

# The Effect Of Combined Dexamethasone–Ondansetron Versus Dexamethasone And Ondansetron Alone For Prevention Of Nausea And Vomiting After Outpatient Gynecological Diagnostic Laparoscopy

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## Abstract

Background: Nowadays, lots of laparoscopic surgeries, especially gynecologic procedures are performed on an outpatient basis and early discharges of patients without any complication is very important. One of the most common causes that impair patient discharge is postoperative nausea and vomiting. The aim of this study is to evaluate the prophylactic effect of combined antiemetic therapy for prevention of PONV in gynecological diagnostic laparoscopy. Methods and materials: In this study, 105 women with ASA physical class of 1-2 who were underwent diagnostic laparoscopy, randomly divided to 3 groups. First group received 8 mg dexamethasone before induction of anesthesia, second group received 4mg ondansetron before the end of surgery and third group received both of them in the same manner. Incidence, severity (Bellville score) and the frequency of PONV as well as need to rescue treatment, total dose of antiemetic therapy and the number of injections and any probable complication were controlled and recorded. Data were analyzed using spss 16. Results: There was not any different in demographic data. The incidence of PONV was low in all groups, but the severity, frequency and rescue anti emetic for treatment were significantly lower in combined therapy group than two groups. There was no significant different in other postoperative complication. Conclusion: Combined antiemetic therapy with dexamethasone and ondansetron for the prevention the of PONV decrease the severity and frequency of PONV and need to rescue treatment, also combination treatment were more effective than using these drugs alone, without any complication.

## INTRODUCTION:

Nowadays, laparoscopic procedures are one of the most common surgeries, particularly in ambulatory setting. Smooth and safe anesthesia along with better surgical condition and early recovery without any complication are the aim of an appropriate anesthesia for these procedures, especially, regarding that the monitoring of laparoscopic surgeries are performed as an outpatient bases (1,2). Postoperative pain, anesthetic related sedation more commonly postoperative nausea and vomiting (PONV) are one of the most important causes of late discharge or even hospitalization of the patients with significant increase in costs. Postoperative or post-anesthesia nausea and vomiting is among the unfavorable complications, which can be associated with serious side effects in severe causes (3-6). In comparison with open surgeries, laparoscopic procedures are

associated with high prevalence (40%-80%) of PONV because of peritoneal irritation of it from abdomen cavity (1-7). Therefore, choice of appropriate anesthesia protocols for prevention of PONV has significant importance, however, despite any presentational strategies; these complications yet remained the main problem especially after gynecologic laparoscopies that necessitate prophylactic treatment.

In the recent years, many protocols and medications were used for prophylaxis of PONV including serotonin receptor antagonists (5-HT<sub>3</sub>), metoclopramide, antihistamine, corticosteroids had been effective to same degree in the prevention of PONV (3-6,8,9).

And now using the combination therapy with different antiemetic has been studied and showed some variable

results (7, 8,10).

Recently with the concern of PONV after outpatient gynecologic laparoscopies and the effectiveness of some antiemetics with different mechanisms, this study has been designed to compare the effectiveness of the combination of dexamethasone –ondansetron with each of these agents alone in the prevention of PONV in outpatient gynecologic laparoscopy in order to reach to an difficult rapid prophylactic protocol and safe discharge of patients with the least costs.

## **METHOD AND MATERIALS:**

After obtaining approval from Medical University ethics committee and written informed consent, 105 female patients aged 20-50 year with ASA class I and II undergoing outpatient diagnostic laparoscopy were enrolled in this study. Patients with ASA class III or higher, those with cardiovascular, respiratory, gastrointestinal disease, diabetes, previous history of PONV or nausea and vomiting due to any reason preoperative use of antiemetics or opioids were excluded from study. Patients were randomly divided to 3 groups By Rand list software. After entrance to operation room, vital signs including heart rate , NIBP, Sao2 measured . Iv-line (with angiocat 18) for intravenous liquids and drug infusion were detected. Before anesthesia induction, group 1 patients received (dexamethasone) 8 mg as IV, group 2 patients (ondansetron) received 4 mg as IV in the end of surgery and group 3 patients received 8 mg dexamethasone in time of induction of anesthesia and 4mg ondansetron in the end of surgery. Immediately after drug infusion, induction was done with 2mg midazolam, 1-1.5µg/kg fentanyl, 2-3 and then 2-3 ml/kg propofol ,0.3-0.4 mg/kg atracoroyum , all patients incubated with laryngeal mask number 3 or 4. For maintenance of anesthesia, we used of 50-75 µ/kg/min .Patients ventilated with tidal volume 7-10ml/kg and fIPPV=10-12 in minute .Intraoperative ,vital signs such as HR,BP(per3 minute),ECG(lead 2),ETco2 measured and recorded. The end of surgery, LMA extubated in deep anesthesia and reversed ,then patient conducted to recovery. In PACU, patients controlled for having nausea and vomiting and if occur, its severity measured with Bellville score (including 0=without nausea and vomiting, 1=sense of nausea,2= sense of nausea,3- having vomiting).If its severity equal with 2 or 3, anti emetic drug (metocloperamide) 10 mg IV infused slowly. Nausea and vomiting frequency and total dose of anti emetic drug, other complications as pain, agitation, lethargy and .....basic vital

