RESPIRATION AND THE AIRWAY

Effect of obesity and thoracic epidural analgesia on perioperative spirometry

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Background. Lung volumes in obese patients are reduced significantly in the postoperative period. As the effect of different analgesic regimes on perioperative spirometric tests in obese patients has not yet been studied, we investigated the effect of thoracic epidural analgesia and conventional opioid-based analgesia on perioperative lung volumes measured by spirometry.

Methods. Eighty-four patients having midline laparotomy for gynaecological procedures successfully completed the study. Premedication, anaesthesia and analgesia were standardized. The patients were given a free choice between epidural analgesia (EDA) (n=42) or opioids (n=42) for postoperative analgesia. We performed spirometry to measure vital capacity (VC), forced vital capacity, peak expiratory flow, mid-expiratory flow and forced expiratory volume in 1 s at preoperative assessment, 30–60 min after premedication and 20 min, 1 h, 3 h and 6 h after extubation.

Results. Baseline values were all within the normal range. All perioperative spirometric values decreased significantly with increasing body mass index (BMI). The greatest reduction in VC occurred directly after extubation, but was less in the EDA group than in the opioid group: mean of −23(± 8)% versus −30(±12)% (P<0.001). In obese patients (BMI>30) the difference in VC was significantly more pronounced than in patients of normal weight (BMI<25): −45(± 10)% versus −33(±4)% (P<0.001). Recovery of spirometric values was significantly quicker in patients receiving EDA, particularly in obese patients.

Conclusion. We conclude that EDA should be considered in obese patients undergoing midline laparotomy to improve postoperative spirometry.

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Introduction

The prevalence of obesity is increasing and about one-third of the population of industrialized countries is at least 20% overweight.1 Obesity is a risk factor for postoperative pulmonary complications since it predisposes to the formation of atelectasis and thus contributes to pulmonary morbidity by jeopardizing respiratory function.2,3 There is a significant negative correlation between perioperative spirometric tests and obesity.4 Despite some controversies,5 many anaesthetists consider perioperative epidural anaesthesia (EDA) as an important part of a multimodal approach to improving patient outcome and analgesia rather than relying solely on systemic opioid administration.6 This may be particularly important for obese patients undergoing extensive laparotomies, although the superiority of EDA in obese patients has not yet been proved. Since there are no studies assessing the impact of body mass index (BMI=weight [kg]/height2 [m2]) and different analgesic regimens on perioperative spirometry following midline laparotomy, we proposed that, compared with systemic opioids, EDA for perioperative analgesia would reduce the magnitude of postoperative deterioration in lung function in obese more than in non-obese patients.
Methods

Study population

The study was approved by the Ethics Committee of the University of Basel. Informed written consent was obtained from each patient before inclusion. We prospectively included 99 adult female patients (ASA I–II) scheduled for midline laparotomy for extensive abdominal gynaecological procedures. Patients who were ASA III only because of their morbid obesity, but without other systemic disease, were also included in the study. They were informed about the advantages, disadvantages and risks of EDA and opioid analgesia by independent anaesthetists not involved in this study. After making a free choice between EDA (n=48, EDA group) and opioids (n=51, opioid group), we invited the patients to participate in the study. For ethical reasons (adverse effects and particularly the neurological risks of thoracic EDA are of greater consequence for the patients than the risks of systemic opioid analgesia) the allocation to the different analgesic regimens was not randomized, and therefore the study was conducted using an observational design. We excluded patients who were pregnant, suffered from bronchial asthma requiring regular therapy, had cardiac disease associated with dyspnoea >NYHA II or had severe psychiatric disorders.

