Comparison between thoracic epidural and systemic opioid analgesia on lung mechanics in obese patients in major gynecological procedures

Department of Anesthesia, Faculty of Medicine, Benha University, Benha, Egypt
Correspondence to Yahya S.A. Dabour, MBBCh, Department of Anesthesia, Faculty of Medicine, Benha University, Benha, 13511, Egypt. Tel: 012-3188173; e-mail: dabour19@gmail.com
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Background
The study was conducted to compare the effects of thoracic epidural analgesia versus systemic opioid analgesia on lung mechanics in obese patients undergoing major gynecological procedures (abdominal hysterectomy, ovarian cyst, ovarian mass, and abdominal explorations). We evaluated their analgesic efficacy over the first 12 postoperative hours after gynecological surgeries, in a randomized, single-blind, clinical trial in 60 patients divided into two equal groups, with 30 patients in each group.

Patients and methods
Sixty patients were randomized into two equal groups, with 30 patients in each group: group I received general anesthesia in combination with intravenous opioids, and group II received general anesthesia in combination with thoracic epidural anesthesia. General anesthesia was induced with fentanyl 1–2 μg/kg and propofol 1–3 mg/kg followed by rocuronium 0.6 mg/kg. Each patient was assessed for pulmonary function tests, pethidine consumption, visual analog pain scale at rest and on movement, vital signs and the presence of complications (nausea, vomiting, sedation, and pruritus) postoperatively by a blinded investigator in the postanesthesia care unit and at 1, 3, 6, and 12 h postoperatively.

Results
Group II patients showed significantly increased postoperative pulmonary function test values compared with group I patients at 1, 3, and 6 h; the postoperative analgesia is more effective with group II than with group I (epidural > systemic opioid), and the postoperative consumption of pethidine in the epidural group is lower than in the opioid group. As regards complications during the study in all groups, complications such as nausea, vomiting, pruritus, and sedation were recorded, which were more in the systemic opioid group than in the epidural group.

Conclusion
Particularly for obese patients, epidural anesthesia and postoperative epidural analgesia improve the postoperative respiratory functions, compared with general anesthesia and systemic analgesia, and reduce postoperative pain in obese patients undergoing major gynecological procedures.

Keywords:
gynecological, lung mechanics, obesity, opioids, thoracic epidural

Introduction
Obesity is becoming a serious problem because its prevalence is increasing and it is well known now that there is a significant negative correlation between lung mechanics and obesity [1]. The severely obese patients have varying degrees of intrinsic reduction of expiratory flow rates and lung volumes [2]. They are predisposed to postoperative atelectasis, ineffective clearing of respiratory secretions, and other pulmonary complications. There is a significant negative correlation between perioperative spirometric tests and obesity, as abdominal surgeries lead to severe pain that is associated with changes in respiratory mechanics, shallow breathing and impaired ability to cough [3].

Epidural anesthesia (EDA) for perioperative analgesia would reduce the magnitude of postoperative deterioration in lung function in obese patients more than in nonobese patients compared with systemic opioids [4]. Despite some controversies, many anesthetists consider perioperative EDA as an important part of a multimodal approach to improving patient outcome and analgesia rather than relying solely on systemic opioid administration [5].
Patients and methods
After obtaining approval by the Benha University Hospital Ethics Committee, and written informed consent from the patient, we studied 60 ASA physical status I–II patients scheduled for elective major gynecological surgeries (abdominal hysterectomy, ovarian cyst, ovarian mass, and abdominal explorations) in a randomized, single-blind, clinical trial. We excluded patients who were pregnant, those with a history of relevant drug allergy, age less than 20 years or more than 60 years, coagulopathy, end-stage obstructive or restrictive pulmonary disease. Patients were randomly allocated into two equal groups: group I (n=30) patients received general anesthesia in combination with intravenous opioids, and group II (n=30) patients received general anesthesia in combination with thoracic EDA.

Randomization was done by an online program, which was used to generate a random number list. Patient randomization numbers were concealed in opaque envelopes, which were opened by the study investigator. The staff members providing postoperative care were blinded to group assignment. All patients were asked to fast 8 h before operation. Intravenous cannula was inserted and the patients were premedicated with midazolam 0.01–0.02 mg/kg, intravenous, 30 min preoperatively, while patients were lying on a semisitting position on oxygen mask.

On admission to the operating room, routine monitors were connected and baseline measurements were recorded, and then an arterial cannula was inserted in the radial artery of the nondominant hand under local anesthesia after performing modified Allen’s test.

