EFFICACY AND TIMING OF SINGLE DOSE DEXAMETHASONE AS PROPHYLACTIC ANTIEMETIC IN MAJOR SURGERIES

FARHAT JALEEL, RIFFAT JALEEL, MOHAMMAD IQBAL AHSAN

ABSTRACT

Objective
To determine the efficacy of single dose intravenous dexamethasone, administered one hour before surgery as prophylactic antiemetic.

Study design
Single blinded, randomized, placebo controlled, interventional study.

Place & Duration of study
Usman Memorial Hospital Karachi, from January 2006 to June 2008.

Patients and Methods
Patients admitted for elective general and gynecological surgery, having ASA I or II class were selected. They were randomly allocated to receive either 2 ml (8 mg) dexamethasone or 2 ml of normal saline, one hour before surgery. Surgery was performed under general anesthesia by a single anesthetist. Wound site was infiltrated with 20 ml of 0.5% bupivacaine. Injection ketorolac 30mg I/V was given prior to extubation and 30 mg I/V twice daily thereafter. Supplemental analgesia was provided with injection nalbuphine 10 mg diluted and supplemental anti emetic used was dimenhydrinate 50 mg I/V as required.

Results
A total of sixty female patients were enrolled. They were divided into two groups, thirty in each (test group and placebo group). Mean age of the patients was 42 years in both the groups. 61.7% patients had cholecystectomy, 15% had herniorrhaphy, 16.7% underwent abdominal hysterectomy and 6.6% had benign ovarian cystectomy. Duration of operation and anesthesia were comparable in both the groups. In the entire 24 hours period after surgery nausea occurred in 30% patients in test group A as compared to in placebo group B 77% (p = 0.000), while vomiting in 10% of test group versus 40% of placebo group (p = 0.007). Timed observations revealed that nausea occurred in 23% versus 70%, 10% versus 30% and 0% versus 6.7% in the first 6 hours, 6 – 12 hours and 12 – 24 post-operative hours respectively. Similarly vomiting occurred in 6.7% versus 40%, 0% versus 6.7% and 3.3% versus 3.3% patients. The number of episodes of nausea and vomiting were significantly reduced in the test group as was the need for supplemental anti emetics.

Conclusion
Dexamethasone given as single I/V injection of 8 mg one hour before surgery is an effective drug for prophylaxis of post operative nausea and vomiting.

Key words
Post-operative nausea, Post-operative vomiting, Dexamethasone, Prophylaxis.

Correspondence: Dr. Farhat Jaleel, General Surgeon, Usman Memorial Hospital, Karachi.
E mail: farhatjaleel@yahoo.com
INTRODUCTION:
Surgery is a major stressful event. Post-operative nausea and vomiting (PONV) makes it an unpleasant experience for the most of the patients. Reported prevalence of PONV is 20 – 30%. It results in profound distress to the patient and increases the risk of aspiration in addition to increasing post-operative morbidity. Retching associated with vomiting increases chances of pain in the wound as well as wound disruption. PONV also results in delay in oral food intake, dehydration, electrolyte imbalance and restricted mobilization. Thereby, it leads to delayed time to convalescence and increases hospital stay and cost.

Etiology of PONV is multifactorial and includes type, technique and duration of anesthesia, type and duration of surgery, drugs, including opioids and antibiotics, intra-abdominal pathology, hypoxia, hypotension, pain as well as psychological factors. Female sex, extremes of age, previous history of PONV or motion sickness are likely predisposing factors.

Commonly used antiemetics for PONV are dopamine antagonists, anticholinergics and 5-HT₃ antagonists. Metoclopramide is very effective anti-emetic but associated with extrapyramidal side effects. Cyclizine and_dimenhydrinate cause sedation, while 5-HT₃ antagonists eg., ondansetron are expensive. Dexamethasone is well known for its analgesic, anti-inflammatory, immune modulating and anti-emetic effects. Its mode of action as an anti-emetic is not yet clear. Several national and international studies have shown beneficial effect of single peri-operative dose of 8 mg intravenous dexamethasone on PONV. A meta-analysis of randomized controlled trials showed that dexamethasone is superior to placebo and comparable to conventional antiemetic drugs. However, some authors have disagreed. Yusek MS and colleagues in Turkey have found conflicting results.

PONV usually occurs on the first post-operative day and is most distressing in the early hours of surgery. Body’s metabolic response to surgery starts immediately with the surgical incision, but the onset of biologic action of dexamethasone is observed after 1 - 2 hours of its administration. Therefore, the drug should ideally be administered 1–2 hours prior to surgery in order to achieve maximum benefit.