General anaesthesia

In both groups, premedication consisted of oral midazolam 7.5 mg given 30–60 min before surgery. In the EDA group, EDA was initiated after local infiltration according to our routine using an 18 gauge Tuohy needle and a 20 gauge multipor epidural catheter inserted at the T7–T8 or T8–T9 interspace. After a negative test dose consisting of lidocaine 2% (3 ml) with 1:200 000 epinephrine, an epidural bolus injection of bupivacaine 15 mg and fentanyl 100 µg in sodium chloride 0.9% (10 ml) were given. Further bolus injections of bupivacaine 0.5% followed according to clinical needs. In both groups, general anaesthesia was induced with propofol 2 mg kg\(^{-1}\) and fentanyl 2 µg kg\(^{-1}\) i.v. Tracheal intubation was facilitated by atracurium 0.5 mg kg\(^{-1}\) i.v. Anaesthesia was maintained with nitrous oxide 66% in oxygen and propofol by infusion using the Bristol formula (10 mg kg\(^{-1}\) h\(^{-1}\) for the first 10 min, 8 mg kg\(^{-1}\) h\(^{-1}\) for a further 10 min and thereafter 6 mg kg\(^{-1}\) h\(^{-1}\) or adjusted to individual needs).\(^7\) Ventilation was controlled using an ADU Ventilator (Datex Ohmeda, S/5 ADU Helsinki, Finland) with a circle system. Repeated doses of fentanyl were given during surgery as necessary based on clinical signs (heart rate, arterial pressure, pupil size and sweating), but not within 60 min of the estimated end of surgery. To have the patient fully alert and cooperative for spirometry, we substituted sevoflurane for propofol 30–60 min before the estimated end of surgery as this was considered, on the basis of clinical observations, to allow for a more rapid recovery.\(^4\) Increments of atracurium 5 mg i.v. were given to maintain muscle relaxation which was monitored by train-of-four stimulation. Neostigmine 2.5 mg and glycopyrrolate 0.5 mg i.v. were given as needed to antagonize residual neuromuscular block. Before extubation of the trachea, four equal twitches in the train-of-four without tetanic fade (50 Hz over 5 s) were required as well as recovery of consciousness (eye opening on demand), protective airway reflexes and adequate spontaneous ventilation.

Postoperative pain management

In both groups, postoperative basic analgesia consisted of paracetamol 1000 mg rectally or orally every 6 h starting directly after the operation. In the EDA group, a continuous infusion of epidural bupivacaine 0.125% with fentanyl 2 µg ml\(^{-1}\) was administered. The infusion rate was adjusted to obtain a sensory level of T\(_5\) (range 5–10 ml h\(^{-1}\)) and adequate analgesia. Adequate analgesia was defined as a pain score ≤20 mm while coughing, which was assessed on the 100 mm visual analogue scale (VAS), where 0 mm represented no pain or no dyspnoea while 100 mm indicated the worst possible pain or dyspnoea. If pain persisted in the EDA group despite a sufficient sensory level, as a first measure an additional epidural dose of fentanyl 100 µg in sodium chloride 0.9% (10 ml) was given. In both groups, according to our standards, increments of methadone 2 mg i.v. were given to the patients in order to achieve adequate analgesia. The total dose of methadone given to each patient was neither limited nor weight adjusted.

Spirometry

Spirometry was standardized with each patient in a 30° head-up position using a Vitalograph 2120 (Vitalograph, Hamburg, Germany). At the pre-anaesthetic visit, a baseline spirometry measurement was taken (T\(_0\)) after a thorough demonstration of the correct usage. Vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in 1 s (FEV\(_1\)) mid-expiratory flow (MEF\(_{25–75}\)) and peak expiratory flow (PEF) were measured and the FEV\(_1\)/FVC ratio was calculated. At each assessment time, spirometry was performed at least three times to be able to meet the criteria of the European Respiratory Society (ERS)\(^5\) and the best measurement was recorded. When the patient arrived in the operating theatre (about 30–60 min after premedication), we repeated spirometry (T\(_1\)) after initiation of effective EDA (where applicable) and before induction of anaesthesia in order to compare the effect of premedication alone with the effect of premedication plus effective EDA on spirometric tests. After extubation, as soon as the patient was alert and fully cooperative, pain and dyspnoea were assessed during coughing using the VAS before and, if necessary, after analgesic therapy. Pain was not assessed during the VC manoeuvre itself. As soon as a patient had a VAS pain score ≤20 mm during coughing (all patients met this criterion within 20 min of extubation), we performed spirometry for the third time (T\(_2\)). Spirometric assessments were
repeated in the postanaesthetic care unit at 1 h ($T_3$), 3 h ($T_4$) and 6 h ($T_5$) after extubation. Prior to each assessment, as soon as the patients were free from pain during coughing, morphine requirements were documented and sensory levels of EDA were evaluated. All postoperative measurements, including spirometry, were performed by postanaesthetic care unit nurses trained to use the spirometer but unaware of the study hypothesis and otherwise not involved in this study.

