

# Comparative Study Of Single Dose Intravenous Dexamethasone, Ondansetron And Ondansetron Plus Dexamethasone As Prophylactic Anti-Emetic Therapy In Patients Undergoing Laparoscopic Gynaecological Surgery

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## Abstract

PONV occurs frequently after day case gynaecological surgery both 5-HT<sub>3</sub> antagonists and dexamethasone are superior to placebo in the prophylaxis of PONV in his setting. Our study has compared. The efficacy of ondansetron plus dexamethasone with each anti-emetic alone for the prevention of PONV in patients undergoing day case gynaecological surgery. Present study was undertaken on 120 patients in the age group of 18 to 65 years with ASA grades I & II undergoing gynaecologic laparoscopic intervention under general anaesthesia. Group 1 received Inj. Ondansetron 4mg with Inj. Dexamethasone 8mg as single dose I V bolus 5 minutes before induction of anaesthesia. Group 2 received Inj. Ondansetron 4mg as single dose I V bolus 5 minutes before induction of anaesthesia. Group 3 received Inj. Dexamethasone 8mg as single dose I V bolus 5 minutes before induction of anaesthesia. A standard anaesthetic protocol was used in all the patients. 5 min prior, the patients received the anti-emetic as per their groups. Induction of general anaesthesia was done with Inj. Propofol 2 – 3 mg / kg IV. Intubating conditions were achieved with Inj. Suxamethonium 2 mg / kg I V. Trachea was intubated with appropriate sized cuffed PVC endotracheal tube. General anaesthesia was maintained with O<sub>2</sub> + N<sub>2</sub>O::40:60, skeletal muscle relaxation was maintained with Inj. Atracurium 0.5mg / kg as loading dose and 0.05mg/kg as supplemental doses. The duration of anaesthesia, surgery, pneumoperitoneum was noted. Nasogastric tube was introduced after induction & suction of gastric contents was done before recovery & was removed after extubation. The patients were evaluated at regular intervals of time in the post operative period for complaints of nausea, vomiting. As per our observations, the incidence of PONV in 0 – 4 hours post operative period was statistically significant. The observations were inconclusive beyond the 4 hour period in combination group as well as either drug group. Combination of Inj. Ondansetron 4mg with Inj. Dexamethasone 8mg proved to be more efficacious over either drug alone.

## INTRODUCTION

Pain is not always the patients prime concern in the post operative period, many patients will place nausea and vomiting as the most unpleasant consequence. PONV has been associated with use of general anaesthesia ever since the ether and chloroform era when the reported incidence was 75-80%. PONV has consequence more far reaching than hitherto appreciated physical, metabolic, psychological, economical. There are a number of factors influencing the occurrence of PONV which may be briefly summarized as :-

- Patient factors
- Pre- operative factors
- Intra operative factors

- Anaesthetic factors
- Anaesthetic technique
- Surgical factors
- Post operative factors

Laparoscopic surgery is one condition where the risk of PONV is particularly pronounced. This technique first gained popularity with its use in gynaecologic procedures which began in 1970. The patient group in these cases was predominantly young. Early ambulation and decreased morbidity are the advantages of the drug therapy.

This study endeavours to compare the efficacy of

Ondansetron and dexamethasone combination and either drug alone in prevention of PONV when given as a single dose IV premedication in Gynaecological laparoscopic surgery under GA. The incidence of Side - effects of these drugs were also be noted.

## PATIENTS AND METHODS

After approval from the hospital ethics committee a prospective, randomized Study was conducted..

Patients included were in the age group of 18 years to 65 years, ASA grade I or grade II. Were in

Patients ASA grade III or above,with a previous history of drug reaction to any of the drugs used in this study.history of PONV, history of motion sickness,those who have received anti-emetics in the previous 24 hours,patients with evidence of respiratory infection. Patients were administered the study drugs preoperatively and general anaesthesia was given.monitoring included cardioscope, pulse oximeter, sphygmomanometer,and capnography.

Patients were followed up immediately after surgery , then after 1 hr, 4 hrs, 12 hrs & 24 hrs.

In the follow up following observation were made :

- Complaints of nausea
- episodes of vomiting

Theses observation were recorded by an independent recovery room personnel who did not know which anti-emetic each patient had received. Every complaint of nausea and every episode of vomiting was recorded.

A rescue anti-emetic in the form of Inj. Granisetron 1mg was given if the patient complained of nausea or had an episode of vomiting.