This study was conducted to determine the efficacy of dexamethasone given one hour prior to surgery, as prophylactic antiemetic for PONV.

PATIENT AND METHODS:
This was single blinded, randomized, placebo controlled, interventional study conducted at Usman Memorial Hospital, a private general hospital, where the authors work as consultants. It was conducted from January 2006 to June 2008. Patients admitted for general and gynecological surgery underwent pre-operative assessment by anesthetist. Patients with ASA I and II class were selected. Patients with history of motion sickness, anxious personality and tobacco addiction were excluded. Informed consent was obtained from the patients.

Patients were randomly allocated to either group A or B. Patients in group A (test group) were administered 2 ml of dexamethasone (Decadron, MSD), equivalent to 8 mg, by slow intravenous injection one hour before scheduled time of surgery. Patients in group B (placebo group) were similarly injected 2 ml of normal saline. The observers (the doctors and nurses) in the ward were unaware of the drug administered. Any immediate side effects, like headache, flushing, vomiting, skin rash were noted down.

After shifting to operation theatre, the patient were reassessed by the anesthetist. General anesthesia was administered as per routine. Anesthetist remained the same during this study period. Similar drugs, dosages and technique of anesthesia were used for each patient. At the end of the surgery, wound was infiltrated with 20 ml of 0.5% bupivacaine and injection ketorolac 30 mg I/V was given prior to extubation.

Later patients were shifted to post-operative ward. All patients were given IV ketorolac 30 mg twice. Supplemental analgesia used was injection nalbuphine 10 mg diluted in 10 ml distilled water. Two ml of this injection was administered I/V on request of the patient. Injection_dimenhydrinate 50 mg I/V was used as supplemental antiemetic as required. Observations were made for the complaint of nausea while vomiting was objectively observed for a period of 24 hours. Whenever the patient complained of nausea or had vomiting, it was noted down. Drug chart was also maintained. Data was entered and analyzed using SPSS version 15. Means with standard deviation were calculated for numerical variables while proportions were calculated for categorical variables. Significance was calculated using t-test, Chi square test or Fisher exact test, where applicable.

RESULTS:
Sixty female patients were studied, thirty in each group. Minimum age was 30 years and maximum 55 years. Mean age was 42 years in both the groups. 61.7% patients had cholecystectomy, 15% had hemiorrhaphy, 16.7% abdominal hysterectomy and 6.6% underwent benign ovarian cystectomy. Duration of surgery, number of episodes of PONV and administration of supplemental
Table I: Baseline Characteristics Of Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (Test group)</th>
<th>Group B (Placebo group)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>42.3 ± 12</td>
<td>42.4 ± 12</td>
<td>0.854</td>
</tr>
<tr>
<td>Duration of surgery, minutes (mean ± SD)</td>
<td>57.8 ± 11.7</td>
<td>59.3 ± 15.6</td>
<td>0.676</td>
</tr>
<tr>
<td>Duration of anesthesia, minutes (mean ± SD)</td>
<td>73.5 ± 5.5</td>
<td>75.4 ± 5.6</td>
<td>0.685</td>
</tr>
</tbody>
</table>

Table II: Number of Episodes of Nausea and Use of Supplemental Drugs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (Test group)</th>
<th>Group B (Placebo group)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of times Nausea (mean ± SD)</td>
<td>0.33 ± 0.5</td>
<td>1.07 ± 0.8</td>
<td>0.000</td>
</tr>
<tr>
<td>Number of times Vomiting (mean ± SD)</td>
<td>0.10 ± 0.3</td>
<td>0.53 ± 0.8</td>
<td>0.006</td>
</tr>
<tr>
<td>Supplemental Opioid (Number of times needed) (mean ± SD)</td>
<td>2.17 ± 0.6</td>
<td>2.2 ± 0.6</td>
<td>0.838</td>
</tr>
<tr>
<td>Supplemental Anti-emetic (Number of times needed) (mean ± SD)</td>
<td>0.3 ± 0.6</td>
<td>0.8 ± 0.9</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Table III: Number of Patients with Post-operative Nausea and Vomiting

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Group A (Test group)</th>
<th>Group B (Placebo group)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 6 Hours</td>
<td>Nausea</td>
<td>7 (23.3%)</td>
<td>21 (70%)</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>2 (6.7%)</td>
<td>12 (40%)</td>
<td>0.002</td>
</tr>
<tr>
<td>6 – 12 Hours</td>
<td>Nausea</td>
<td>3 (10%)</td>
<td>9 (30%)</td>
<td>0.053</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>0</td>
<td>2 (6.7%)</td>
<td>0.492</td>
</tr>
<tr>
<td>12 – 24 Hours</td>
<td>Nausea</td>
<td>0</td>
<td>2 (6.7%)</td>
<td>0.492</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>First 24 Hours</td>
<td>Nausea</td>
<td>9 (30%)</td>
<td>23 (76.7%)</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>3 (10%)</td>
<td>12 (40%)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

algesics and antiemetics are listed in table I. Frequency of PONV in the two groups is compared in table II and III.

