Effect of Adding Hydrocortisone to Intraperitoneal Bupivacaine in Laparoscopic Bariatric Surgery

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Abstract

Background: Bariatric surgery is the effective management of obesity; however, postoperative pain is associated with a great morbidity. The management of pain is important for the enhancement of patient recovery. Local anesthetics can be injected during laparoscopic surgery into the peritoneum throughout the ports produced either before the beginning of laparoscopy or before the closure of the wound to reduce postoperative pain. Our aim is to evaluate if there is an additive analgesic effect by the administration of intraperitoneal hydrocortisone with streamed intraperitoneal bupivacaine as a method of postoperative pain relief in laparoscopic bariatric surgeries. Patients and Methods: One hundred patients listed for laparoscopic bariatric surgery were the subject of this study. Patients were randomly allocated into two groups: Group I received 100 mg of 0.5% isobaric bupivacaine plus 20 mL normal saline intraperitoneally and Group II received intraperitoneal 100 mg of 0.5% isobaric bupivacaine + 100 mg hydrocortisone + 20 mL of saline at the end of the laparoscopic procedure. The primary outcome was the Visual Analog Scale (VAS) score for pain. The secondary outcomes were the time of first analgesic request, total opioid requirement, heart rate, and mean blood pressure. Results: VAS showed a significant decrease at 4, 6, and 12 h postoperative in Group II compared to Group I. There was a marked decrease in total meperidine requirement with prolonged time of the first analgesic request in Group II compared to Group I. Conclusion: Intraperitoneal hydrocortisone with bupivacaine had improved postoperative pain relief with a decrease in analgesic requirement.

Keywords: Bariatric surgery, hydrocortisone, intraperitoneal bupivacaine, laparoscopy, pain

Introduction

Obesity became one of the main health problems all over the world. It resulted in decreased life expectancy, greater morbidity and mortality, and increased health-care costs. Bariatric surgery is effective in the management of obesity than nonsurgical methods. Recently, laparoscopic approaches to bariatric surgery have improved significantly. Lesser pain and enhanced healing time compared to open surgeries are the causes of popularity of laparoscopy.[1] Perioperative pain management of the obese patients is very essential for not only the comfort but also for the better surgical outcome.[2] It is suggested that postoperative pain relief using nonopioid analgesia had a greater margin of safety concerning respiratory side effects, such as sleep apnea and slow respiratory rate, compared with systemic opiates. Hence, different approaches for pain management including opioid drugs, nonsteroidal anti-inflammatory drugs, and infiltration of local anesthetic (LA) were recommended as the most favorable combination in laparoscopic surgeries.[3]

LA can be installed intraperitoneal throughout the ports formed either at the beginning of laparoscopic procedure or before the closure of the wound. It is usually injected through the trocar site over the visceral peritoneum or into the surgical bed or subdiaphragmatic. The subdiaphragmatic injection of LA usually decreases the incidence of shoulder pain.[4] Numerous studies had used this technique of analgesia. Bupivacaine,[5] levobupivacaine,[6] lidocaine,[7] and ropivacaine[8] were administrated intraperitoneally in different doses to produce analgesia in several types of surgeries. Steroids have also been used for postoperative pain relief in different kinds of

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surgery; intraperitoneal hydrocortisone can reduce pain after laparoscopic cholecystectomy without significant adverse effects.[2,9]

Up to the best of our knowledge, in bariatric surgeries using laparoscopy, there is no clinical trial that compared the effect of adding hydrocortisone to intraperitoneal bupivacaine with intraperitoneal bupivacaine alone on postoperative pain.

We hypothesize that adding steroids as hydrocortisone to intraperitoneal bupivacaine would have a superior pain relief effect than using intraperitoneal bupivacaine alone after laparoscopic bariatric surgery.