signs and in the end , discharge of patient time control and recorded. All data analyzed with statistical methods (frequency, percentage,  $\mu \pm SD$ ), chi-square , Fisher for independent groups and by spss 16.0. P value <0.05 was statistically significant.

Statistical analysis :According to previous studies (Yanak Erkan et al.)(14), a sample size of 35 patients would be required in each group to have a 95% chance with a one sided test of detecting a 20% relative reduction in PONV with 80% power and with an expectation 10% dropout rate. The spss version 16 was used for statistical analysis. Results were calculated as mean± standard deviation. Parametric data were analyzed with one- way analysis of variance (ANOVA), and Chi- square test or fisher exact test were used for non parametric variables. P value less than 0.05 was considered significant.

## **RESULTS:**

105 women studied in 3 groups:

35 patients in group 1 (dexamethasone) 8 mg as IV, 35 patients in group 2 (ondansetron) received 4 mg as IV in the end of surgery and concordance with extension of trocars, 35 patients in group 3 received 8 mg dexamethasone in time of induction of anesthesia and 4mg ondansetron in the end of surgery.

The age of patients was 19-46 (group1=  $30.51 \pm 6.9$ , group 2 =  $31.11 \pm 6.2$  , group 3 =  $33.66 \pm 5.7$ ) . Weight of patients was in ( group 1=  $67.66 \pm 9.8$ , group2=  $67.97 \pm 8.7$  , group 3 =  $69.86 \pm 9.1$ ). 31 patients in group 1 and group 2 had ASA 1, also in group 3, 28 (80%) had ASA 1. Medium time of operation in was (group 1 =  $48.14 \pm 18.4$  , group 2 =  $47.86 \pm 19.3$  , group 3 =  $46.57 \pm 18.6$ ).

Mean of basic systolic blood pressure was in ( group1=  $121.83 \pm 10.43$  , group 2 =  $123.91 \pm 12.5$  , group 3 =  $122.98 \pm 14.36$ ) and mean of diastolic blood pressure was in (group 1 =  $76.17 \pm 12.1$ , group 2 =  $77.20 \pm 12.7$  , group 3 =  $75.8 \pm 12.5$ ). In the entrance time to recovery unit , mean of systolic blood pressure was in (group 1=  $118.43 \pm 16.02$  , group 2=  $117.63 \pm 12.7$ , group 3 =  $121.34 \pm 11.9$ ) and mean of diastolic blood pressure was in (group 1 =  $73.80 \pm 10.3$ , group 2 =  $70.83 \pm 12.2$  , group 3 =  $75.03 \pm 11.5$ ). None of these variables had no statistically significant relationship.

In group 1, 22 persons had not nausea and 13 patients had nausea or vomiting that nausea severity score was in 2 patients = 1 , 4 patients = 2 and in 7 patients = 3. Also,

frequency of vomiting in group 1 was in five patients equal or higher than 3 times and in 6 patients was less than 3 times. In group 2, 27 patients had no nausea and 8 patients had vomiting or nausea that nausea severity score was in 3 patients = 1, in 2 patients = 2 and in 3 patients = 3. In group 3, 28 had no nausea and 7 patients had vomiting or nausea that nausea severity score was in 5 patients = 1, in 2 patients = 2. Also, frequency of vomiting in group 3 was in only 1 patient higher than 1 times and less than 3 times. This shows that in group user of combination of dexamethasone and ondansetron, severity of nausea and vomiting was significantly less than other groups ( $p=0.02$ ) and also, its frequency was significantly less than other groups ( $p=0.04$ ).

Using of additional drug or drugs in severe cases as rescue treatment was shown in table 1.