Technique of thoracic epidural
The patient was in the sitting position and supported by an attendant. A standard regional anesthesia tray was prepared with the following equipment:

1. Sterile towels and 4"x4" gauze packs.
2. Twenty milliliter syringes with local anesthetic.
3. Sterile gloves, marking pen and surface electrode
4. One 1.5" 25-G needle for skin infiltration.
5. An 18-G 8-cm epidural needle (Perifix; B. Braun Melsungen AG, 34212 Melsungen, Hessen, Germany).

Before induction of general anesthesia, epidural block was initiated, and the patient was made to sit supported by an attendant on the edge of the operating bed with legs on a stool, leaning forward with arms crossed. After patient positioning, the skin of the back was prepared with an iodine-containing sterilizing solution. The back was draped in a sterile manner, as we followed full sterile precautions, including gown, mask, and gloves, and then the thoracic interspace (T8–T9 or T9–T10) was identified. Low thoracic approach was chosen to spare block of intercostal muscles, and affection of pulmonary functions would be minimized. Midline approach was chosen (because some of the patients were obese and paramedian approach would be difficult), and a skin wheal of local anesthetic (5 ml lidocaine 2%) was produced using a 25-G needle at the midpoint between the two adjacent vertebrae to anesthetize the potential tract of the epidural needle. An 18-G Tuohy epidural needle (Perifix; B.Braun Melsungen AG) was inserted and directed through the dermis into the interspinal ligament, which was verified by firm resistance; at this point, the needle trocar was removed and a glass syringe filled with air was connected, and then the needle was advanced by two-handed grip on the syringe and needle with continuous firm pressure on the hub as the needle moves forward, until loss of resistance was elicited. Epidural catheter (B.Braun Melsungen AG) was threaded through the needle, the needle was removed and the catheter was adjusted to keep 4 cm in the epidural space. A test dose of 4 ml of 2% plain lidocaine with 1 : 20 000 ephinephrine (0.005 mg/ml) was injected to rule out subarachnoid or intravenous placement of the catheter. At least 15 min before surgery, a loading dose of bupivacaine 0.5% (8 ml) and 100 μg of fentanyl were injected in the epidural catheter, and we waited until establishment of analgesia was evidenced by diminished sensation to pin prick. Further bolus injections of bupivacaine 0.5% were sensation to pin prick. Further bolus injections of bupivacaine 0.5% were given according to clinical needs (heart rate, arterial blood pressure, pupil size, and sweating). In both groups, general anesthesia was induced with propofol 2 mg and fentanyl 1–2 μg/kg, intravenous. Tracheal intubation was facilitated by rocuronium 0.6 mg/kg, intravenous, and anesthesia was maintained with sevoflurane 2%. Increments of rocuronium were given to maintain muscle relaxation whenever needed at a dose of 0.5 mg/kg. Analgesia was maintained intraoperatively using fentanyl, and repeated doses were given according to clinical signs (heart rate, arterial blood pressure, pupil size, and sweating), but not within 1 h of the estimated end of the surgery to achieve rapid recovery. Ventilation was controlled using lean body weight used to calculate a tidal volume of 8–10 ml/kg with a respiratory rate that avoids excessive hypercapnea or hypocapnea.
Neostigmine 0.04–0.08 mg/kg, together with atropine 0.01–0.02 mg/kg, was given as needed when extubation criteria were found, as well as recovery of consciousness (eye opening on demand), protective airway reflexes and adequate spontaneous ventilation.

Postoperative pain management
In group I, basic analgesia was achieved using pethidine (1 mg/kg) every 8 h intramuscularly to obtain adequate analgesia and pain score of 20 mm while coughing.

In group II, basic analgesia was achieved using a continuous epidural infusion of bupivacaine (0.125%) with fentanyl (2 μg/ml) through the epidural catheter, and the infusion rate was adjusted to obtain a sensory level of T5 (range: 5–10 ml/h) and adequate analgesia.

In both groups, if additional analgesia was needed it was achieved by pethidine (0.5 mg/kg). Adequate analgesia was defined as pain score less than 20 mm while coughing, which was assessed on the 100-mm visual analog scale (VAS), in which 0 represented no pain and 100 mm indicated the worst possible pain or dyspnea.

Spirometry
Spirometry was standardized with each patient in a 30 head-up position using an automated flow-sensing spirometer (Spirolab III, ver 4.3; Italy; MIR Group Organization, 5462 S. Westridge Drive, New Berlin, WI, USA). At the preanesthetic visit, a baseline spirometry measurement was taken based on American Thoracic Society/European Respiratory Society, 2005, recommendations with all participants in a sitting position. If possible, at least three and up to a maximum of eight forced expiratory maneuvers were performed in an effort to meet the American Thoracic Society standards. Spirometric measurements taken were vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and peak expiratory flow rate (PEFR). Spirometric assessments were repeated at 1, 3, 6, and 12 h postoperatively, as soon as the patients were free from pain during coughing.