**Statistical analysis**

We measured the weight and height of each patient to obtain the exact BMI. In order to quantify the effect of obesity, we allocated the patients according to their BMI as follows: normal weight (BMI<25), mildly obese (BMI 25–30) and obese (BMI>30). To allow for comparisons between the patients and the groups, pulmonary function values were calculated as the percentage deviation from baseline ($T_0$). To compare data within the groups, repeated-measure analysis of variance (ANOVA) was applied. To compare data between the groups, a Wilcoxon rank-sum test was performed. For post hoc comparisons, a Bonferroni test was applied and probability values were calculated. The Spearman rank correlation test was used to calculate the correlation coefficients between spirometric measurements and BMI as the BMI data were skewed. A $P$-value <0.05 was considered significant. The Statview for Windows software package (SAS Institute Inc., Cary, NC, USA, Version 5.0.1) was used for statistical calculations.

**Results**

We recruited 99 women scheduled for laparotomy. The planned surgery was altered for three patients, seven subjects declined to continue and measurements were unsatisfactory in five. Consequently, we present data for 84 female patients with 42 individuals per group (Table 1). The number of patients for each BMI group was as follows: normal weight (EDA $n=25$, opioid $n=24$), mildly obese (EDA $n=8$, opioid $n=11$) and obese (EDA $n=9$, opioid $n=7$). Patients with unacceptable spirometric tracings did not differ in age or weight from those with acceptable measurements nor did they have extreme values of BMI. The distribution of non-smokers between the groups was similar with 38 (90%) in the EDA group and 35 (83%) in the opioid group. The smokers (2–15 pack-years) were evenly distributed over the BMI range with a minor tendency towards lower BMI. Antagonism of muscle relaxation was necessary in only two patients of the opioid group and in none of the EDA group. All patients met the extubation criteria. The mean duration of surgery was 180 (SD 45) min, with a maximum of 260 min.

**Vital capacity**

The baseline VC values were within the normal range. After premedication, there was a small but significant decrease in VC compared with baseline values in all patients (Table 2) but there was no difference between the two groups. The decrease was greater in those with a higher BMI, although the effect in normal-weight patients was minimal (Fig. 1 and Table 3). In both groups, the lowest values were found directly after extubation. The opioid group showed a significantly greater decrease in VC at all postoperative assessments as well as a slower recovery of VC than the EDA group (Fig. 1). At every point, VC values decreased significantly with increasing BMI (Fig. 1). There was a significant correlation between BMI and VC for all assessments ($P<0.005$).

**Table 1** Anthropometric data for 84 patients undergoing midline laparotomy with thoracic epidural analgesia ($n=42$) or with an opioid-based regime ($n=42$) as postoperative pain relief. Values are median (range, SD)

<table>
<thead>
<tr>
<th>AEPA</th>
<th>Epidural Analgesia</th>
<th>OpioidAnalgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>48 (26–88)</td>
<td>46 (23–90)</td>
</tr>
<tr>
<td>BMI 24 (5.6)</td>
<td>24 (5.6)</td>
<td>24 (5.8)</td>
</tr>
</tbody>
</table>

**Table 2** Absolute and relative values of vital capacity, forced vital capacity, forced expiratory flow rate in 1 s, mid-expiratory flow rate and peak expiratory flow rate for patients with epidural or opioid analgesia. Values are mean (SD). Changes are shown as percentage of preoperative value. All changes within the groups were significant (repeated measure ANOVA); the significances between the groups (Wilcoxon rank-sum test) are indicated (*significant; NS, not significant)
Other spirometric values

The baseline values of all other variables (FVC, FEV₁, MEF₂₅₋₇₅ and PEF) were within normal ranges. At each measurement, they changed in parallel with VC with the exception of the EDA group showing lower PEF and MEF₂₅₋₇₅ values after premedication (T₁) than the opioid group (Table 2). All these parameters correlated significantly with BMI (P<0.005). The ratio FEV₁/FVC did not change in either group throughout the study period.

Intraoperative opioid requirement, postoperative pain scores and pain relief

There were no differences in pain scores between the groups when spirometry was performed; the maximum VAS value was 20 mm. There was no correlation between the VAS scores and the reduction in spirometric measurements in either group of patients. During the whole study period, no patient in either group complained of dyspnoea.

