POV 8 | POV 12 | POV 24 |
|-------------|-------|--------|--------|-------|-------|--------|--------|
| Combination | 3.2%  | 6.3%   | 0%     | 0%    | 3.2%  | 3.2%   | 3.2%   |
| Combination | 0%    | 3.2%   | 9.4%   | 3.2%  | 3.2%  | 0%     | 0%     |

POV – postoperative vomiting

**Table 6.** Presentation of the mean value of postoperative nausea in the fourth hour in relation to the administered analgesic postoperative therapy

| Mean value of postoperative nausea in the fourth hour | NSAID | Opioids | NSAID and opioids | p     |
|---|-------|---------|-------------------|-------|
|   | 1.36  | 40      | 5.26              | 0.002 |

NSAID – non-steroidal anti-inflammatory drugs

by VAS scale 1–100 in patients in terms of analgesia that they received regardless of which group of patients they belonged to).

In our study, there is a statistically significant correlation between the intensity of postoperative pain and degree of postoperative nausea (Table 7).

## DISCUSSION

Contemporary literature points to the fact that female sex possesses a strong predictive factor for the occurrence of PONV [14], and a high incidence of PON and POV is expected. In addition to sex, the type of surgical intervention in terms of gynecological laparoscopic surgery also influences the highly expected incidence of PONV, up to 80% [3]. For ethical reasons, this study did not include a control group that would receive a placebo, and the total incidence of PON and POV remains only at prediction level. The total expected incidence of PON calculated by a simplified Apfel score was about 40% [6]. In our study, the total incidence of PON amounts to 12.7%, incidence of PON in the group receiving combined therapy was 10.74%, and in the group receiving monotherapy, it was 14.75%. As in can be concluded, therapy administered to both groups was effective in terms of reduced PON in comparison to the expected levels. Although the incidence was 4% lower in the group of patients receiving combined therapy, there

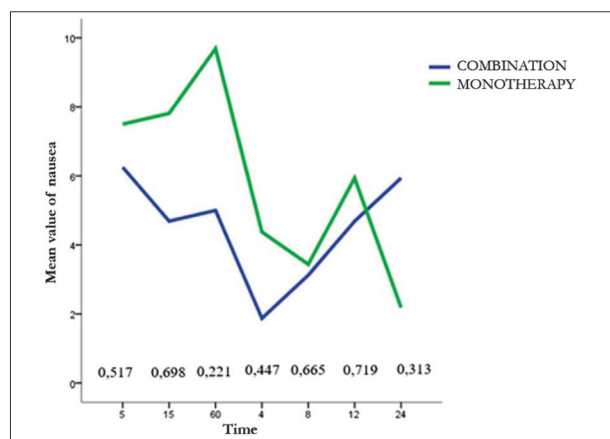
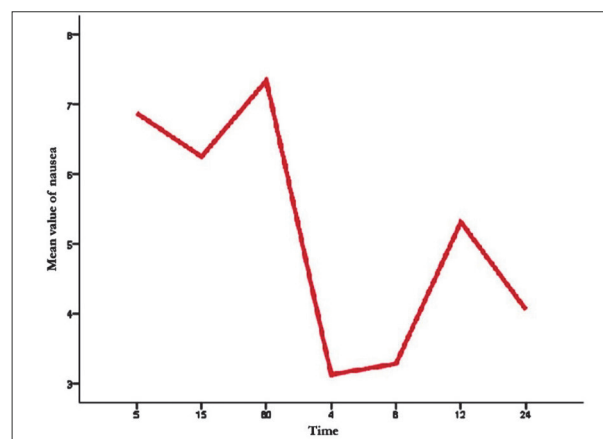
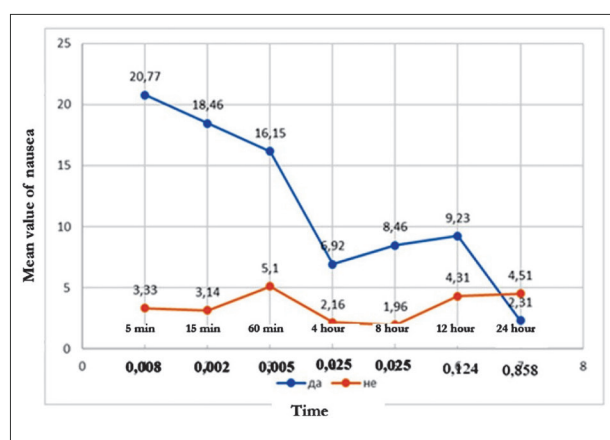
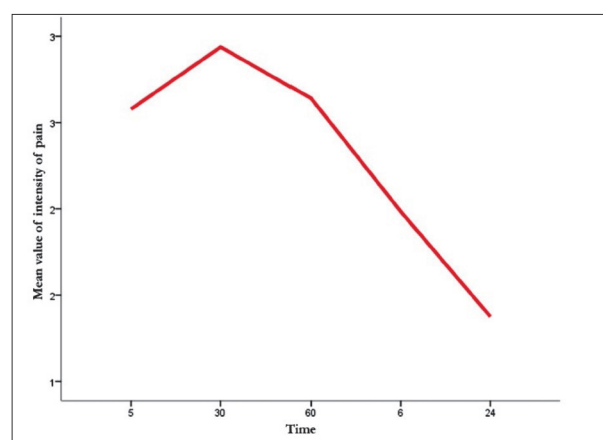
**Table 7.** Correlation of PON depending on pain intensity

