Intra-peritoneal Bupivacaine alone or in combination with Morph inc in Patients Undergoing Vertical Bypass Gastroplasty


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Abstract

Background and knowledge: Intra-peritoneal instillation of local anesthesia and morphine has been used to alleviate post-operative pain in laparoscopic surgery. Controversy exists about the efficacy of this technique.

Methods: We studied 48 patients scheduled for Vertical Bypass Gastroplasy (VBG). All of them received the same technique of general anesthesia (GA). Patients were randomly allocated into four equal groups. They received equal volumes of the test drug instilled in the peritoneal cavity at the end of laparoscopy, 50 ml of normal saline (Group S): 50 ml of bupivacaine 0.25% (Group B), 50 ml of bupivacaine 0.25%, plus morphine 40 mcg.kg-1 (maximum of 5 rug) Group M or (Group D) patients received the same regimen as Group M in addition, they received 75 mg intra-muscular diclophenac after induction of general anesthesia. Wound edges were infiltrated with 10 ml bupivacaine 0.25% in all patients. Morphine 25-50 mcg.kg-1 was given intravenously every 10 mm as a rescue analgesic to control postoperative pain in Post Anesthesia Care Unit (PACU). Post operative pain was evaluated using Visual Analogue Scale (VAS). vital signs and morphine consumption, and time to receive rescue analgesia were measured at different intervals. The incidence of post-operative complications (respiratory depression. oxygen de-saturation. arid nausea and vomiting) was recorded as well as hospital stay.

Results: There was significant decrease in VAS, HR, MBP and morphine consumption in Groups M & D when compared to Groups S & B on admission and on discharge from PACU. There were significant decrease in time to receive rescue analgesia as well as significant reduction in hospital study in Groups M and D when compared to Groups S and B. However, there was no significant difference between group S & B regarding the same parameters.

Conclusions: The presented technique is safe and easy to use with good postoperative morphine sparing analgesia, excellent patient satisfaction and short hospital stay.

Introduction

Laparoscopic surgery, compared to open procedures, is a minimally invasive technique associated with reduced postoperative pain.(1-3) nevertheless, pain after laparoscopy may be perceived as moderate or even severe by some patients.(4) Intra-peritoneal instillation of local anesthetics has been proposed to minimize postoperative pain after laparoscopic surgery. However, a controversy exists regarding the effectiveness and clinical value of this procedure for pain control after laparoscopic cholecystectomy.(5) Several reports are available on the efficacy of intra-peritoneal administration of local anesthesia for analgesia after laparoscopic gynecologic surgery.(6-8) All these studies, reported an attenuation of postoperative pain when local anesthetics (bupivacaine or ropivacaine) were administrated at the end of surgery. Intra-peritoneal instillation of opioids for postoperative analgesia has been evaluated as an alternative approach. It has been suggested that peripheral antinociceptive effects of opioid agonists could be elicited inw activation of opioid receptors localized on peripheral sensory nerves.

However, Schulte-Steinberg et at. failed to demonstrate any atalgesic ellèet of intra-peritoneal morphine (0.25 mg) after laparoscopic cholecystectomy.(10) This result was explained, in part, by the very small dose of morphine delivered at the surgical site. Although non steroidal ant-inflammatory drugs (NSAIDs) provide morphine-sparing effects (2), they do not appear, on their own, to provide sufficient...
reliable postoperative analgesia for minimally invasive laparoscopic surgery. However, there is a synergistic effect between NSAIDs and opioids when the latter is used intra-peritoneal or systemically. On the basis of these data, we conducted a double blind randomized study where we hypothesized that intra-peritoneal administration of higher doses of morphine (3-5 mg) and 100-150 mg bupivacaine with or without diclofenac at the end of laparoscopic vertical bypass gastroplasty surgery would provide more effective postoperative analgesia compared to placebo.

The aim of this work is to evaluate the efficacy and safety of intraperitoneal instillation of bupivacaine, bupivacaine and morphine, or in addition to bupivacaine and morphine IM 75 mg diclofenac on postoperative pain relief and morphine consumption and its related complications.

Both techniques will be compared with the traditional method used in King Faisal Specialist Hospital & Research Center (KFSII&RC) for pain control after laparoscopic Vertical Bypass Gastroplasty (VI3G).

