Abstract

**Purpose:** To compare the efficacy of ondansetron-dexamethasone combination with ondansetron alone for prevention of postoperative nausea and vomiting (PONV).

**Methods:** This double blind, randomized, prospective, placebo controlled study was carried out in 120 patients, aged 20-60 yr, American Society of Anesthesiologists-I and II physical status posted for exploratory laparotomy for various clinical conditions under general anaesthesia. The patients were divided into three groups of 40 each.

Patients in each group received either 4ml Normal Saline or injection Ondansetron 4mg(2ml) + 2ml Normal Saline or injection Ondansetron 4mg (2ml) + injection Dexamethasone 8mg(2ml), one of the three regimes for prevention of PONV before induction.

Nausea and vomiting were looked from 0 min upto 24 hours. Retching and vomiting were grouped together under common term 'emetic episodes'.

**Results:** Though ondansetron was effective in controlling postoperative nausea, the ondansetron plus dexamethasone combination was more effective overall. Though ondansetron was effective in reducing postoperative emetic episodes, the combination of ondansetron plus dexamethasone was more effective. The requirement for rescue antiemetic was less in ondansetron group and least in ondansetron plus dexamethasone group. There was no significant difference between pain intensity and sedation between these groups at any time. Only adverse effect reported was headache in ondansetron and ondansetron plus dexamethasone groups.

**Conclusion:** Ondansetron plus dexamethasone combination is more effective in reducing incidence of PONV without causing any major side effects. Throughout the study, ondansetron plus dexamethasone combination was superior to ondansetron alone in all respects pointing towards the potentiating effect of dexamethasone.

**Keywords:** PONV, Ondansetron, Dexamethasone, General Anaesthesia

1. Introduction

Nausea and vomiting is a common and distressing postoperative complication with an incidence of 25-43% after both inpatient and day care surgery. Patients rate freedom from postoperative nausea and vomiting (PONV) as their most
important postoperative requirement. Surgical complications such as abdominal wound dehiscence, bleeding beneath skin flaps and loss of vitreous fluid following intraocular surgery may follow PONV.

The search for rapid acting antiemetic with long duration without above side effects led to the introduction of ondansetron, a 5HT3 receptor antagonist, shown to be effective in reducing PONV following various surgical procedures. Dexamethasone has been found to be effective in the control of nausea and vomiting following chemotherapy and also effective in reducing incidence of PONV following surgery.

The present study was carried out to determine effect of ondansetron alone and in combination with dexamethasone for patients undergoing exploratory laparotomy for various clinical conditions under general anaesthesia as the incidence of PONV is described as high in these patients.

2. Material And Methods:

The present study has been carried out in the Department of Anaesthesiology J.N.M.C and Acharya Vinobha Bhave Rural Hospital, Sawangi during the period of July 2010 to August 2012. This is a randomized, prospective, double blind, Placebo controlled study in which 120 patients posted for exploratory laparotomy for various clinical conditions under general anaesthesia were studied, after the approval from the institutional Ethical Committee and written informed consent. All the patients belonging to ASA I - II of different age groups and weighing 30-80 kg were included in this study. At the pre-anaesthetic visit the patients were familiarized with post-operative questionnaires and postoperative nausea and vomiting score, as described later, Tablet diazepam 10 mg was given the night before surgery to all patients.

The patients were divided into three groups of 40 each.

Patients received one of the three regimes for prevention of PONV before induction.

Group P : Received 4 ml Normal saline I.V.

Group O : Received injection Ondansetron 4 mg (2 ml) + 2 ml Normal Saline.

Group OD : Received injection Ondansetron 4 mg (2 ml) and injection Dexamethasone 8 mg ( 2 ml).

Standard protocol of Balanced anaesthesia followed for each patient with endotracheal intubation.

Efforts were made to keep gastric distension to minimum using low airway pressure ventilation. After endotracheal intubation, nasogastric tube was placed to ensure baseline emptying of stomach, air and gastric contents. Intra operative hydration was corrected with crystalloids, blood loss was assessed and corrected.