**Aim of the study**

The aim of this study is to evaluate if there is an additive analgesic effect by the administration of intraperitoneal hydrocortisone with streamed intraperitoneal bupivacaine as a method for pain relief after laparoscopic bariatric surgery. The primary outcome is the assessment of postoperative visual analog score. The secondary outcomes are total opioid requirement, the time to first analgesic request, and postoperative hemodynamics.

**Patients and Methods**

This double-blind randomized controlled study was conducted in Mansoura University Hospitals, in the period between September 2017 and March 2019 after obtaining approval of the Institutional Research Board Number R.16.02.03, Mansoura Faculty of Medicine. Written informed consent was obtained from all patients before inclusion in the study.

**Inclusion criteria**

One hundred obese patients with a body mass index (BMI) ≥35 kg/m² and 20–60 years old with the American Society of Anesthesiologists physical Class I–II who were planned for laparoscopic bariatric surgeries under general anesthesia were included in this study.

**Exclusion criteria**

Patients with a history of significant cardiac, hepatic, or renal diseases; sensitivity to amide LA drugs or hydrocortisone and psychological or neurological disorders and patients receiving steroids or opioid analgesic medication within 24 h before the operation were excluded. Patients were also excluded in case of conversion from a laparoscopy to an open laparotomy.

Patients were randomly divided into two equal groups. Randomization was done through sealed opaque envelopes to avoid bias. Either Group I received 100 mg of 0.5% isobaric bupivacaine plus 20 mL normal saline intraperitoneally or Group II received 100 mg of 0.5% isobaric bupivacaine and 100 mg hydrocortisone plus 20 mL of normal saline intraperitoneally.

**Perioperative management**

Patients received ranitidine 150 mg and metoclopramide 10 mg the night before and 60 min before arrival in the operating room. Subcutaneous enoxaparin 60 mg will be administered 12 h before the scheduled operation for thromboprophylaxis.

All medications in the study protocol were based on the dosing body weight (ideal body weight (IBW) ×0.4 × [actual body weight – IBW]) as described by Han et al.[10]

On arrival to the operating room, the patient’s monitoring includes electrocardiography; noninvasive blood pressure, pulse oximetry, and capnography were attached to the patients; preoxygenation through the face mask was done; anesthesia was induced with propofol 1.5–2.5 mg.kg⁻¹ and fentanyl 2 µg.kg⁻¹; and rocuronium 0.6 mg.kg⁻¹ was given to facilitate tracheal intubation. Anesthesia was initially maintained with 0.7–1.2 minimum alveolar concentration (MAC) of sevoflurane in combination with air (1 L/min) and oxygen (1 L/min) mixture to maintain the mean arterial blood pressure (MAP) and heart rate (HR) which are ≥20% of the baseline values. Fentanyl 0.5 µg.kg⁻¹ increments were administered when the MAP and HR are ≥20% of the baseline values despite a MAC of sevoflurane ≥1.0. Rocuronium 0.1 mg.kg⁻¹ was used to maintain surgical relaxation.

Ventilation was on pressure-controlled mode to deliver a tidal volume of 8 mL.kg⁻¹, inspiratory/expiratory ratio of 1:2, and positive end-expiratory pressure of 5 cm H₂O. Respiratory rate was titrated to maintain end-tidal carbon dioxide (CO₂) tension around 35 mmHg.

All operations were done by the same surgeons. During CO₂ pneumoperitoneum, the intra-abdominal pressure was maintained at 12–14 mmHg. The patient position was altered from the supine to the reverse Trendelenburg position (40°). Hemodynamic control was standardized hypotension (defined as MAP value <25% of the basal value on two readings in 3 min), with no response to decrease the sevoflurane MAC to 0.7 and a 5 mL/kg/mL ringer lactate or acetate bolus over 5 min, which was treated with intravenous (i.v.) boluses of ephedrine (3 mg) or norepinephrine (5 µg i.v.). Hypertension (increase >20% basal MAP) was treated by deepen anesthesia and i.v. fentanyl 20 µg or nitroglycerine perfusion. Tachycardia (>20% increase from basal HR) was treated with propranolol 0.5 increment. Bradycardia (HR <45) for ≥2 min was treated with atropine 0.5 mg i.v.

