Abstract. – OBJECTIVE: General anesthesia in obese patients is both challenging and demanding. With the rates of obesity in the general population increasing, more patients undergo bariatric surgery. The aim of this study was to compare the performance, effectiveness and recovery from anesthesia of sevoflurane and propofol in combination with remifentanil, with and without bispectral index (BIS) monitoring in super obese patients undergoing bariatric surgery.

PATIENTS AND METHODS: In this prospective, double-blind, randomized, controlled study a total of 100 super obese patients (body mass index, BMI > 50 kg/m²) undergoing bariatric surgery were randomly allocated in four groups: a sevoflurane group (n = 25), a sevoflurane with BIS monitoring group (n = 25), a propofol group (n=25) and a propofol with BIS monitoring group (n=25). Hemodynamic parameters, depth of anesthesia, recovery from anesthesia and postoperative pain were recorded.

RESULTS: The mean age of patients was 37.7 ± 9.2 years and the median BMI was 57.86 ± 9.33. There were no statistically significant differences between the four groups with respect to patient characteristics, comorbidities and duration of surgery. The intraoperatively mean arterial pressure was significantly higher in both propofol groups. No significant difference was observed between the four groups in respect to heart rate changes during anesthesia. Although the time to eye-opening and extubation was significantly shorter in both propofol groups, recovery from anesthesia, assessed with the Aldrete, Chung and White recovery scores, was significantly faster in sevoflurane groups. No significant difference was observed in postoperative pain between the four groups.

CONCLUSIONS: Although both propofol and sevoflurane provide adequate general anesthesia, sevoflurane may be preferable in super obese patients because of superior hemodynamic stability and faster recovery from anesthesia.

Key Words: Sevoflurane, Propofol, BIS, VAS, Super obese, Bariatric surgery anesthesia.

Introduction

A balanced general anesthesia must include hypnosis, amnesia, analgesia, muscle relaxation and hemodynamic stability. Since there is not an ideal anesthetic drug that includes all of these properties, modern general anesthesia usually involves the administration of a variety of anesthetic agents, including hypnotic agents, opioids, benzodiazepines, inhalational agents and muscle relaxants. The choice of anesthetic drug combination is customized to the patient’s characteristics and needs, and the type and duration of surgery.

Due to the growing prevalence of obesity, the number of super obese patients (BMI > 50 kg/m²) undergoing bariatric surgery is constantly increasing. Most super obese patients present with several comorbidities and are at a higher risk of perioperative complications. In this patient population, general anesthesia is both demanding and challenging. Fast induction, perioperative hemodynamic stability and fast recovery are prerequisite.

Propofol, one of the commonly used intravenous anesthetics and sevoflurane, one of the newer volatile liquid anesthetic agents, have many desirable properties. Propofol offers fast induction and decreased prevalence of postoperative nausea and vomiting and is commonly used in ambulatory procedures. Sevoflurane, a low-soluble inhalation anesthetic, has been shown to have a cardioprotective effect, preventing from myocardial ischemia and arrhythmias. Patients regain full cognitive function after general anes-
thetics, history of substance abuse (alcohol or other drugs), contra indications for placement of thoracic epidural catheter (previous spine surgery, coagulation abnormalities) and patients who refused to participate were excluded from the study.

**Study Protocol**

Preoperative cardiovascular (resting 12-lead ECG, transthoracic echocardiography), pulmonary (baseline chest radiograph, pulmonary function testing), endocrinological and psychiatric evaluation was performed in all patients. Scheduled for elective early morning bariatric surgery all patients were fasted after midnight the day before and received premedication with ranitidine (150 mg per os at bedtime and 50 mg intravenously half an hour prior to surgery).

Heart rate (HR), invasive mean arterial pressure (MAP) and pulse oximetry were monitored during the entire procedure and baseline values were obtained prior to induction of general anesthesia. A radial arterial line and a central venous line, through internal jugular vein catheterization with a triple lumen catheter, were placed at the operating theater. Additional hemodynamic monitoring with ECG, central venous pressure (CVP), core body temperature and urine output, through a temperature-sensing Foley catheter, capnography and blood gas analysis was applied to all patients. BIS monitoring (BIS, Aspect Medical Systems) was used only in the appropriate groups. A BIS level between 40 and 55 was considered to be an appropriate state for adequate surgical anesthesia.

A thoracic epidural catheter was placed utilizing the paramedian approach and loss of resistance technique, at approximately T5-T7 interspaces, as assessed by palpation. Appropriate epidural catheter placement was confirmed by administering a test dose of 3 ml lidocaine 2% (total dose 60 mg). The presence of adequate sensory blockade, as assessed by decreased perception of cold, was confirmed before induction of general anesthesia. The epidural catheter was used only for postoperative analgesia.