Totally effective anti-emetic response was defined as no vomiting and no request for additional anti-emetic.

Nausea was graded using a 4 point linear VAS (Visual Analogue Scale).

\* = No nausea

N1 = Mild nausea

N2 = Moderate nausea

N3 = Severe nausea.

Patients were questioned regarding complaints of headache and dizziness and were assessed for the presence of sedation, hypotension, extrapyramidal reaction and hypersensitivity reactions.

The observations were tabulated and special observations recorded, tabulated and analyzed statistically using and Z test for proportions wherever appropriate.

## RESULTS

In our study :

the mean age in the 3 groups were found to be

Group 1 – 35.65, Group 2 – 32.62, Group 3 – 33.82 respectively.

the mean weight of the patients in the 3 groups were found to be 58.75,

56.65, 57.65 respectively.

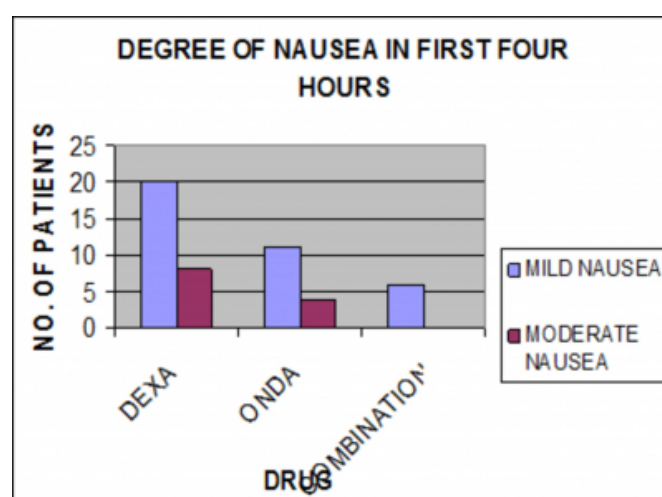
Therefore the age and the weight distribution was comparable in the 3 groups.

Average number of patients with a past history of PONV was 31, as compared to migraine 20 and menstruation 11.

Average number of patients for diagnostic scopy was found to be 17.3 as compared to 33.6 for laparoscopic sterilization.

**Figure 1**

Table 1

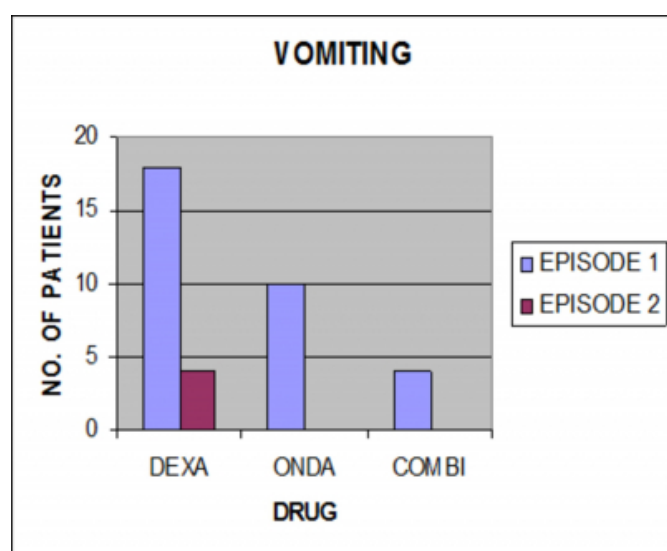


The 95% confidence interval for the difference of proportions is (0.36- 0.73). The calculated value of Z is 5.98 which is beyond the confidence interval (CI). So the

proportion of patients who experienced nausea during first four hours post operative period is significantly less in combination group than the dexamethasone. Similarly 95% confidence interval for combination versus ondansetron group is 0.03-0.41 and the calculated Z value is 2.36 which is beyond the CI so the combination group is better than Ondansetron group.

**Figure 2**

Table 2: Severity Of Vomiting In The First Four Hours



The 95% confidence interval for the difference of proportions for the combination group versus dexamethasone group is 0.26 – 0.63. The calculated Z value is 4.89 which is beyond the CI, hence the combination group is better than the dexamethasone group.

The 95% confidence interval for the difference of proportions for the combination group versus ondansetron is – 0.01 to 0.31.

The calculated Z value is – 1.8 which is beyond the CI, hence the combination group is better than the ondansetron group.