After the end of the laparoscopic procedure and evacuation of insufflated CO₂, patients were either Group I (n = 50): received 100 mg of 0.5% isobaric bupivacaine plus 20 mL normal saline intraperitoneally or Group II (n = 50): received 100 mg of 0.5% isobaric bupivacaine and 100 mg hydrocortisone plus 20 mL of normal saline intraperitoneally.

All the study solutions looked identical and were prepared by a local pharmacy. All the operating room staff were uninformed of the patient allocation group.

Before wound closure, 10 mL of bupivacaine 0.25% was injected at laparoscopic ports entering site, and residual neuromuscular block was reversed with neostigmine (0.05 mg.kg⁻¹ i.v.) and atropine (20 µg.kg⁻¹ i.v.). After completing the surgery, inhalational anesthesia was discontinued.
Ondansetron (4 mg i.v.) was given for the prevention of postoperative nausea and vomiting. Postoperative 30 mg of i.v. ketorolac every 6 h was given. Patients were assessed for pain using the Visual Analog Scale (VAS) in the postoperative anesthesia care unit (0 h) and at 2, 4, 6, 12, and 24 h based on a 0–10 scale (with 0 meaning no pain and 10 meaning the most intense pain ever felt). Rescue doses of i.v. meperidine 25 mg requirements were also recorded. It was given as rescue analgesia for VAS >4. Time for the first analgesic request, postoperative HR, and blood pressure were recorded and analyzed.

Statistical methods

Sample size calculation

The power of this study was calculated using G * Power analysis (program version 3: Faul F, Erdfelder E., LangAG2007, Universitat Dusseldorf), assuming alpha (Type I error) = 0.05, beta (Type II error) = 0.2, and power = 80%. Forty-six patients were necessary in each group to detect a difference of 30% between the two groups. Therefore, 4 patients were added in every group to be 50 patients for the risk of any missing data.

Statistical analysis

Statistical analysis was done using the SPSS program version 22 for Windows (IBM Corporation, Armonk, NY, USA). The normality test was done by Kromogorov–Smirnov test. Normally distributed continuous data were analyzed by Student’s t-test. Nonnormally distributed continuous data were analyzed by Mann–Whitney U-test. Categorical data were analyzed by Chi-square or Fisher’s exact test as appropriate. The results were interpreted as mean (standard deviation) or number and percentage of patients. P < 0.05 was statistically significant.

RESULTS

One hundred and twenty-three patients were assessed for eligibility, 23 patients were excluded either due to not meeting inclusion criteria, the patient refused to participate, or laparoscopy converted into open surgery due to adhesions. One hundred patients completed the study [Figure 1].

There was no statistically significant difference between either group regarding the patient’s demographic data and duration of surgery [Table 1].

As regards the VAS, there was no significant difference between both the groups at the basal value and 2 h and 24 h postoperative with a significant decrease in pain score at 4, 6, and 12 h postoperative in Group II compared to Group I [Table 2].

There was no significant difference among the two groups as regards HR immediately postoperative and at all recorded time intervals [Table 3].

