Laparoscopic gastric plication (LGP) is a technique in the restrictive category of bariatric procedures that reduces the gastric volume. Nausea and vomiting are the most common complications after this procedure. The goal of this research is to determine the preventive effective dose of promethazine on postoperative nausea and vomiting (PONV) after laparoscopic gastric plication.

Methods: After induction of general anesthesia the patients were divided into two groups, the promethazine 50mg group, which was given promethazine 50mg IM plus dexamethasone 8mg IV and the promethazine 25mg group, which was given promethazine 25mg IM plus dexamethasone 4mg IV. The primary endpoints were the incidence and intensity of nausea and vomiting, and severity of abdominal pain score in postoperative periods.

Results: Sixty-four morbid obese patients were enrolled into the study. Promethazine 50mg group was found to significantly reduce the incidence of PONV in the first 12 hours compared with the other group, (21.87% vs 37.5%, P=0.068). At the same time the intensity of PONV in base of numeric rating scale was lower in promethazine 50mg group compared to another group (2.63±0.85 vs 4.65±1.23, P=0.089). The mean severity of abdominal pain was higher in promethazine 25mg group, thus these patients needed more analgesia in comparison with another group.

Conclusion: In morbidly obese patients undergoing laparoscopic gastric plication, prophylactic administration of dexamethasone 8mg and promethazine 50mg was more effective in the first 12 hours after surgery in reducing the incidence of PONV, and severity of abdominal pain.

Keywords: laparoscopic gastric plication; nausea; vomiting; promethazine; dexamethasone; metoclopramide.
All surgeries were done by two general surgeons who had completed a fellowship in advanced laparoscopic surgery. The technique of LGP used, was based on the standard method in the last paper of the author [6].

All patients received general anesthesia; they were induced with propofol 1.5mg/kg, fentanyl 2µg/kg, midazolam 0.06 mg/kg, and atracurium 0.5mg/kg. For anesthesia maintenance a combination of isoflurane, fentanyl 1µg/kg/hr, and propofol was used. Propofol was the standard drug between two groups and these patents were morbid obese with BMI>40. In some situations we added less than one MAC isoflurane to decrease blood pressure during surgery.

After induction the patients were randomly allocated by using a computer-generated table into two following groups, the promethazine 50mg group, which was given promethazine 50mg IM plus dexamethasone 8mg IV and the promethazine 25mg group, which was given promethazine 25mg IM plus dexamethasone 4mg IV.

Prior to extubation all patients received propacetamol 1g IV. The study was double-blinded and the anesthesiologist responsible for the postoperative patient evaluations was not involved in drug administration. The evaluations were performed q12hrs for the first 48hr following the surgery.

The primary endpoints were the incidence of nausea and vomiting, in postoperative periods. The intensity of nausea and vomiting score was evaluated as a scale comparable to a numeric rating scale (NRS).

Abdominal pain was evaluated at the same time by using a visual analogue scale (VAS) (0 = no pain and 10 = worst possible pain). Postoperative pain score and the total analgesic requirement for the first 48 hours were recorded. Meperidine 50 mg IV was used as rescue analgesia in both groups when pain score exceeded 3. In patients in whom nausea and vomiting wasn’t tolerable ondansetron 4mg IV was used as rescue treatment.

The sample size was determined prospectively with 30 patients in each group. In regards to high incidence of PONV after laparoscopic gastric plication, a 50% reduction in the incidence of PONV at any time within the first 48hrs of treatment could be determined with a statistical power of 80% (β=0.85).

Statistical analysis was performed using SPSS version 14. Student’s t-test was used to compare the continuous variables between the groups. Repeated measure test (General Linear Model), Fisher’s exact test, and chi-2 were used to compare the incidence and the severity of nausea, vomiting, and pain at multiple time points. A P-value < 0.05 was considered statistically significant. Data are presented as mean [standard deviation (SD)], numbers, or percentages.

**Results**

Sixty four morbid obese patients were enrolled in this study from May 1, 2015 to 30 October 2016 with similar demographic characteristics in both groups (Table 1). The incidence of ponv in first 12 hour after operation in patients that took promethazine 50mg was lower than the other group, 21.87% vs 37.5% (P=0.068). At the same time the intensity of ponv in base of numeric rating scale was lower in promethazine 50mg group in compare to other group 2.63±0.85 vs 4.65± 1.23 (P=0.089). The incidence and severity of ponv was similar and reduced in the next following times after operation in both groups. The mean severity of abdominal pain was higher in promethazine 25mg group, thus these patients needed more analgesia in comparison with the other group.