Operative data included type of surgery (ovarian mass, ovarian cyst, ectopic pregnancy, gall stones, appendicular lump, appendicular abscess, exploratory laparotomy), induction dose of propofol, amount of opioids administered, duration of surgery, estimated blood loss and urine output.

At the end of procedure Patients were shifted to the recovery room for postoperative observation. Nausea and vomiting were looked from 0 min upto 24 hours. Retching and vomiting were grouped together under common term ‘emetic episodes’.

Postoperatively rescue antiemetic was given if vomiting occurred, or nausea lasting more than 10 minutes. Injection metoclopramide was used as a rescue antiemetic in the dose 10 mg I.V.

Pain was observed with visual analog scores (VAS) on a scale of 0 -10 at 2, 12 and 24 hours interval.

Mild Pain : 1 – 3

Moderate Pain : 4 - 7

Severe Pain : 8 - 10

Sedation was observed with a five - point rating scale:

Completely awake, open eyes : 4

Drowsy, closed eyes : 3
Asleep, responds to oral call : 2
Asleep responds to touch or pain : 1
Does not respond : 0

We also observed the patients for side effects if any. The primary end point was a complete response, as defined by no nausea or emetic episode during 24-hour period.

The data was collected and expressed as Mean ± Standard Deviation. For statistical analysis one way analysis of variance (ANOVA) test by SPSS software 15.0 for windows 7 was used, and ‘p’ value < 0.05 was considered as statistically significant.

3. Observations and Results

Table 1: Patient characteristics (Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Ondansetron</th>
<th>Ondansetron + Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in Years</td>
<td>36.62 ± 9.39</td>
<td>35.82 ± 8.94</td>
<td>36.30 ± 9.46</td>
</tr>
<tr>
<td>Weight in Kilogram</td>
<td>53.20 ± 8.05</td>
<td>52.65 ± 5.73</td>
<td>49.85 ± 5.41</td>
</tr>
<tr>
<td>Duration of surgery</td>
<td>99.25 ± 9.17</td>
<td>97.50 ± 8.40</td>
<td>98.50 ± 8.02</td>
</tr>
</tbody>
</table>

Table 2: Distribution of Patients according to type of surgery in all the three groups:

All the patients underwent exploratory laparotomy for various surgical and gynecological pathologies.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Placebo</th>
<th>Ondansetron</th>
<th>Ondansetron + Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Pathology</td>
<td>09</td>
<td>10</td>
<td>08</td>
</tr>
<tr>
<td>Fallopian Tube Pathology</td>
<td>04</td>
<td>03</td>
<td>06</td>
</tr>
<tr>
<td>Appendicular Pathology</td>
<td>13</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Gallbladder Pathology</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Number of patients</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
</tbody>
</table>

All the groups were comparable with regards to age, weight and duration of surgery (p >0.05). The patients underwent exploratory laparotomy for different clinical conditions. (Table no. 1 & 2)

Table 3: Incidence of Nausea in all the three groups at varied time intervals:

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Ondansetron</th>
<th>Ondansetron + Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hours</td>
<td>14 (35%)</td>
<td>04 (10%)</td>
<td>02 (5%)</td>
</tr>
<tr>
<td>12 hours</td>
<td>30 (75%)</td>
<td>16 (40%)</td>
<td>04 (10%)</td>
</tr>
<tr>
<td>24 hours</td>
<td>32 (80%)</td>
<td>20 (50%)</td>
<td>04 (10%)</td>
</tr>
</tbody>
</table>

At 2 hours, 14 (35%) patients had nausea in the Placebo group compared with 4 (10%) in the Ondansetron group and 2 (5%) in the ondansetron plus dexamethasone group. The difference between placebo and ondansetron plus dexamethasone group was statistically significant (p < 0.05).