There was no significant difference among the two groups as regards MAP immediately postoperative and at different time intervals after surgery [Table 4].

| Table 1: Patient demographic data, duration of surgery |
|------------------------------------------------------|
| **Group I (n=50)** | **Group II (n=50)** | **P** |
| Age (years) | 35.7±8.5 | 33.8±9.3 | 0.31 |
| Gender, n |  |  |  |
| Male | 22 | 19 | 0.48 |
| Female | 26 | 30 |  |
| Body weight (kg) | 124.2±17.8 | 123.6±16.8 | 0.87 |
| BMI | 45.3±7.2 | 46.1±6.8 | 0.59 |
| Hypertension, n (%) | 6 (12.5) | 9 (18.4) | 0.42 |
| DM, n (%) | 6 (12.5) | 7 (14.3) | 0.79 |
| Duration of surgery (min) | 75.3±17.5 | 73.1±14.3 | 0.51 |

| Table 2: Visual Analog Scale |
|-----------------------------|
| **Group I (n=50)** | **Group II (n=50)** | **P** |
| VAS at recovery room | 4 (2-5) | 4 (2-3) | 0.432 |
| VAS 2 h | 3 (1-6) | 3 (2-5) | 0.859 |
| VAS 4 h | 3 (2-6) | 2 (1-5)* | 0.006 |
| VAS 6 h | 3 (2-5) | 2 (1-4)* | 0.024 |
| VAS 12 h | 4 (2-6) | 2 (1-4)* | 0.038 |
| VAS 24 h | 4 (1-6) | 4 (1-5) | 0.609 |

*Significant difference comparing Group II to Group I. Data are expressed in median and range. P value is significant if <0.05. Group I=Bupivacaine group, Group II=Hydrocortisone bupivacaine group, VAS=Visual Analog Scale

| Table 3: Heart rate measurements during the first postoperative day |
|---------------------------------------------------------------|
| **Group I (n=50)** | **Group II (n=50)** | **P** |
| HR at recovery room | 77±9 | 81±9 | 0.410 |
| HR 2 h | 79±3 | 78±4 | 0.369 |
| HR 4 h | 85±4 | 82±7 | 0.346 |
| HR 6 h | 79±9 | 77±6 | 0.510 |
| HR 12 h | 82±9 | 78±5 | 0.41 |
| HR 24 h | 79±3 | 78±4 | 0.858 |

Data are expressed in mean±SD. P value was insignificant. Group I=Bupivacaine group, Group II=Hydrocortisone bupivacaine group, HR=Heart rate, SD=Standard deviation

| Table 4: Mean blood pressure measurement during the first postoperative day |
|--------------------------------------------------------------------------|
| **Group I (n=50)** | **Group II (n=50)** | **P** |
| MBP at recovery room | 83.9±9.5 | 81.7±9.6 | 0.266 |
| MBP 2 h | 80.2±5.8 | 78.7±4 | 0.155 |
| MBP 4 h | 79.3±4.7 | 78.1±5.6 | 0.759 |
| MBP 6 h | 89.7±9.6 | 86.1±7.8 | 0.698 |
| MBP 12 h | 86.8±6.8 | 84.4±8.5 | 0.112 |
| MBP 24 h | 87.5±6.7 | 86.6±8.8 | 0.227 |

Data are expressed in mean±SD. P value is significant if <0.05. Group I=Bupivacaine group, Group II=Hydrocortisone bupivacaine group, SD=Standard deviation, MBP=Mean blood pressure

There was a statistically significant decrease in the total analgesic requirement (63.97 ± 21.81) in Group II compared to
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Group I (81.35 ± 17.82) with *P*< 0.001. The time for the first analgesic request was prolonged in Group II (105.62 ± 54.92) compared to (87.38 ± 63.87) in Group I [Table 5].

**DISCUSSION**

Postoperative pain following laparoscopic bariatric surgery affects the great benefit of laparoscopy as a minimally invasive surgical procedure. The recovery from laparoscopic surgeries had a revolution in decreasing pain postoperatively; however, reducing the residual pain is essential in bariatric surgeries as it is critical for bariatric patients with their high BMI to pass the postoperative period uneventfully.[11] Achieving effective pain management usually results in lesser postoperative complications with early initiation of oral intake; moreover, an efficient pain control encourages early ambulation, which significantly decreases the risk of deep-vein thrombosis and pulmonary embolism, facilitates patient’s ability to take deep breaths to reduce the pulmonary complications as atelectasis and pneumonia.[12]