**Induction of General Anesthesia**

Administration dose for all anesthetic drugs was based either on the ideal body weight (IBW), or the empirical formula of corrected body weight (CBW = IBW + [0.4 x excess weight]).

In both Sevoflurane groups, rapid sequence induction (RSI) to anesthesia was performed with the administration of a bolus dose of propofol 2 mg·kg⁻¹ CBW, followed by a bolus dose of...
remifentanil 1 µg·kg⁻¹ IBW and succinylcholine 1 mg·kg⁻¹ TBW and subsequent intubation of the trachea. The correct positioning of the endotracheal tube was confirmed by capnography and bilateral lung auscultation. Anesthesia was maintained with end-tidal sevoflurane concentrations of 1-3% (Siemens Multigaz Gas Analyzer). In the BIS monitoring group the sevoflurane concentrations were also adjusted to maintain a BIS level between 40 and 55. For every positive sympathetic response expressed with rise of blood pressure or heart rate > 15% of the baseline, a bolus inhalation of 8% sevoflurane (fresh gas flow 6 L/min, semi-closed circuit) was administered for 2 minutes. If the positive sympathetic response persisted and HR < 70/min, nifedipine 10 mg was administered sublingually, whereas if HR > 70/min diltiazem 10-20 mg was administered IV, followed by esmolol infusion if the response to diltiazem was unsatisfactory. The duration and frequency of positive sympathetic stress responses that required pharmacologic intervention were recorded.

In both propofol groups general anesthesia was induced with a gradually reduced continuous IV propofol infusion (21 mg·kg⁻¹ CBW for 5 min, 12 mg·kg⁻¹ CBW for 10 min and then 6 mg·kg⁻¹ CBW), followed by a bolus dose of remifentanil 1 µg·kg⁻¹ IBW and succinylcholine 1 mg·kg⁻¹ IBW. Anesthesia was maintained with continuous intravenous administration of propofol at 6-10 mg/kg/hr CBW and remifentanil at 0.1-1 µg/kg/min. In the BIS monitoring group the rate of propofol administration was also adjusted to maintain a BIS level between 40 and 55. For every rise of BP or HR > 15% of the baseline, a bolus dose of remifentanil 1 µg · kg⁻¹ IBW was administered, followed by a gradual increase in the continuous infusion rate of remifentanil to 1.0 µg/kg/min. The increased dose was interrupted when hemodynamic alterations returned to baseline. For any decrease in blood pressure < 15% of the baseline, continuous infusion rate of remifentanil was reduced and if no response was evident in 3 minutes etilefrine was administered. For every drop of HR < 45/min a bolus dose of atropine 0.5 mg was administered, followed by a repeated dose if no response was evident in 5 minutes. The duration and the frequency of the hemodynamic changes were recorded.

Neuromuscular blockage was accomplished intraoperatively in all groups by administering a bolus dose of cisatracurium 0.1 mg · kg⁻¹ IBW and maintained by continuous infusion. The depth of neuromuscular blockade was assessed by peripheral nerve stimulation of the ulnar nerve using a train-of-four monitor (TOF-Watch SX; Organon Ltd., Dublin, Ireland), and drugs were titrated to one or less twitches. The cisatracurium infusion was interrupted approximately 30 minutes before the end of operation. Reversal of neuromuscular blockage was achieved postoperatively with the administration of neostigmine and atropine, when the patient had at least 3 twitches on the TOF monitor.

An oxygen/air mixture was used for all patients (fresh gas flow 3 L/minute, semi-closed circuit), with the oxygen concentration of the inspired gases set to 40%. If arterial blood saturation, as monitored by pulse oximetry fell below 92%, oxygen concentration was raised to 50%. The lungs of the patients were mechanically ventilated with a Siemens Kion ventilator (Siemens-Elema AB, Solna, Sweden).

All patients received 1500 ml of colloid solution (gelofusine) and at least 3000 ml of ringer lactate solution for fluid replacement. The total amount of crystalloid was guided by continuous monitoring of the central venous pressure (CVP), with the endpoint of keeping urine output higher than 0.5 ml/kg/h.

All patients were extubated in the Post Anesthesia Care Unit (PACU) when they were able to open eyes, follow commands, demonstrate good inspiratory effort and ability to cough, and exhibited a spontaneous respiratory rate > 12 breaths/min, with end-tidal carbon dioxide concentration < 55 mm Hg. The time interval between the last skin suture and the trachea extubation was recorded. All episodes of postoperative hypertension, nausea, vomiting and pain exacerbation were also recorded. Recovery of anesthesia was evaluated utilizing the scoring systems of Aldrete, Chung and White 10, 30 and 60 minutes after the completion of the procedure15-18. Pain was assessed subjectively utilizing the visual analogue scale (VAS) score, ranging from 0 for “no pain” to 10 for “unbearable pain”. Epidural analgesia with continuous administration of 10 mg/h levobupivacaine plus 2 µg/ml/h fentanyl was initiated postoperatively in the PACU and continued until the second postoperative day.