|                |                     | VAS<br>5 minutes | VAS<br>30 minutes | VAS<br>60 minutes | VAS<br>6 hours | VAS<br>24 hours |
|----------------|---------------------|------------------|-------------------|-------------------|----------------|-----------------|
| PON 5 minutes  | Pearson correlation | <b>0.412**</b>   | <b>0.391**</b>    | 0.190             | 0.088          | 0.053           |
|                | Sig. (2-tailed)     | <b>0.001</b>     | <b>0.001</b>      | 0.133             | 0.490          | 0.676           |
|                | n                   | <b>64</b>        | <b>64</b>         | 64                | 64             | 64              |
| PON 15 minutes | Pearson correlation | <b>0.421**</b>   | <b>0.443**</b>    | 0.085             | <b>0.302*</b>  | <b>0.281*</b>   |
|                | Sig. (2-tailed)     | <b>0.001</b>     | <b>0.000</b>      | 0.506             | <b>0.015</b>   | <b>0.025</b>    |
|                | n                   | <b>64</b>        | <b>64</b>         | 64                | <b>64</b>      | <b>64</b>       |
| PON 60 minutes | Pearson correlation | -0.045           | -0.043            | <b>0.346**</b>    | 0.223          | <b>0.280*</b>   |
|                | Sig. (2-tailed)     | 0.726            | 0.739             | <b>0.005</b>      | 0.076          | <b>0.025</b>    |
|                | n                   | 64               | 64                | <b>64</b>         | 64             | <b>64</b>       |
| PON 4 hours    | Pearson correlation | 0.097            | 0.207             | 0.095             | -0.015         | 0.058           |
|                | Sig. (2-tailed)     | 0.444            | 0.101             | 0.454             | 0.908          | 0.647           |
|                | n                   | 64               | 64                | 64                | 64             | 64              |
| PON 8 hours    | Pearson correlation | 0.141            | 0.200             | 0.125             | -0.003         | -0.008          |
|                | Sig. (2-tailed)     | 0.265            | 0.113             | 0.324             | 0.980          | 0.949           |
|                | n                   | 64               | 64                | 64                | 64             | 64              |
| PON 12 hours   | Pearson correlation | -0.058           | 0.067             | 0.013             | 0.232          | 0.226           |
|                | Sig. (2-tailed)     | 0.648            | 0.601             | 0.919             | 0.065          | 0.072           |
|                | n                   | 64               | 64                | 64                | 64             | 64              |
| PON 24 hours   | Pearson correlation | -0.049           | 0.017             | 0.063             | <b>0.286*</b>  | <b>0.282*</b>   |
|                | Sig. (2-tailed)     | 0.701            | 0.891             | 0.621             | <b>0.022</b>   | <b>0.024</b>    |
|                | n                   | 64               | 64                | 64                | <b>64</b>      | <b>64</b>       |