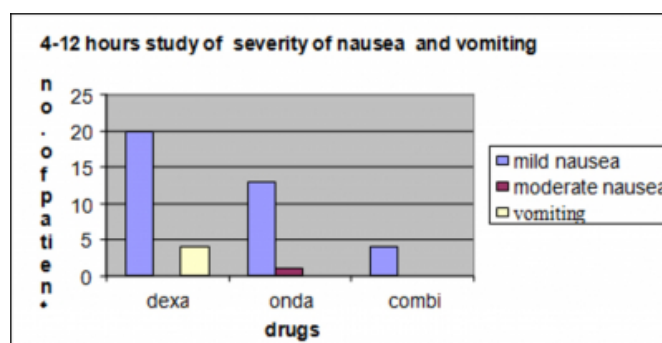
Nausea in ondansetron versus dexamethasone: 95% CI is 0.11 – 0.53

calculated Z value is – 3.08, which is beyond the CI hence ondansetron proves to be better than dexamethasone.

Vomiting in ondansetron versus dexamethasone: 95% CI is 0.09 – 0.50 calculated Z value is – 2.87, which is beyond the CI hence ondansetron proves to be better than dexamethasone.

**Figure 3**

Table 3



Applying the Z tests of proportions of equality, nausea and vomiting were studied and compared in 4 – 12 hours in post-operative period.

Combination group versus dexamethasone group:

Nausea: 95% CI is 0.21 – 0.58

Calculated Z value is – 0.33 which is beyond the CI so combination group is better than the dexamethasone group.

Vomiting: 95% CI is 0.007 – 0.192

Calculated Z value is – 2.1 which is beyond the CI so combination group is better than the dexamethasone group.

Combination group versus ondansetron group:

Nausea: 95% CI is 0.7 – 0.42

Calculated Z value is – 2.8 which is beyond the CI so combination group is better than the dexamethasone group.

Vomiting: statistical data insufficient so testing not possible.

Ondansetron group versus dexamethasone group:

Nausea: 95% CI is – 0.06 – 0.36

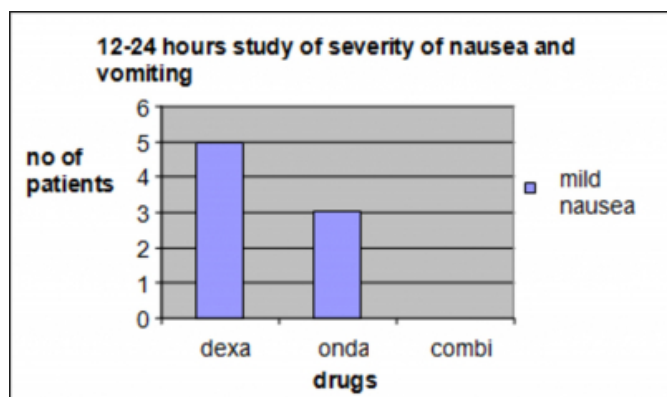
Calculated Z value is – 1.37 which is beyond the CI so ondansetron group is better than the dexamethasone group.

Vomiting: 95% CI is 0.007 – 0.192

Calculated Z value is – 2.1 which is beyond the CI so ondansetron group is better than the dexamethasone group.

**Figure 4**

Table 4



The study of severity of nausea and vomiting over 12-24 hours is statistically in conclusive. The bar diagram depicts combination group has minimal incidence as compared to individual drugs in the study.

**Figure 5**

Table 5: Incidence Of Adverse Effects

SIDE EFFECTS	DEXAMETHASONE	ONDANSETRON	COMBINATION
DROWSINESS	5	0	1
DIZZINESS	7	0	0
HEADACHE	0	4	3
FLUSHING	0	0	2
HEARTBURN	3	0	0

Headache, drowsiness and dizziness are the msot frequently occurring side effects but they prove to be statistically insignificant in all the three groups.

## DISCUSSION

It is generally accepted that outpatient surgical procedures are cost effective and efficient method of patient care. Nausea and vomitting after surgery can negate the benefits of outpatient surgery by increasing recovery time, intensity of nursing care and patient morbidity. Laparoscopic procedures have been known to cause more significant PONV because of the creation of pneumoperitoneum involved in the procedure. This has its effects by two to mechanisms , one of which is the stimulation of mechanoreceptors in the gut which are stimulated due to mechanical stretching of the structures in the creation of pneumoperitoneum. The second mechanism results from the absorption of CO<sub>2</sub>, which is used in the creation of

pneumoperitoneum. CO<sub>2</sub> is known to cause increased PONV by stimulation of nociceptors in the brain <sub>1</sub> .