**Statistical Analysis**

All data were collected by a blinded investigator. The Shapiro-Wilk test was used to check whether data were normally distributed. For the statistical analysis chi-squared test, Mann-Whitney U-test, unpaired Student’s t-tests, independent-samples Kruskal-Wallis test and ANOVA
were used as appropriate. $p$ values $<0.05$ were considered statistically significant. The demographic data were expressed as mean ± SD and range, and categorical data as n and percentage (%). Statistical analysis was performed using SPSS version 21.0 (IBM SPSS Statistics for Windows, Armonk, NY, USA).

**Results**

**Demographic Data**

A total of 100 patients were enrolled in the study. The mean age of patients was 37.7±9.2 years and sixty nine (69%) of patients were female. No difference was observed between the groups with respect to age, sex, BMI, weight, height, hypertension, diabetes, restrictive lung disease, obstructive sleep apnea (OSA), fatty liver disease, gastric ulcer, gastroesophageal reflux disease (GERD), smoking, alcohol consumption, depression, operation duration or stay (Table I).

**Intraoperative Effects**

The mean arterial blood pressure (MAP) and heart rate (HR) measures were decreased after induction to anesthesia. The changes in MAP values over time were significantly different between the sevoflurane and propofol groups ($p < 0.001$). The MAP values were significantly higher in the propofol groups ($p < 0.001$). There were no statistically significant differences in the MAP values between the propofol groups with respect to BIS monitoring ($p > 0.05$) and between the sevoflurane groups with respect to BIS monitoring ($p > 0.05$) (Figure 1). The changes in HR values over time were not significantly different between the four groups ($p = 0.46$) (Figure 2). To control hypertension and tachycardia 41 patients in the propofol groups were given bolus doses of remifentanil (mean total events 2.17±1.79). Respectively in the sevoflurane groups a bolus inhalation of 8% sevoflurane was only given to 18 patients (mean total events 0.72±0.93). The requirement for succinylcholine was similar between the four groups.

**Postoperative Effects**

The time from discontinuation of anesthesia to eye-opening and extubation was significantly shorter in the propofol groups regardless of the BIS monitoring. Time to eye-opening was 3.46±2.63 minutes in the propofol group.

---

**Table I. Demographic data (mean ± SD).**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group Sevoflurane (n = 25)</th>
<th>Group Propofol (n = 25)</th>
<th>Group Sevoflurane &amp; BIS (n = 25)</th>
<th>Group Propofol &amp; BIS (n = 25)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>42 ± 8</td>
<td>36 ± 9</td>
<td>36 ± 10</td>
<td>37 ± 9</td>
<td>0.298</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>10/15</td>
<td>8/17</td>
<td>7/18</td>
<td>6/19</td>
<td>0.651</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>61 ± 10</td>
<td>59 ± 11</td>
<td>57 ± 9</td>
<td>55 ± 6</td>
<td>0.662</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>170 ± 35</td>
<td>162 ± 27</td>
<td>157 ± 26</td>
<td>152 ± 20</td>
<td>0.477</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167 ± 9</td>
<td>166 ± 9</td>
<td>166 ± 9</td>
<td>166 ± 9</td>
<td>0.377</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>192 ± 29</td>
<td>194 ± 27</td>
<td>187 ± 28</td>
<td>176 ± 24</td>
<td>0.478</td>
</tr>
<tr>
<td>Stay</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
<td>0.223</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>12</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>0.189</td>
</tr>
<tr>
<td>Restrictive lung disease</td>
<td>24</td>
<td>24</td>
<td>25</td>
<td>25</td>
<td>0.564</td>
</tr>
<tr>
<td>OSA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.152</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>6</td>
<td>13</td>
<td>7</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>15</td>
<td>11</td>
<td>11</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>0.068</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>15</td>
<td>3</td>
<td>12</td>
<td>10</td>
<td>0.005</td>
</tr>
<tr>
<td>Fatty liver disease</td>
<td>21</td>
<td>17</td>
<td>17</td>
<td>13</td>
<td>0.117</td>
</tr>
<tr>
<td>GERD</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>0.965</td>
</tr>
<tr>
<td>Smoking</td>
<td>10</td>
<td>9</td>
<td>10</td>
<td>13</td>
<td>0.687</td>
</tr>
<tr>
<td>Alcohol</td>
<td>12</td>
<td>10</td>
<td>4</td>
<td>6</td>
<td>0.061</td>
</tr>
<tr>
<td>Depression</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>0.528</td>
</tr>
</tbody>
</table>

*BMI = body mass index, OSA = obstructive sleep apnea, GERD = gastroesophageal reflux disease.*
3.76±2.3 minutes in the propofol with BIS monitoring group, 13.06±7.8 minutes in the sevoflurane group and 14.21±8.07 minutes in the sevoflurane with BIS monitoring group (p < 0.001). Time to extubation was 10.67±4.26 minutes in the propofol group, 10.96±5.45 minutes in the propofol with BIS monitoring group, 25.19±13.7 minutes in the sevoflurane group and 24.7±11.68 minutes in the sevoflurane with BIS monitoring group (p < 0.001) (Figure 3).