VAS – visual analogue scale; PON – postoperative nausea;

\*\*correlation is significant at the 0.01 level (2-tailed);

\*correlation is significant at the 0.05 level (2-tailed)

**Figure 1.** Difference in the degree of postoperative nausea**Figure 2.** Postoperative nausea as a subjective category was measured by visual analogue scale**Figure 3.** Presentation of the degree of nausea in patients who had kinetosis**Figure 4.** Postoperative pain was measured by visual analogue scale

is no statistical significance either in the incidence or in the level of nausea between patients of the two groups.

In terms of demographic characteristics, preoperative and intraoperative anesthesiological intervention was homogenous without statistically significant difference, except for the smoker status length before surgery and intra-abdominal pressure value during the creation of pneumoperitoneum. This is significant information, because both of these characteristics are listed in literature as predictive factors in the occurrence of PONV. Non-smoker status is known in literature as an independent predictor of occurrence of PONV [6]. Over the past 15 years, research has proven that non-smoker status reduces the likelihood of PONV by 34%. One of the possible explanations for protective action of smoking is the induction of enzyme CYP450, facilitating faster breakdown of medications used in anesthesia [15]. In our study, a statistically significantly higher number of smokers was in the group receiving monotherapy – 56.3%, compared to the group receiving combined therapy – 28.1%, so that non-smoking status did not feature as a predictive factor of PONV. Explanation for this result should perhaps be sought in the fact that, in our study, we regarded former smokers as non-smokers, or in the efficiency of combined therapy that might be even more superior if the groups of patients in this segment had been homogenous.

The intra-abdominal pressure values during laparoscopic surgery were statistically significantly higher in the monotherapy group, which corresponds to the fact that the incidence of vomiting was higher in this group of patients. Cohen et al. [16] proved that, in addition to ophthalmological, gynecological, and laparoscopic interventions, surgical interventions also have a high incidence of PONV. Two observational studies point to the fact that intra-abdominal surgery has a higher incidence of PONV than other surgeries. In their study, identified the pathophysiological and pharmacological role of visceral innervation on the emetic reflex [17, 18].

The positive anamnesis in terms of anamnestic data about prior kinetosis is one of the most commonly listed risk factors for PONV. Kinetosis is a relatively common disorder affecting about 33% of population transported by various means of transport [19].

In our study, the patient who had had the anamnestic data about prior kinetosis had significantly higher values of PONV in the first eight hours after the surgical intervention compared to the patients who had not had anamnestic data about prior kinetosis.

PONV is normally monitored during the first 24 hours; PON and POV in the first four hours are defined as the

so-called early PONV, and in the later period of 4–24 hours as late or delayed PONV [21]. In our study, the mean value of PONV during the first four hours after surgery was significantly higher than in the later period. After the 8<sup>th</sup> hour, up to the 12<sup>th</sup> hour there was a slight increase in the mean value of PON.

The highest incidence of PON was in the 60th minute in patients treated by monotherapy, as high as 25%, whereas the highest incidence in the group in combined therapy occurs in the 15th postoperative minute, amounting to 15.7%. As regards POV, the highest incidence corresponds to PONV, so that in the group, receiving monotherapy it was in the 60th postoperative minute and amounted to 9.4%, and in the group in combined therapy, the incidence of POV was the highest in the 15th minute and was 6.3%.