At 12 hours, 30 (75%) in the placebo group had nausea compared with 16 (40%) in the Ondansetron group and 4 (10%) in the ondansetron plus dexamethasone group. The difference was statistically significant when
a) Placebo group was compared with ondansetron group (p < 0.05).
b) Placebo group was compared with ondansetron plus dexamethasone group (p < 0.001).
c) Ondansetron group was compared with ondansetron plus dexamethasone group (p < 0.05).

At 24 hours, 32 (80%) patients in placebo group had nausea compared with 20 (50%) in Ondansetron group and 4 (10%) in ondansetron plus dexamethasone group. The difference was statistically significant when:
a) Placebo group was compared with ondansetron group (p < 0.05).
b) Placebo group was compared with ondansetron plus dexamethasone group (p < 0.001).
c) Ondansetron group was compared with ondansetron + dexamethasone group (p < 0.01).

**Table 4: Incidence of Emetic episode in all the three groups at varied time intervals:**

<table>
<thead>
<tr>
<th>Time</th>
<th>Placebo</th>
<th>Ondansetron</th>
<th>Ondansetron + Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hours</td>
<td>10 (25%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12 hours</td>
<td>20 (50%)</td>
<td>6 (15%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>24 hours</td>
<td>18 (45%)</td>
<td>10 (25%)</td>
<td>2 (5%)</td>
</tr>
</tbody>
</table>

At 2 hours, 10 (25%) patients in the Placebo group had an emetic episode, whereas none of the patients in ondansetron group or ondansetron + dexamethasone group had an emetic episode. The difference was statistically significant when:
a) Placebo group and ondansetron group were compared (p < 0.05).
b) Placebo group and ondansetron plus dexamethasone group were compared (p < 0.05).

At 12 hours 20 (50%) patients in the Placebo group had an emetic episode as against 6 (15%) in ondansetron group and 2 (5%) patients in ondansetron plus dexamethasone group.
The difference was statistically significant when:
a) Placebo group and ondansetron group were compared (p < 0.05)
b) Placebo group and ondansetron plus dexamethasone group were compared (p < 0.05).

At 24 hours, 18 (45%) patients in the Placebo group had an emetic episode compared to 10 (25%) in the ondansetron group and 2 (5%) patients in the ondansetron plus dexamethasone group.
The difference was statistically significant between placebo group and ondansetron plus dexamethasone group (p < 0.05).

**Table 5: Rescue Antiemetic given in all the three groups at varied time intervals:**

<table>
<thead>
<tr>
<th>Time</th>
<th>Placebo</th>
<th>Ondansetron</th>
<th>Ondansetron + Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30(75%)</td>
<td>12 (30%)</td>
<td>04(10%)</td>
</tr>
</tbody>
</table>

**Graph 1:** Mean Visual analog scores in all the three groups at varied time intervals
Table 6: Side Effects in all the three groups:

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Ondansetron</th>
<th>Ondansetron + Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Nil</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

4. Discussion

Postoperative nausea and vomiting is a common sequel of general anesthesia and a leading cause of delayed discharge and unanticipated hospital admissions after ambulatory surgery. Many factors have been thought to contribute to PONV and we tried to control most of them. Patients with a low threshold for vomiting such as gastroparesis, motion sickness, previous PONV and obesity were excluded from the study.

We selected ondansetron (5HT\textsubscript{3} receptor antagonist) as our study drug and the dose was selected as 4mg as it was found to be the optimal dose for prevention of PONV as mentioned in different studies\textsuperscript{12,13}. Suggestion on mechanism of action of dexamethasone include central or peripheral inhibition of production or secretion of serotonin, central inhibition of synthesis of prostaglandins or changes in the permeability of blood brain barrier to serum proteins\textsuperscript{6,8,9}. We selected dexamethasone as our study drug and dose selected was 8mg as it was found to be optimal dose for prevention of PONV as we found that ondansetron 4 mg reduced postoperative nausea with the effect being more pronounced at 12 and 24 hour duration than at 2 hours. The combination of ondansetron plus dexamethasone significantly reduced nausea at 2, 12 and 24 hours compared to Placebo group as well as ondansetron group. Thus combination of ondansetron plus dexamethasone was more effective in prevention of nausea, though ondansetron used alone significantly reduces the incidence of nausea as well owing to potentiation.