As in laparoscopic surgeries, postoperative pain is caused by many factors, so multimodal management usually needed for optimum relief of pain. Intraperitoneal administration of various drugs was given along with LA for the relief of pain after laparoscopic surgeries such as bupivacaine with morphine or meperidine, levobupivacaine with epinephrine, and lidocaine with tenoxicam.[13,14]

In this prospective randomized controlled study, adding intraperitoneal hydrocortisone to bupivacaine showed potentiation of the postoperative analgesic effect than intraperitoneal bupivacaine alone with decreased in the postoperative analgesic requirement and prolonged the first analgesic rescue time; however, there was no difference in the patients’ hemodynamics between the two groups.
Adding hydrocortisone to bupivacaine has an added benefit than bupivacaine only because steroid reduced the pain through numerous mechanisms such as inhibition of bradykinin release, of decrease phospholipase enzymes so decreasing cyclooxygenase and lipoxygenase mediators of inflammatory pathway, and inhibition of other inflammatory mediators as interleukin 6 and tumor necrosis factor.[15]

Amini et al. studied the analgesic effect of intraperitoneal injection of hydrocortisone alone prior to gas insufflation in laparoscopic cholecystectomy, and they found that intraperitoneal hydrocortisone can decrease postoperative pain without postoperative complications, which is in parallel to the results of the current study.[16] Furthermore, our results agreed with Asgari et al. who studied the additive effect of intraperitoneal hydrocortisone and bupivacaine on postoperative pain in gynecological surgery, and they found that hydrocortisone with bupivacaine has a greater analgesic effect than bupivacaine only.[17]

In a study of Sarvestani and Amini, they found that the intraperitoneal administration of bupivacaine with hydrocortisone prior to CO₂ insufflation reduced the pain postoperative same as the intraperitoneal bupivacaine without postoperative adverse effects in laparoscopic cholecystectomy, which is in contrast to the results of the current study and this may be due to their intraperitoneal administration in a different timing as intraperitoneal injection was done after the end of laparoscopic procedure in the current study.[18]

The results showed no significant difference in the postoperative HR and mean blood pressure, which is in parallel to the results of Abdulla who investigated the addition of hydrocortisone to ropivacaine intraperitoneally, and they found no difference between ropivacaine group and hydrocortisone ropivacaine group as regards the patient hemodynamic postoperatively.[19]

In agreement with the results of this study, Sharma et al. who studied intraperitoneal hydrocortisone with bupivacaine in laparoscopic cholecystectomy found that bupivacaine with hydrocortisone has significantly low VAS score at 6 h than bupivacaine alone also they found that opioid requirement was less in hydrocortisone group than hydrocortisone bupivacaine group.[15]

Time for the first analgesic request was prolonged in hydrocortisone bupivacaine group than in bupivacaine group, which is in agreement with the results of Asgari et al. who studied the same drugs in laparoscopic gynecological surgery,[17] however, this is in contrast to the results of Amini et al. who studied hydrocortisone versus bupivacaine; this difference may be explained by the use of drug combination in our study instead of hydrocortisone alone in the previous study.[16]

Limitations of the study
This study did not investigate the effect of intraperitoneal hydrocortisone on nausea, vomiting, and return of bowel function, as their incidence is affected by numerous factors in bariatric surgery, and this could be investigated in further studies. Further studies with different doses and concentration of the studied drugs and a greater number of the studied patients are recommended to be carried out to provide maximum postoperative pain relief with minimal adverse effects after bariatric surgeries.

**Conclusion**
Intraperitoneal hydrocortisone with bupivacaine had more effective postoperative pain relief with a decrease in postoperative meperidine requirement and prolonged the time of postoperative analgesic rescue than the use of intraperitoneal bupivacaine alone without associated adverse effects.

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**Conflicts of interest**
There are no conflicts of interest.

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