Our study clearly showed a correlation between pain and PON, especially in early postoperative period. Data analysis produced results showing a statistically significant difference in the mean value of PON in the fourth hour in patients who received NSAID and opioids, as well as combination of these ( $p = 0.002$ ), for postoperative analgesia (Table 6). Earlier studies had proved that the administration of opioids in postoperative analgesia, regardless of administration route, in the first 24 hours have nausea and vomiting as adverse effects [22]. Only descriptive statistical analysis was used in the study.

## CONCLUSION

As a common complication in patients undergoing gynecological laparoscopic surgical interventions, PONV requires administration of antiemetics for prevention of complications that can be associated with the occurrence of PONV in postoperative period. Our study has proved that the effect of combination of dexasone and metoclopramide is not inferior compared to the effect of monotherapy with granisetron. From the clinical aspect, this information is significant because the cost of combined therapy is significantly lower than the cost of monotherapy.

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## REFERENCES

- Odom-Forren J. Postanesthesia recovery. In: Nagelhout JJ, Plaus K, editors. *Nurse Anesthesia*. St. Louis, Mosby: Saunders/Elsevier; 2014; 1:1224–43.
- Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014; 118(1):85–113.
- Cao X, White PF, Ma H. An update on the management of postoperative nausea and vomiting. *J Anesth*. 2017; 31(4):617–26.
- Kakuta N, Tsutsumi YM, Horikawa YT, Kawano H, Kinoshita M, Tanaka K, et al. Neurokinin-1 receptor antagonism, aprepitant, effectively diminishes post-operative nausea and vomiting while increasing analgesic tolerance in laparoscopic gynecological procedures. *J Med Invest*. 2011; 58(3-4):246–51.
- Pym A, Ben-Menachem E. The effect of a multifaceted postoperative nausea and vomiting reduction strategy on

- prophylaxis administration amongst higher-risk adult surgical patients. *Anaesth Intensive Care*. 2018; 46( 2):185–9.
6. Milnes V, Gonzalez A, Amos V. Aprepitant: A New Modality for the Prevention of Postoperative Nausea and Vomiting: An Evidence-Based Review. *J Perianesth Nurs*. 2015; 30(5):406–17.
  7. Kovac AL. Update on the management of postoperative nausea and vomiting. *Drugs*. 2013; 73(14):1525–47.
  8. drugs.com[internet] A-Z Drug index. Available from: <http://www.drugs.com>
  9. Awad K, Ahmed H, Abushouk AI, Al Nahrawi S, Elsherbeny MY, Mustafa SM, et al. Dexamethasone combined with other antiemetics versus single antiemetics for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: An updated systemic review and meta-analysis. *Int J Surg*. 2016; 36(Pt A):152–63.
  10. Habib AS, Gan TJ. Combination therapy for postoperative nausea and vomiting- a more effective prophylaxis? *Ambul Surg*. 2001; 9(2):59–71.
  11. Alkaissi A, Dwaikat M, Almasri N. Dexamethasone, metoclopramide, and their combination for the prevention of postoperative nausea and vomiting in female patients with moderate-to-high risk for PONV undergoing laparoscopic surgery. *J Evolution Med. Dent Sci*. 2017; 6(75):5353–9.
  12. Wallenborn J, Gelbrich G, Bulst D, Behrends K, Wallenborn H, Rohrbach A, et al. Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone: randomised double blind multicentre trial. *BMJ*. 2006; 333(7563):324.
  13. D'souza N, Swami M, Bhagwat S. Comparative study of dexamethasone and ondansetron for prophylaxis of postoperative nausea and vomiting in laparoscopic gynecologic surgery. *Int J Gynec Obstet*. 2011; (113):124–7.
  14. Apfel CC, Heidrich FM, Jukar-Rao S, Jalota L, Hornuss C, Whelan RP, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. *Br J Anaesth*. 2012; 109(5):742–53.
  15. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder J, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *N Engl J Med*. 2004; 350(24):2441–51.
  16. Cohen MM, Duncan PG, DeBoer DP, Tweed WA. The postoperative interview: assessing risk factors for nausea and vomiting. *Anesth Analg*. 1994; 78(1):7–16.
  17. Bonica JJ, Crepps W, Monk B, Bennett B. Postanesthetic nausea, retching and vomiting; evaluation of cyclizine (marezine) suppositories for treatment. *Anesthesiology*. 1958; 19(1):532–40.
  18. Bellville JW, Bross IDJ, Howland WS. Postoperative nausea and vomiting IV: factors related to postoperative nausea and vomiting. *Anesthesiology*. 1960; 21:186–93.
  19. Srivastava A, Pai Raghavendra K, Parate LH. A comparative study of palonosetron versus palonosetron and dexamethasone for the prevention of postoperative nausea and vomiting in subjects undergoing laparoscopic surgeries: A randomized double-blind control study. *Karnataka Anaesthesia Journal*. 2016; 2(1):19–24.
  20. Pace NL, Carlisle J, Eberhart LHJ, Kranke P, Trivella M, Lee A, Bennett MH. Prediction models for the risk of postoperative nausea and vomiting. *Cochrane Database of Systematic Reviews*. 2014; 9 (Art. No.: CD011318)
  21. White PF, Sacan O, Nuangchamnon N, Sun T, Eng MR. The relationship between patient risk factors and early versus late postoperative emetic symptoms. *Anesth Analg*. 2008; 107(2):459–63.
  22. Aleyasin A, Hayatshahi A, Saffarieh E, Torkamandi H, Aghahosseini M, Hanafi S, et al. No Superiority of Granisetron Over Metoclopramide in Prevention of Post-operative Nausea and Vomiting: A Randomized Clinical Trial. *J Obstet Gynaecol India*. 2014; 64(1):59–62.