Our results were comparable with various studies conducted by Claybon et al 1994\textsuperscript{12}, Pearman et al 1994\textsuperscript{13}, Sung et al 1993\textsuperscript{16} and Helmer et al 1993\textsuperscript{17}.

We also found that ondansetron 4 mg reduced postoperative emetic episodes more effectively at 2 and 12 hours as against at 24 hours. The combination of ondansetron with dexamethasone was more effective as compared to ondansetron alone in reducing the incidence of postoperative emetic episodes at 2 hrs, 12 hrs and 24 hrs.

Our results were in confirmation with the results of the studies conducted by Rajeeva et al 1999\textsuperscript{18}, Biswas et al 2003\textsuperscript{19} and Elhakim et al 2002\textsuperscript{20}.

In our study, the requirement for rescue antiemetic was observed in 15 ( 75% ) patients in placebo group compared with 6 ( 30% ) in ondansetron group and only 2 patients ( 10% ) in ondansetron plus dexamethasone group ( Table no. 5 ). The difference was statistically significant at p <0.01 when ondansetron group was compared with placebo group.
The difference was statistically significant at p <0.001 when ondansetron plus dexamethasone group was compared with placebo group. However, the difference was not significant when ondansetron group was compared with ondansetron plus dexamethasone group p >0.05.

Results were comparable with studies conducted by Lopez et al 1996\textsuperscript{11} and Bano et al 2008\textsuperscript{21}. This effectively proves that ondansetron plus dexamethasone combination drastically reduces the need for rescue antiemetics. The findings in our study coincide with those of the above studies.

In our study we compared the incidence of postoperative pain in all the three groups at 2 hours, 12 hours and 24 hours according to the visual analog scale. It was observed that there was no significant difference in pain intensity between the groups at anytime (Graph 1).

These findings coincide with those of Lopez et al 1996\textsuperscript{11} and Wang et al 2012\textsuperscript{22} found no significant differences in pain intensity between all the three groups at any time interval.

In our study we compared the incidence of sedation in all the three groups at 2 hours, 12 hours and 24 hours using the five point sedation scale (Graph 2).

There was no significant difference in sedation with no patients in category 0, 1 or 2 of sedation at anytime during the study.

These findings are similar to those of Lopez et al 1996\textsuperscript{11} who found no significant difference in sedation with no patients in any of the groups being in category 0, 1 or 2 at anytime during the study.

The only adverse effect we found in our study was headache reported in 3 patients in ondansetron and 4 in the ondansetron plus dexamethasone group (Table no.6)

In the study conducted by Lopez et al 1996\textsuperscript{11}, headache was the most common adverse effect. Even Pearman et al 1994\textsuperscript{13} in his study noted headache to be the most common adverse effect. This might be related to ondansetron.

5. Conclusion

1) Though ondansetron was effective in controlling postoperative nausea, the ondansetron plus dexamethasone combination was more effective overall.
2) Though ondansetron was effective in reducing postoperative emetic episodes, the combination of ondansetron plus dexamethasone was more effective.
3) The requirement for rescue antiemetic was less in ondansetron group and least in ondansetron plus dexamethasone group.
4) There was no significant difference between pain intensity and sedation between these groups at any time.
5) Only adverse effect reported was headache in ondansetron and ondansetron plus dexamethasone groups.

It can thus be concluded from the study that ondansetron plus dexamethasone combination is more effective in reducing incidence of PONV without causing any major side effects. Throughout the study, ondansetron plus dexamethasone combination was superior to ondansetron alone in all respects pointing towards the potentiating effect of dexamethasone.

References