Parameters of assessment
The primary outcome was pulmonary function tests: VC, FVC, FEV1 and PEFR; all these parameters were taken preoperatively at baseline, and 1, 3, 6, and 12 h postoperatively.

Secondary outcome measures included VAS recorded postoperatively at 0, 0.5, 1, 3, 6, and 12 h, total dose of postoperative pethidine requirements, and side effects related to narcotics, epidural, and major surgical procedures.

Statistical analysis
Statistical analyses were performed using a standard statistical program (SPSS, version 16; SPSS Inc., Chicago, Illinois, USA). Quantitative data were presented as mean±SD. Qualitative data were presented as numbers and percentages. Quantitative data were analyzed by using unpaired Student’s t-test. Qualitative data were analyzed by using χ2 test and Z test. P value less than 0.05 was considered statistically significant and P value less than 0.01 was considered highly statistically significant.

Results
Sixty patients were entered into the study undergoing elective gynecological surgeries, and 30 patients were randomized to receive general anesthesia in combination with intravenous opioids. In all, 30 patients were randomized to receive general anesthesia in combination with thoracic EDA.

Table 1 shows that on comparing the two groups as regards demographic data there was no significant difference among the two studied groups. In the two groups as regards VC, a statistically insignificant value was found at the preoperative period and a statistically significant decrease at 1, 3, and 6 h postoperatively in the opioid group (Table 2).

On comparing the two groups as regards FVC that there was a statistically insignificant value at preoperative period and statistically significant decrease at 1, 3, and 6 h postoperatively in the

Table 1 Comparison between both groups as regards age, weight, BMI, height, and operative time

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Opioid group (mean±SD)</th>
<th>Epidural group (mean±SD)</th>
<th>t-Test</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.51±6.36</td>
<td>51.66±6.29</td>
<td>0.63</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163±10.73</td>
<td>162.6±11.62</td>
<td>0.48</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>92.55±5.82</td>
<td>90.46±5.38</td>
<td>1.62</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>28.39±5.29</td>
<td>27.62±6.27</td>
<td>0.64</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>156.78±23.19</td>
<td>155.44±20.19</td>
<td>0.29</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Student’s t-test; significant if P < 0.05.
opioid group (Fig. 1). On comparing the two groups as regards FEV1 there was a statistically insignificant value preoperatively and a statistically significant decrease at 1, 3, and 6 h postoperatively in the opioid group (Table 3).

As regards PEFR, in the two groups, there was a statistically insignificant value preoperatively and statistically significant decrease at 1, 3, and 6 h postoperatively in the opioid group (Fig. 2). On comparing the two groups as regards postoperative analgesic requirements a statistically significant increase was observed in analgesic requirement in the opioid group postoperatively (Table 4).

On comparing the two groups as regards VAS, there was a statistically significant decrease at 0, 0.5, 1, and 3 h in the epidural group postoperatively (Fig. 3). In addition, comparing the two groups as regards complications, there was a statistically insignificant value among the two studied groups (Table 5).

**Discussion**

Obese patients undergoing major abdominal surgeries were anesthetized, in the past, by general anesthesia alone despite the associated adverse effects of general anesthesia on these already compromised patients. Despite some controversies, many anesthetists consider perioperative EDA as an important part of

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Comparison between both groups as regards vital capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC (l)</td>
<td>Opioid group (mean±SD)</td>
</tr>
<tr>
<td>Preoperative</td>
<td>3.356±0.384</td>
</tr>
<tr>
<td>Postoperative</td>
<td></td>
</tr>
<tr>
<td>1 h</td>
<td>2.55±0.49</td>
</tr>
<tr>
<td>3 h</td>
<td>2.96±0.49</td>
</tr>
<tr>
<td>6 h</td>
<td>3.101±0.413</td>
</tr>
<tr>
<td>12 h</td>
<td>3.311±0.387</td>
</tr>
</tbody>
</table>

VC, vital capacity. Student’s t-test; significant if P<0.05. **Highly significant.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Comparison between both groups as regards forced expiratory volume in 1 s</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (l)</td>
<td>Opioid group (mean±SD)</td>
</tr>
<tr>
<td>Preoperative</td>
<td>3.11±0.318</td>
</tr>
<tr>
<td>Postoperative</td>
<td></td>
</tr>
<tr>
<td>1 h</td>
<td>2.29±0.394</td>
</tr>
<tr>
<td>3 h</td>
<td>2.64±0.354</td>
</tr>
<tr>
<td>6 h</td>
<td>2.89±0.342</td>
</tr>
<tr>
<td>12 h</td>
<td>3.076±0.328</td>
</tr>
</tbody>
</table>