**Patients and methods**

After Local Ethics Committee approval and written informed consent. 48 patients aged 18-40 years, ASA II - III, with Body Mass Index (BMI) 3 8-45 kg.m2 were scheduled for laparoscopic vertical bypass gastroplasty (VBG) were randomly divided into four equal groups. They received 50 ml 0.9% saline (Group A), bupivacaine 0.25% 50 ml (Group B), bupivacaine 0.25% 50 ml plus morphine 40 mcg.kg-1 (maximum 5 mg) (Group M) or (Group D) received the same regimen as Group M in addition, 75 mg intramuscular diclofenac administered into peritoneal cavity in all groups at end of laparoscopy. In addition to Wound edges were infiltrated with 10 ml bupivacaine 0.25% in all groups. Postoperative pain was evaluated using visual analogue scale (VAS), where 0 means no pain and 10 the worst imaginable pain. Exclusion criteria included patients with a history of malignancy, or those who had contraindications to diclofenac (allergy, liver disease, esophago-gastro-duodenal disease, renal insufficiency, abnormal coagulation), or with proved allergy to local anesthetic. All patients received the same technique of general anesthesia. Intra-operative analgesia was maintained by fentanyl 2μg.kg-1 at induction followed by fentanyl infusion of 1 1μg.kg-1.h-1. All surgeries were carried out by the same surgical team. In recovery room, all the patients received 25-50 mcg.kg-1 intravenous morphine as a rescue medication, if needed, every 10 minutes to control postoperative pain. Postoperative patient controlled morphine analgesia (PCA) was used according to the hospital Protocol.

**Measurements**

Heart rate (HR) and Mean Blood Pressure (MBP) were measured preoperatively, before and after intraperitoneal drug administration, on admission to Post Anesthesia Care Unit (PACU), and on discharge from PACU (2 hours postoperatively). Respiratory rate (RR) and oxygen saturation (SO2) were measured preoperatively, on admission to PACU, and on discharge PACU Visual Analogue Scale (VAS) was assessed on admission to and on discharge from PACU.

The time to first analgesic requirement (mm). Postoperative morphine consumption during the first 2 hours and after 24 hours was recorded.

The incidence of complications including respiratory depression (RR less than 10), oxygen desaturation (SaO2 < 87%) on admission to recovery room, re-intubation during the first 24 hours postoperatively, and the incidence of nausea and vomiting were recorded as the number of patients needed medical treatment in each group. hospital stay (day).
**Statistical analysis**

ANOVA test was used to compare and analyze results between groups, while subgroup analysis was achieved by Tuqey’s approach. The statistical analysis of means within the groups is achieved via paired t test(12)

**Results**

There were no significant differences between the four groups of patients with regard demographic data, body mass index duration of anesthesia as show in table.

**Assessment of homodynamic measurements** Table 2, Shows that, there were no significant decrease in HR & MBP on admission and on discharge from PACU in groups M and D Compared to groups S & B. When Groups M and D were Compared, no significant differences were found.

**Assessment of pain** : Table 3 & Figure 1 show, the Visual Analogue Scale in the four groups. Pain Scores were statistically lower in patients in groups M and D as compared to groups S & B, both on admission and in discharge from PACU at 2 hours postoperatively.

<table>
<thead>
<tr>
<th>Table 1 . Demographic Data</th>
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<td>Age (Yr)</td>
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<tr>
<td>Gender (male/female)</td>
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<td>BMI (kg-m-2)</td>
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<tr>
<td>Duration of surgery (min)</td>
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<td>Duration of Anesthesia (min)</td>
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* Data are expressed as Mean+SD.

<table>
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<tr>
<th>Table (2). preoperative Changes in Heart Rate (HR) and Mean Blood pressure (MBP).</th>
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<tr>
<td>Preoperative HR</td>
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<td>Before instillation HR</td>
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<td>After instillation HR</td>
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<tr>
<td>On Admission to PACU HR</td>
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<td>On Discharge from PACU HR</td>
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Data are expressed as Mean + SD.
* P<0.01 when compared with Groups sand B.
** P <0.05 when compared with Groups and B.