There were significant differences between the groups regarding intraoperative and postoperative opioid requirements. Mean intraoperative fentanyl doses were 0.30 (0.10) mg in the EDA group versus 0.62 (0.17) mg in the opioid group.

Postoperatively, seven patients in the EDA group received a single dose of epidural fentanyl 100 μg, while four patients received a single dose of methadone 2 mg i.v. Postoperative analgesic requirements were higher in the
opioid group, as indicated by mean methadone doses of 0.9 (1.1) mg immediately after extubation, 4.5 (2.2) mg between T2 and T3, 4.1 (2.1) mg between T3 and T4, and 4.4 (1.9) mg between T4 and T5. This resulted in a total methadone dose within the first six postoperative hours of 14 (3.6) mg for the opioid group compared with 0.2 (0.7) mg for the EDA group. There was no correlation between the opioid consumption and the reduction of VC within either the EDA or the opioid groups.

Discussion

Spirometric measurements as a measure of respiratory function

Although spirometry is only a surrogate measure of respiratory function in the perioperative period, it is an accurate, reproducible and simple investigative tool that can be used easily in the immediate perioperative period in both the operating theatre and the postanaesthetic care unit. Healthy patients may be able to cope with less than a full VC range during normal tidal breathing, but important respiratory functions such as coughing and deep breathing may be significantly impaired in critically ill patients or in patients with pre-existing pulmonary disease. In order to increase the accuracy of spirometry, factors that potentially interfere with breathing and volition, such as pain, should be eliminated or at least minimized as far as possible in order to produce reliable measurements.

Effect of premedication and initiation of effective EDA

The effect of premedication was similar to that shown in a previous study,4 although EDA was introduced as a new variable. Premedication resulted in a BMI-related reduction of VC with no significant difference between the groups and no further change by effective EDA. However, there was a comparatively wide range of individual responses to the effect of premedication. VC is known to be a good index of respiratory muscle strength in patients with neuromuscular disorders.9 Benzodiazepines have a spinaly mediated relaxant action on respiratory muscles9 and could have been expected to affect EDA. Benzodiazepines have a spinally mediated relaxant action on muscle strength in patients with neuromuscular disorders.9

Thus, if premedication is given to obese patients, they should be closely observed in the preoperative period for signs of respiratory impairment.

Surprisingly, EDA did not influence spirometric measurements (except for a reduction of PEF and MEF25–75 values), 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.12 13

Anaesthesia and immediate postoperative respiratory function

As previously described,4 the lowest spirometric values are observed during the first assessment after extubation. The decrease in VC, FVC, FEV1, MEF25–75 and PEF followed the same pattern (Table 2), and the FEV1/FVC ratio did not change. This suggests a restrictive pattern of respiratory compromise in the immediate postoperative period, as previously described.4 14

Postoperative impairment of spirometric measurements was probably not related to insufficient cooperation since all patients were alert and fully compliant within 20 min of extubation. Additionally, any lack of cooperation would have affected the whole study population to a comparable degree. The reduction of spirometric volumes observed in our study may have been caused by impaired respiratory mechanics, obesity and atelectasis formation promoted by general anaesthesia in the supine position, as well as by abdominal surgery.15–17 A reduction in both inspiratory and expiratory reserve volumes would not only have an impact on VC,14 but might interfere directly with the ability to cough effectively as a result of decreased inspiratory capacity and thus predispose to respiratory complications.3 14

Body mass index and immediate postoperative respiratory function

As previously reported,4 the compromise of spirometric measurements correlated significantly with increasing BMI, persisted over the entire study period and was more severe in obese patients. Six hours after an operation, the mean VC reduction in the opioid group was 42% for obese but only 21% for normal-weight patients. These data differed significantly from those obtained within the EDA group, in which there was a mean reduction in VC of 24% for obese and 13% for normal-weight patients.