FEV1, forced expiratory volume in 1 s. **Significant. "Highly significant.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Comparison between both groups as regards total analgesic requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesic requirement</td>
<td>Opioid group (mean±SD)</td>
</tr>
<tr>
<td>Postoperative pethidine in mg</td>
<td>197±24.5</td>
</tr>
</tbody>
</table>

Student’s t-test; significant if P<0.05. **Highly significant.
the multimodal approach for improving patient outcome and analgesia rather than relying solely on systemic opioid administration. This may be particularly important for obese patients undergoing major surgeries. In our study, a comparison was made between the effect of thoracic epidural analgesia and systemic opioids on the perioperative lung mechanics on obese patients undergoing major gynecological procedures, and patients were divided into two equal groups:

Group I received general anesthesia in combination with intravenous opioids.

Group II received general anesthesia in combination with low thoracic EDA.

In the present study, the results of demographic data were nearly the same in all groups and are of no significance or concern to our study.

In the present study, pulmonary function tests (VC, FVC, FEV1, and PEFR) were decreased in both epidural and opioid groups from baseline data in the whole readings and shifted towards baseline at 12 h, and there was a significant decrease in the opioid group than in the epidural group. The VC showed nearly the same values of both epidural and opioid groups preoperatively and a significant decrease in the whole postoperative period (1, 2, and 3 h) and then a nonsignificant decrease at 6 and 12 h; this was the same in FVC, FEV1, and PEFR. The FEV1/FVC was not significantly different among the two groups, as both FEV1 and FVC decreased. The better effect of thoracic epidural on pulmonary function over the systemic opioid group can be explained by the better postoperative analgesia, decreased incidence of atelectasis compared with systemic opioids, as well as the rapid recovery allowing patients to sigh and cough, and because of respiratory depression and a decrease in all respiratory functions caused by systemic opioids. Our study was also in agreement with that of Ulke and Sentürk [6], who reported that reduction in functional residual capacity after abdominal and thoracic surgeries is a well-known change with general anesthesia, and adequate analgesia is not the only contributing factor to prevent respiratory complications, but other factors such as preservation of diaphragmatic function and early extubation must be considered.

The results were in agreement with those of von Ungern-Stenberg et al. [7], in a similar study, who found that thoracic EDA had less influence on spirometric measurements, even though initiation of EDA may have accounted for some degree of muscle relaxation, as shown by changes in dynamic rather than static spirometric measurements of respiratory function. They found that the decrease in FVC and FEV1 after initiation of EDA was mainly attributable to change of position, as baseline measurements performed in the sitting position were compared with subsequent measurements in the supine position. They also reported that, during forced expiration (e.g. spirometry), the principal expiratory muscles are those of the abdominal wall and, to a lesser extent, the internal intercostal muscles, and thus EDA with sensory levels extending from approximately T4–L1, are likely to be accompanied by some degree of muscle paralysis, even if low concentrations of local anesthetics were used, and it is more likely to block the muscles of the abdominal wall (innervation T6–L1) than the diaphragm (C3–C5) or the intercostal muscles (T1–T11). This blockade of abdominal muscles

<table>
<thead>
<tr>
<th>Complications</th>
<th>Opioid group [N (%)]</th>
<th>Epidural group [N (%)]</th>
<th>$\chi^2$-Test</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>7 (70)</td>
<td>3 (21.4)</td>
<td>1.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Pruritus</td>
<td>5 (35.7)</td>
<td>2 (20)</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>1 (10)</td>
<td>3 (21.4)</td>
<td>1.05</td>
<td></td>
</tr>
<tr>
<td>Sedation</td>
<td>2 (14.3)</td>
<td>0 (0)</td>
<td>2.05</td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0 (0)</td>
<td>1 (7.14)</td>
<td>1.01</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15 (100)</td>
<td>9 (100)</td>
<td>5.74</td>
<td></td>
</tr>
</tbody>
</table>

*$P$ is significant if <0.05.
because of low thoracic EDA is reflected by a reduction of the dynamic parameters PEFR and Maximal expiratory flow rate 25 per cent–75 per cent (MEF25–75), which depend more on active exhalation, but it is without significant changes in comparatively static spirometric measurements.