<table>
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<tr>
<th>Table 3. postoperative pain Scores Measured on 10 cm Visual Analogue Scale (VAS)</th>
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<tr>
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<tr>
<td>On Admission to PACU</td>
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<td>On Discharge from PACU</td>
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</table>

Data are expressed as Median.
* P<0.05 when compared with Groups S & B.
** P <0.01 when Compared with Groups S & B.
Figure 1. Postoperative pain Scores Measured on 10 cm visual Analogue Scale (VAS)

Assessment of Time to first Rescue Analgesic requirement: Table 4, shows that the time to first analgesic requirement was 33.5+7.15 min in Group S, 40.66+9.4 min in Group B, 106.25+7.55 min in Group M and 116.08+3.05 min in Group D. There was significant increase in time for first analgesic requirement in Groups M and D when compared to Groups S and B (P<0.01), while there was no difference between Group M and D.

Assessment of Morphine consumption: Table 4. Figure 2 shows the morphine consumption in the four groups 2 hours (on discharge from PACU) and 25 hours after surgery. There was significant reduction in morphine consumption in groups M and D with mean 6.16+2.3, 5.1+1.58 (p<0.05) and 34.8+8.33, 31.66+7.7 (P<0.01) on discharge from PACU and 24h after surgery respectively, compared to Groups S and B With mean 12.91+3.28, 10.33+1.82 and 73+22.42, 68+31.51 discharge form PACU and 24h after surgery respectively.

Table 4 Time for rescue Analgesia and Morphine consumption in PACU and 24 Hour after surgery

<table>
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<tr>
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<th>Grope S</th>
<th>Grope B</th>
<th>Group M</th>
<th>Group D</th>
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<tbody>
<tr>
<td>Time to Rescue Analgesia (min)</td>
<td>33.5+7.15</td>
<td>40.66+9.4</td>
<td>106.25+7.55**</td>
<td>116.08+3.05**</td>
</tr>
<tr>
<td>Morphine Consumption on Discharge from PACU (mg)</td>
<td>12.91+3.28</td>
<td>10.33+1.82</td>
<td>6.1+2.3*</td>
<td>5.1+1.58*</td>
</tr>
<tr>
<td>Morphine Consumption 24h after surgery (mg)</td>
<td>76+22.42</td>
<td>68+8.33</td>
<td>34.83+8.33***</td>
<td>31.66+7.7**</td>
</tr>
</tbody>
</table>

Data are expressed as Mean + SD.
*P<0.05 when compared with Groups & B.
** P< 0.01 when compared with Groups & B
Figure 2. morphine consumption in PACU and 24 Hours after surgery.

Table (5) Hospital stays in days

<table>
<thead>
<tr>
<th></th>
<th>Group S</th>
<th>Group B</th>
<th>Group M</th>
<th>Group D</th>
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<tbody>
<tr>
<td>Hospital stay (Days)</td>
<td>3.91+0.9</td>
<td>3.66+1.15</td>
<td>2.28+0.9*</td>
<td>2.25+0.86*</td>
</tr>
</tbody>
</table>

- Data are expressed as Mean ± SD.
- *P <0.01 when compared with Groups S & B.

**Assessment of the incidence of complications:**

There were no significant changes in oxygen saturation and respiratory rate between the four groups on admission to PACU (P > 0.01). In group (5) 2 patients (16%) suffered from transient oxygen desaturation during the first 24 hrs compared to 0 patients in the other 3 groups (P < 0.01). In group (5) 7 patients (58%) suffered from postoperative vomiting compared to 6 patients (50%) in group B and 3 patients (25%) in group M and D (P < 0.01).

**Discussion**

In their recent article, Charghi et al(12) concluded that in grossly obese patients undergoing gastric bypass surgery patient controlled analgesia with intravenous morphine is an acceptable strategy for pain management and may confer some advantages when compared to epidural analgesia. However the high prevalence of postoperative respiratory complications following bariatric surgery urge a hard trial to find out a safer postoperative analgesic regimen that may reduce this incidence. The intra-peritoneal administration of local anesthetics and or opioids, being an easy way of applying these drugs, draws much attention of the anesthesiologists and may be one of the solutions.