## Поређење ефикасности комбинације дексазона и метоклопрамида са монотерапијом гранисетроном у превенцији постоперативне мучнине и повраћања

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### САЖЕТАК

**Увод/Циљ** Постоперативна мучнина и повраћање (ПОМП) једна је од најчешћих постоперативних компликација. Инциденција ПОМП код одрасле популације је 20–30%, а може да буде и до 80% у популацији са повишеним ризиком, као што су гинеколошке и лапароскопске операције.

Циљ ове студије је поређење ефикасности комбиноване у односу на монотерапију у превенцији ПОМП код гинеколошких и лапароскопских операција.

**Метод** Спроведена је опсервациона проспективна кохортна студија на узорку од 64 болеснице (32 болеснице по групи) оперативно лечене у Служби за гинекологију и акушерство Опште болнице у Суботици, у периоду јануар–март 2017. Надлежни анестезиолог је за превенцију ПОМП у складу са протоколом давао болесницама комбинацију дексазона и метоклопрамида или гранисетрон у монотерапији. За статистичку обраду добијених резултата коришћен је комерцијални програмски пакет *SPSS*, верзија 20.

**Резултати** Демографске карактеристике болесница су хомогене и статистички значајну разлику показују само у карактеристикама дужина пушачког статуса и максималном интраабдоминалном притиску током оперативног захвата. Укупна инциденција постоперативне мучнине у петом, 15. и 60. минути после операције била је 15,6%, 17,2% и 18,7%, а у четвртном, осмом, 12. и 24. сату после операције била је 12,5%, 7,8%, 10,9% и 6,2%. Инциденција постоперативног повраћања у петом, 15. и 60. минути после операције била је 1,6%, 4,7% и 4,7%, а у четвртном, осмом, 12. и 24. сату после операције била је 1,6%, 3,2%, 1,6% и 1,6%.

**Закључак** У истраживању смо доказали да ефекат комбинације дексазона и метоклопрамида није слабији у односу на ефекат монотерапије гранисетроном.

**Кључне речи:** постоперативна; мучнина; повраћање