Median of infusion times of rescue treatment were in group 1 =  $0.26 \pm 0.5$ , in group 2 =  $0.17 \pm 0.56$ , group 3 =  $0.16 \pm 0.2$ . The comparison of 3 groups showed no significant differences ( $p=0.1$ ).

The survey of probably complications in recovery unit indicated that: pain was seen in 45.7% (group 1), 37.1% (group 2), 61% (group 3) and 34.4% (group 1), 31.1% (group 2), 28.6% (group 3) agitated.

Mean time of discharge of recovery was in group 1 =  $3.2 \pm 1$ , group 2 =  $3.3 \pm 7.4$ , group 3 =  $3.5 \pm 0.8$  hours. No significant differences between groups ( $p=0.43$ ).

Of all patients (105), only 6 person (4 of group dexamethasone, 1 of group ondansetron and 1 of combination group) need to hospitalization because of frequently vomiting in 2 patients, other admitted due to surgery and monitoring, agitation.

## **DISCUSSION:**

The results of our study shows that anti- emetics combination therapy has more beneficial effect for prevention of PONV in gynecologic laparoscopies as compared with single drug administration. Regarding to all patients undergoing diagnostic gynecologic laparoscopy are women and often young, have some strong risk factors for PONV. On the other hand, their procedure was done as an ambulatory surgery and their safe discharge without any problem is significantly important. So prophylactic use of antiemetics for prevention of PONV and to avoid late discharge or uneven hospitalization of these patients is an important issue. According to all three groups are well

matched, the difference in the incidence and severity of PONV should be attributable to the effects of administered medicine. Dexamethasone was administered at induction of anesthesia due to delayed its onset time, and has been found to be effective as an antiemetic agent due to central block of nucleus tracks solitaires and its effect lasts for a long time because a biologic half – life of 36 to 75 hours and should theoretical has a larger duration of prophylaxis. however the results of our study showed that the combination of two drugs (dexamethazone and ondansetron) with different mechanism significantly lower the incidence and severity of nausea and vomiting after gynecological laparoscopy more than each drug used alone, and with fewer patients requiring rescue treatment. Ondansetron is the most commonly used prophylactic serotonin subtype 3 antagonists in daily clinical practice for the prevention of PONV. According that the half – life of ondansetron is approximately 3.5 – 4 hours in adults, it was suggested to administrate the drug at the end of surgery especially in procedures last more than 2 hours (13).

Also, this study showed that, Severity of emetic episodes especially itching and vomiting was lower in patients received combination therapy and rescue treatment in severe cases was low in this group. Some other study has the same results. One study conducted with Dabboes et al resulted had the combination of dexamethasone with ondansetron and grainstron in prevention of nausea and vomiting was more effective than each medication used alone (10).

Michel J et al compared different doses of dexamethasone with ondansetron and resulted that combination therapy especially with doses higher than 4 mg of dexamethasone have better control for the prevention of PONV (11).

Biswas BN et al study on postoperative nausea and vomiting after laparoscopic tubal ligation also show the same results (12).

Maddi MM et al showed that dexamethasone and metoclopramide with combined dexamethasone – ondansetron and showed that combination therapy was more better for prevention of PONV (13).

In our study the incidence of PONV was not different in three groups. Although the overall incidence was decreased. In contrast to our and these studies, Yamak K et al showed that dexamethasone alone was more effective than ondansetron and grainstron for prevention of PONV after laparoscopic cholecystectomy (14). Also Sublin et al resulted

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that combination therapy with dexamethasone and ondansetron had no prophylactic effect for PONV after laparoscopic cholecystectomy(7)

However Coloma M et al studied the effect of dexamethasone on the recovery profiles after outpatient surgeries and showed that in addition to prevention effect of dexamethasone on PONV, it can decrease postoperative pain and discharge time of outpatient surgeries probably via its anti inflammatory effects (17).

### CONCLUSION:

Regarding to multifactorial origins causes of PONV and different mechanisms responsible for it, and also contribution of patient factors, type of surgery and anesthesia related factors, using combined antiemetic agents with different antiemetic mechanisms can prevent PONV more effective than each one alone.

**Table 1**

The comparison of nausea and vomiting severity and frequency

maximum	Std.error	Std.deviation	mean	N	Vomiting frequency
5	0.200	1.183	0.31	35	Ondansteron group
5	0.248	1.467	0.71	35	Dexamethasone group
2	0.057	0.338	0.06	35	Ondansetron + dexamethasone group
5	0.110	1.128	0.36	105	

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