Therefore Laparoscopic gynaecological procedures were chosen for the study. Knowing that no single drug has been found to be universally effective in the prevention of PONV it was decided to compare the efficacies of the two drugs in combination & single drug alone. Inj. Ondansetron 4mg & Inj. Dexamethasone 8mg as a single intravenous drug & in combination were studied. <sub>234</sub>

In the present study the two groups were comparable with respect to the age of the patients as well as ASA grades of the patients in each group. The procedures performed in each group were comparable in proportion.

In our study Inj. Ondansetron 4mg was the selected dose as it is said to be the lower acceptable dose to prevent PONV & did not alter vital signs nor prolong sedation Inj. Dexamethasone 8mg was selected as it is the standard used in our hospital & all studies before. <sub>5</sub>

The reported dose of Dexamethasone for prevention of PONV is 0.15mg / kg up to a maximum of 10mg I V yet favourable doses were also noted with a single dose of Inj. Dexamethasone 8mg in adult patients. <sub>6</sub>

The duration of anaesthesia, surgery & that of pneumoperitoneum have also been found to be significant influences on PONV. In our study the duration of anaesthesia was maximum 30 minutes & the duration of pneumoperitoneum was not more than 12 minutes on an average so statistically inconclusive.

Visceral / pelvic pain is a common cause of increased incidence of PONV. Anderson & Krogh found that the relief of pain was associated with reduction in the incidence of nausea. Preoperative Dexamethasone administration improves pain scores, reduces analgesic requirements, allows earlier oral fluid intake & improves post operative swallowing. These results may be attributed to the anti – inflammatory effect produced by Dexamethasone which may reduced local oedema & pain. <sub>7</sub>

Propofol to be an anti-emetic agent in subhypnotic doses of 10mg I V bolus. Modulation of subcortical structure could be a possible mechanism. Median plasma concentration of Propofol associated with an anti – emetic property was shown to be 343ng / ml. The concentration can be achieved by Propofol infusion of 10 – 20 mcg / kg / min. Propofol

given at the end of surgery as a bolus has been widely proclaimed as the sandwich technique & this has been shown to reduced PONV. <sup>8</sup>

In our study we found that the incidence of nausea in zero to 4 hours group was Group 1 – 17.3, Group 2 – 32.2, Group 3 – 47.2 Severe nausea was not observed in either group & the incidence of mild & moderate nausea were significantly less in group 1 & 2.

The incidence of episodes of vomiting in 0 to 4 hours was statistically significant in Dexamethasone group where one episode was 42.2% And Incidence Of Two Episodes Were 10%.The incidence of vomiting in group 1 and 2 was 10% each , these patients were posted for MTP with laparoscopic tubal ligation, on obstetricians demand Inj. Methergin 2 cc I M was given for uterine contractility. These patients had vomiting which responded to Inj. Metoclopramide 10mg. This incidence can be considered as treatment failure in group 1 & group 2 patients. Our study demonstrated a significant difference between group 1,2,3 in 0 to 4 hours period. This difference failed to maintain statistical significance overall (0-24hours).Mild nausea was observed in group 3 patients over 24hours. <sup>2</sup>

95% confidence intervals show a trend suggesting that the combination group (Dexamethasone & Ondansetron) has definitely some benefit over individual drugs.

There is no statistically significant difference in anti – emetic efficacy or side – effect profile when one of 5 HT antagonist is combined with Dexamethasone & that both combination regimes are significantly more effective than 5 HT alone. <sup>9</sup>

No patient required hospital admission for PONV. The most frequently reported adverse events were dizziness, headache, drowsiness but there were no statistically significant difference between the groups. <sup>10</sup>

From the above discussion and comparison of various studies it has been concluded by various authors the need to use anti – emetic as a part of premedication to prevent PONV in laparoscopic interventions under general anaesthesia. The incidence of vomiting in group 3 was statistically significant. Methergin induced vomiting in group 1 & group 2 was the only significant finding. There were no incidences of severe vomiting in either group. The

hallmark of this study has been the incidence of PONV in 0 – 4 hours post operative period was statistically significant. The observations were inconclusive beyond the 4 hour period in combination group as well as either drug group can be answered by the limited sample size.

So we conclude, Combination of Inj. Ondansetron 4mg with Inj. Dexamethasone 8mg proved to be more efficacious over either drug alone. The incidence of side - effects was minimal with the combination as well as either drug given alone.

## ACKNOWLEDGMENTS

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