However, there was controversy about the efficacy of this technique in reducing post laparoscopic pain. The difference in outcome of studies on intra-peritoneal instillation of local anesthetics may result from the nature of surgery, dose, type and timing of instillation of local anesthetic. Also the failure in some studies to show an analgesic effect may result from the wide area on which the local anesthetic spread in the peritoneal cavity that cannot be managed by increasing the dose of local anesthetic(13)
Although it is not possible to increase the dose of local anesthetic without increasing the risk of systemic toxicity but by optimization of the dose and adding morphine as in the hypothesis of the present research postoperative analgesia can be augmented.

The mean plasma concentration of bupivacaine after intra-peritoneal instillation of 100-150 mg plain bupivacaine ranges between 0.92 to 1.14 μg ml-1, which is well below the toxic concentration of 3 μg m1-1 and goes with the doses used in the used in the present research\(^{(14-16)}\). The rationale behind the use of intra-peritoneal route of administration is that the visceral nociceptive conduction can be blocked through the peritoneum exposed to local anesthetic and or morphine. Again absorption from the large peritoneal surface may also occur, which may be a further mechanism of analgesia.

In the present study the use of local anesthetic, in combination with an opioid, potentiates analgesia in PACCU by prolonging the First call for rescue analgesia in group M and D compared to the other 2 groups and also reduce the total dose of morphine consumption during the first 24 hours. This was proved by Colbert et al., who found that in 100 patients undergoing laparoscopic tubal ligation, pain scores at rest and on movement were significantly lower in patients who had a combination of intra-peritoneal 50 mg meperidine and 80 ml bupivacaine 0.125% compared with those who had a combination of intramuscular meperidine 50mg and intra-peritoneal 80 ml bupivacaine 0.125% \(^{(17-18)}\).

On the contrary, Moiniche et al. concluded that the clinical benefit of this procedure, at least regarding pain scores, was questionable \(^{(5)}\). In the present study, patients reported low postoperative pain scores on admission to PACU in group M and D compared to group S and B. They also needed small doses of supplemental analgesics. This situation may be related to the good amount of morphine and bupivacaine used compared with other studies \(^{(18)}\).

Also in 1997, Willoamson and coworkers described the use of large volumes of dilute local anesthetic (80 ml lidocaine 0.5% or 80 ml bupivacaine 0.125%, both with epinephrine) administered before surgery into the peritoneal cavity for the treatment of pain after laparoscopy \(^{(19)}\). They demonstrated significant reductions in mean pain Scores in the local anesthetic groups from eight to 24 hr after surgery compared to the control group. In contrast to our study, Schulte-Steinberg et al. despite the use of 3 mg morphine at the surgical site \(^{(10)}\), they observed a negative result and the inefficacy of intra-peritoneal morphine. They have attributed the lack of efficacy of intra-peritoneal morphine in reducing postoperative pain after laparoscopic cholecystectomy to an insufficient dosage which is doubled in the present work \(^{(10)}\).

However, in a recent study to augment postoperative analgesia after laparoscopic cholecystectomy with the fractionated injection of local anesthetic (before and at the end of surgery) is considered an alternative solution \(^{(20)}\). Also in agreement with the present research, Hernandezpazalon et al. used bupivacaine 0.25% 30 ml plus morphine 2 mg intraperitoneal with significant postoperative pain relief \(^{(21)}\). In the present study the less incidence of postoperative vomiting can be explained by the fewer doses of morphine used in group M and D, while he incidence of transient oxygen de-saturation that occurred in group M and D, while he incidence if transient oxygen de-saturation that occurred in group S was related to over-sedation by morphine. Although there was less hospital stay in group M and D compared to group S and B but the presence of other discharge criteria limits the evaluation of the presented technique on hospital stay in spite of surgeries were done by the same team.

**Conclusions**

The intra-peritoneal route of administration of local anesthetic and morphine followed by morphine patient...
controlled analgesia is simple, Sate and. it

does not involve additional central neural
axia1 block. It is particularly suited to
particularly suited to the practice of
anesthesia for Bariatric surgery. Proper
instillation of the drugs in the peritoneal
space for a good. time with or without the
use of Diclofenae. ensures adequate
postoperative postoperative analgesia.
The search goes on for the use of this
technique in other forms of Bariatric
surgeries using newer, less toxic local
anesthetics hat have a longer duration of
action and. lead ultimately to
improvements in convalescence and to a
reduction in the risk of prolonged hospital
admission after minimally invasive
surgery.

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