Thoracic epidural analgesia and respiratory function

The effect of EDA on spirometric measurements is controversial. High-thoracic EDA was shown to decrease spirometric measurements by blocking intercostal muscle innervation.18 19 A recent study showed a 25–30% decrease in FVC and FEV1 after initiation of EDA in patients undergoing cardiac surgery. This decrease was mainly attributable to change of position, since baseline measurements
performed in the sitting position were compared with subsequent measurements in the supine position.\textsuperscript{20} In contrast with the latter results, and in line with our study, others have not found that EDA has any influence on spirometry or lung dynamics.\textsuperscript{21–24}

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. EDA with sensory levels extending from approximately T\textsubscript{4} to L\textsubscript{1} is likely to be accompanied by some degree of muscle paralysis, even if low concentrations of local anaesthetics are used,\textsuperscript{13} and is more likely to block the muscles of the abdominal wall (innervation T\textsubscript{6}–L\textsubscript{1}) than the diaphragm (C\textsubscript{3}–C\textsubscript{5}) or the intercostal muscles (T\textsubscript{1}–T\textsubscript{11}). This blockade of abdominal muscles because of low-thoracic EDA is reflected by a reduction in inspiratory parameters before impairing static spirometric measurements (e.g. VC).\textsuperscript{19,25–27} Even a subtle decrease in abdominal muscle tone because of EDA will affect dynamic parameters before impairing static parameters.

Some older studies show a reverse relationship between reduced spirometric measurements and increased postoperative complication rates.\textsuperscript{28} Despite the lack of evidence that EDA reduces in-hospital mortality, a recent large randomized trial showed a significant reduction in postoperative respiratory failure rates (23% versus 30%).\textsuperscript{2} However, since lung volumes were not measured, this trial did not answer the question as to whether a reduction in spirometric values was predictive of postoperative complications.

Overall, the positive effects of EDA on spirometric tests, which became even more important in obese patients, might add to other benefits of EDA shown in previous studies, such as earlier mobilization, more rapid recovery of bowel function, thus allowing oral nutrition, and less disturbance of mental status in the elderly.\textsuperscript{29,30}

**Postoperative pain and respiratory function**

Spirometric measurements have been used to quantify postoperative pain.\textsuperscript{31,32} Therefore it is crucial for a patient to be free of pain during spirometry and thus to be as close to preoperative baseline conditions as possible to avoid factors that affect test performance. Pain probably influenced the results of earlier studies in which insufficient postoperative pain relief might have contributed to a greater decrease of VC.\textsuperscript{28,33}

Although all our patients were free of pain during coughing (VAS≤20 mm), there might also have been some degree of abdominal tension because of volume shifts into the third space.\textsuperscript{14} The pain score during the VC manoeuvre itself was not measured. Theoretically, reduction of abdominal wall tension induced by EDA might result in a decrease of diaphragmatic strain and ease displacement of the abdominal contents during breathing, and thus might have contributed to the measured differences between the two techniques. Therefore inspiratory volumes would be increased in the EDA group, improving all spirometric measurements provided that active expiration is intact.\textsuperscript{12}

Sedation induced by the larger doses of opioids required during surgery and for postoperative analgesia might have interfered with spirometry of subjects not receiving the benefits of EDA, although there was no correlation between the opioid requirements and spirometric performance within the groups.

**Limitations**

An observational rather than a randomized study design was used in our study. With randomization, this study would not have been finished within a reasonable time span in our hospital. Many patients refuse thoracic EDA for fear of neurological complications after being informed about its risks. In consequence, the patients opted for systemic opioid analgesia technique.

The potential for a selection bias was minimized by the support of anaesthetists not involved in this study who were responsible for giving patients preoperative information. Patients were only asked for informed consent once they had decided on their perioperative pain regimen. Additionally, postoperative spirometry was performed by trained nurses who were unaware of the study hypothesis and were not involved in this study.

Our findings do not allow us to draw conclusions regarding the mechanism of VC loss or to distinguish between the loss of inspiratory and expiratory power. Nevertheless, the primary aim of our study was to examine the potential of different perioperative anaesthetic regimens for modifying spirometrically measured lung volumes, and to assess whether there were clinically relevant differences in postoperative respiratory impairment during the immediate postoperative period when the impact of surgical trauma and anaesthesia are likely to peak and trigger postoperative pulmonary morbidity.\textsuperscript{4}

We conclude that obesity is an important risk factor for perioperative impairment of spirometric measurements in patients undergoing laparotomy. The moderate reduction of spirometric tests induced by midazolam as premedication was not enhanced further by EDA. The reduction postoperatively was significantly greater in obese than in normal-weight patients. In all patients, 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. The use of EDA should be considered for obese patients undergoing midline laparotomy.

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