In contrast, a study conducted by de Leon-Casasola et al. [8] showed no improvement in pulmonary outcome with the use of thoracic epidural anesthesia (TEA); however, these studies consisted mostly of healthy low-risk patients and did not control postoperative analgesia, and/or lacked sufficient statistical power. Also in the present study, VAS was significantly lower in the epidural group than in the opioid group from 0 to 12 h postoperatively; this was also confirmed by patient satisfaction score that showed significantly higher values in the epidural groups (45.044±8.9) compared with the opioid group (35.73±7.48). This could be explained by the quality of analgesia and the reduced pulmonary functions complications caused superiorly by EDA over systemic opioids.

This was in agreement with a systemic review conducted by Pergialiotis et al. [9], who found that patient-controlled epidural analgesia seems to be superior to traditional patient-controlled intravenous analgesia during the postoperative management of gynecologic oncology patients. They also reported that the need for morphine equivalents was more frequent among patients of the patient-controlled analgesia (PCA) group and for postoperative days 1 and 2, respectively. This was confirmed by Ulke and Sentürk [6], who reported that dynamic analgesia, rapid mobilization, and blunted stress response with TEA performed alone, or combined with general anesthesia, is not only the method of choice for postoperative analgesia in many operations but also obtains a large number of other, nonanalgesic advantageous effects as the synergistic effect of local anesthetic and opioids combination is well known, and it provides better analgesia during activity. The use of combination may reduce the dose-related adverse effects of either agent alone, and EDA is particularly effective at providing dynamic analgesia, early mobilization, and rapid functional recovery.

Our results are not in agreement with those of Moawad and Mokbel [11], who performed a comparative study between fentanyl–bupivacaine patient-controlled epidural analgesia and fentanyl patient-controlled intravenous analgesia as postoperative analgesia after major abdominal surgery; they found that in the first hour postoperatively the Numeric Pain Rating Scale (NPRS) for pain score in the patient controlled intravenous analgesia with fentanyl (PCA) group was significantly less than the pain score in the patient-controlled epidural analgesia (PCEA) group, because of the rapid onset of intravenous fentanyl compared with epidural fentanyl–bupivacaine combination. There are two possible explanations for this. The peak effect of intravenous fentanyl occurs 2–5 min after intravenous bolus administration, whereas the analgesic onset of fentanyl after epidural administration is delayed for 10–20 min. This delay may be explained by the time taken for fentanyl to traverse the dura and cerebrospinal fluid and bind to opiate receptors in the neuraxis of the spinal cord. An alternative explanation may be that the analgesic effects of epidural fentanyl appear largely mediated by systemic absorption.

As regards the total postoperative analgesic requirement, the total analgesic requirement postoperatively was 197±24.5 mg in the opioid group versus 60.12±16.2 mg in the epidural group for the whole 12 h postoperatively; this is because of the effectiveness of thoracic EDA on pain relief, and thus there was no need of extra added opioid analgesia and the consumption was lower. In our study, only two patients of the epidural group needed extra added systemic opioids.

This was in agreement with von Ungern-Stenberg et al. [7], who conducted a study on 84 patients having midline laparotomy who were divided into two equal groups: one group received TEA and the other group received systemic opioids; they found that there was a significant difference between the two groups as regards intraoperative analgesics. The fentanyl dose was 300 μg in the epidural group versus 600 μg in the opioid group, and postoperative
analgesic requirement was 3.6 versus 0.7 mg in the epidural group.

In our study, side effects were not significant among both epidural and opioid groups. This is because of the fact that both groups received opioids either epidurally or systemically. This is in agreement with Parris [12] in a similar study comparing epidural and systemic opioids. In our study, vomiting was seven in the opioid group versus three in the epidural group. Pruritus was five in the opioid group versus two in the epidural group. Sedation was two in the opioid group versus 0 in the epidural group. This is because of the fact that both groups received opioids either intravenously or epidurally, but the effect of opioids was more but not significantly evident in the systemic opioid group.

Limitations of our study are one of the possible shortcomings of our study; the study did not include a placebo-control group and the study limited assessment of postoperative analgesia to the first 12 postoperative hours.

We conclude that obesity is an important risk factor for perioperative impairment of spirometric measurements in patients undergoing major gynecological surgeries. The severity of postoperative lung volume reduction measured by spirometry was reduced by the presence of EDA, and postoperative restoration of lung volumes was significantly quicker. Therefore, we recommend that, whenever possible, epidural analgesic techniques should be adopted in the obese patients particularly if they are undergoing major abdominal surgeries to improve postoperative pulmonary functions.

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Nil.

Conflicts of interest
There are no conflicts of interest.

References