**DISCUSSION:**
The safety and efficacy of dexamethasone for prevention of chemotherapy induced nausea and vomiting is well recognized since 1981.\(^1\)\(^2\) Since then it has been used in various trials for PONV in gynecological, laparoscopic, abdominal, ENT and orthopedic surgeries with successful results. Mechanism of action of dexamethasone as an antiemetic is unknown. Glucocorticoids are important modifiers of the post-operative physiologic inflammatory, humoral and immunologic responses by regulation of the trauma-induced humoral mediators. The postulated mechanism is centrally mediated via inhibition of prostaglandin synthesis or inhibition of the release of endogenous...
opioids. Glucocorticoids bind to the intracellular glucocorticoid receptors and effects are predominantly mediated through an altered protein synthesis via gene transcription. Other suggested mechanisms include central or peripheral inhibition of production or secretion of serotonin and changes in permeability of the blood-brain barrier to serum proteins.

Our study has shown that dexamethasone reduced the incidence of PONV. It also reduced the number of episodes of nausea and vomiting and the need for supplemental antiemetics. In our study frequency of overall post-operative nausea during 24 hour period in the test group was 30% as compared to 77% in the placebo group, while frequency of vomiting was 10% and 40%, respectively. This result is in accordance with various other similar studies. Bisgaard T reported frequency of PONV 32.5% in dexamethasone and 52.5% in placebo group. Laq N found that 26% versus 54% patients had PONV in early post-operative hours, while 42% versus 82% patients had PONV in later hours. Kashmiri ZA observed 10% versus 33% PONV in the recovery room, 27% versus 43% in first 12 hours and 30% versus 80% in the second 12 hours, when they compared dexamethasone with placebo.

Wallenborn J suggests that late PONV is likely to occur in patients who experience nausea and vomiting in early post-operative phase. Therefore, reducing nausea and vomiting is important during this period. As quoted earlier, the action of dexamethasone starts after 1 – 2 hours of its administration therefore, for the drug to show its full prophylactic action, it should be available in the body before skin incision is made. This will result in reduction of nausea and vomiting in the early post-operative period, which can have a positive psychological effect on the sense of well being and also reduce PONV in later hours. This effect is reflected in our study where, in addition to overall reduction, frequency of PONV in later hours of surgery was far less as compared to early hours. Bisgaard T has used dexamethasone 90 minutes before surgery and his results are similar to ours. His study showed that nausea was seen in 10/40 and vomiting in 1/40 patients during 0 – 6 post-operative hours, while nausea was seen in 5/40 and vomiting in 1/40 patients during 6 – 24 hours, in patients in whom dexamethasone was used. In contrast, Laq N and Kashmiri ZA used dexamethasone immediately prior to induction of anesthesia. In these two studies, although dexamethasone significantly reduced the occurrence of PONV as compared to saline / placebo, but the frequency was increased in the later hours of the day. PONV was observed in 26% patients during first 4 post-operative hours and 42% patients between 4 – 10 hours by Laq N. Kashmiri ZA reported 10%, 27% and 30% incidence of PONV in the recovery room, first 12 hours and second 12 hours, respectively. These results support our observation that if dexamethasone is given 1 – 2 hours prior to surgery, its total antiemetic effect is more pronounced.

In our study, the need for supplemental analgesics was similar in both the groups but that for supplemental antiemetics was significantly lower in the test group. This observation matches other studies, except Bisgaard T, who found that the need for analgesics was also reduced in the dexamethasone group. Corticosteroids may be associated with certain side effects like infections, hyperglycemia, osteoporosis, gastro-intestinal bleeding, depression and euphoria. These adverse effects have not been reported with single dose of dexamethasone. Perianal pruritis was observed in 3 patients by Bano F. Bisgaard T has reported 2 patients with wound infection, one in each of test and control groups (non significant). We did not observe any of these side effects in our patients.

CONCLUSION:

Dexamethasone given as single I/V injection of 8 mg one hour before surgery in an effective drug for prophylaxis of PONV.

REFERENCES:


Efficacy and Timing of Single Dose Dexamethasone as Prophylactic Antiemetic in Major Surgeries