**Table 1- Patient’s characteristic between two groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Promethazine 50mg (n=34)</th>
<th>Promethazine 25mg (n=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.41±12.05</td>
<td>30.58±13.37</td>
<td>0.4</td>
</tr>
<tr>
<td>Male/Female</td>
<td>20/12</td>
<td>22/10</td>
<td>0.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>40.87±3.38</td>
<td>40.67±3.68</td>
<td>0.3</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>100.23±19.54</td>
<td>102.05±21.91</td>
<td>0.1</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>187.38±39.59</td>
<td>197.95±58.85</td>
<td>0.2</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>201.51±38.84</td>
<td>229.20±50.82</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean severity of pain (vas)</td>
<td>3.23±0.45</td>
<td>4.85±1.67</td>
<td>0.06</td>
</tr>
<tr>
<td>Total pethidine Use (mg)</td>
<td>32.1±2.6</td>
<td>68.5±4.6</td>
<td>0.00</td>
</tr>
</tbody>
</table>

MAP=mean arterial pressure BMI=body mass index

**Discussion**

This study shows that from recovery to 12 hr following surgery the combination of dexamethasone 8mg and promethazine 50mg achieved a greater total response rate than dexamethasone 4mg and promethazine 25mg. During this period the incidence and severity of nausea and vomiting in the combination dexamethasone 8mg and promethazine 50mg group was lower than the other group.

Laparoscopic gastric plication as a surgical restrictive therapy for treatment of morbid obesity has been shown to have acceptable results since its application 12 years ago [6]. One of the most common problems with this operation is PONV. LGP, like other gastric restrictive therapies, induces increased intra gastric pressure. The degree of plication and the rate of increased intra gastric pressure is higher in patients who undergo LGP, in comparison to patients who underwent other gastric restriction procedures (such as sleeve gastrectomy) [6]. The feeling of postoperative gastric fullness is a potential etiology for nausea in LGP cases, which would be corrected after patient adaptation to the reduced stomach volume [7]. The mechanism for nausea after LGP is that the vagal input from the plicated stomach can activate the emetic center of the brainstem and can also activateafferent action from the chemoreceptor trigger zone (CTZ).

The patients in this study have multiple risk factors that can increase the incidence of PONV, such as female gender, younger age, general anesthesia with volatile anesthetics, and gastric surgery. These risk factors were similar between the two study groups and therefore do not affect the results significantly.

Promethazine is a centrally acting drug with antihistamine and anticholinergic properties that are effective for the prevention of PONV [8]. It also helps reduce nervousness, restlessness, and agitation, all of which are common after any surgery. Co-administration of promethazine with opioids or codeine increase subjective happiness in patients [9]. Deep IM injections of promethazine have a 4-6hr effect and have been shown to be safe in most patients. In this study the anticholinergic effect of promethazine is the likely...
etiology that reduced the gastric irritability and frequency of PONV. In some current guidelines promethazine, in combination with other antiemetics, was found to be more effective in reducing PONV, severity of nausea, and pain than promethazine monotherapy [10]. A combination prophylactic therapy of PONV with promethazine and other drugs has been published by some authors [11-12].

Dexamethasone is a well documented anti-inflammatory drug which is also centrally acting [13]. It is absorbed rapidly following IM injection and reaches maximum plasma concentration at 1 hour, with a half-life about 190 minutes. It also potentiates euphoric effects of opioids and reduces the postoperative pain intensity, nausea, vomiting and need for rescue analgesia as compared to placebo [14-16].

In our previous study administration of promethazine 50mg /dexamethasone 8mg during the postoperative period significantly controlled ponn after surgery [17].

In a study by Benevides et al combination of dexamethasone with haloperidol and ondansetron reduced PONV, the necessity of rescue antiemetics and opioid consumption after Laparoscopic Sleeve Gastrectomy [18].

Conclusion
To conclude, in patients undergoing LGP, prophylactic administration of dexamethasone8mg and promethazine 50mg was more effective in the first 12 hours after surgery in reducing the incidence of PONV, and severity of abdominal pain.

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References