The recovery from anesthesia was assessed utilizing the Aldrete, the Chung and the White recovery scores, determined 10, 30 and 60 minutes after the completion of the procedure. The time to achieve Aldrete score ≥ 8 was not significantly different between the four groups (p = 0.481). The time to achieve Chung score ≥ 8 and the time to achieve White score ≥ 12 was significantly shorter in both sevoflurane groups (p = 0.001 and p = 0.002 respectively) (Table II).

The postoperative pain was assessed subjectively with the VAS score. Neither the immediate postoperative pain, nor the change of the pain over time was statistically different between the four groups (p = 0.873) (Figure 4).

**Discussion**

In this study, we evaluated the effectiveness of sevoflurane as a sole anesthetic agent in super obese patients undergoing elective bariatric surgery and compared it to the commonly used propofol, in
combination with remifentanil. We also evaluated the usefulness of BIS monitoring in this patient population. We demonstrated that both sevoflurane and propofol in combination with remifentanil can be safely and effectively used in this demanding patient population. However, sevoflurane offered better hemodynamic stability, based on the lower intraoperative mean arterial pressures observed and better control of the positive sympathetic response to surgical stress, expressed with fewer hypertension and tachycardia episodes. In addition the use of sevoflurane offered faster recovery times and excellent pain control without additional need for opioid administration.

Propofol has been compared to sevoflurane in a variety of settings, but there is no data regarding their relative merits and disadvantages in morbid obesity. Álvarez et al.19 evaluated total intravenous anesthesia (TIVA) with midazolam, remifentanil, propofol and cis-atracurium in morbidly obese patients and found it to be effective, secure, predictable and economic.

An analysis of the Abbott laboratories database indicated that there is no difference in postoperative recovery times between sevoflurane and propofol, but this analysis did not present any data on morbidly obese patients.30 There is evidence that immediate and intermediate postoperative recovery is more rapid after desflurane anesthesia in morbidly obese patients, when compared with the use of propofol or isoflurane.21 Desflurane promotes postoperative desaturation, an advantage that persists for at least for 2 hours after surgery, resulting in improved mobility. In our study the time to eye-opening and extubation was significantly shorter with the use of propofol. However, postoperative recovery was more rapid after sevoflurane anesthesia. This result is comparable with a recent systematic literature analysis comparing recovery after anesthesia with propofol, isoflurane, desflurane or sevoflurane in adults demonstrated that patients receiving sevoflurane recovered somewhat faster compared to those receiving propofol, but postoperative nausea and vomiting were less frequent with propofol.22,23

Propofol may be advantageous compared to sevoflurane because sevoflurane has been shown to prolong the Q-T interval and the heart rate adjusted Q-T interval, whereas propofol shortens the Q-T interval without affecting heart rate adjusted Q-T interval.11,24

Propofol also differs from sevoflurane in that reversal of rocuronium induced neuromuscular blockage with neostigmine is delayed more profoundly when sevoflurane is administered as a sole anesthetic agent.25,26 This difference may be an advantage of propofol compared to sevoflurane for gastric bypass surgery in morbidly obese patients, because this particular operation requires administration of large amounts of non-depolarising muscle relaxants in order to achieve adequate surgical exposure and, therefore, delay in antagonizing the neuromuscular blockade could result in delayed or unsatisfactory postoperative recovery.

However, there is also evident suggesting that sevoflurane may have some advantages, com-

### Table II. Recovery Scores (mean ± SD).

<table>
<thead>
<tr>
<th>Time to reach (min)</th>
<th>Sevoflurane</th>
<th>Sevoflurane &amp; BIS</th>
<th>Propofol</th>
<th>Propofol &amp; BIS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldrete score &gt; 8</td>
<td>2.22 ± 0.74</td>
<td>2.57 ± 1.93</td>
<td>3.48 ± 3.52</td>
<td>4.52 ± 6.48</td>
<td>0.481</td>
</tr>
<tr>
<td>Chung score &gt; 8</td>
<td>2.52 ± 1.47</td>
<td>3.79 ± 2.65</td>
<td>13.28 ± 12.03</td>
<td>12.17 ± 9.95</td>
<td>0.001</td>
</tr>
<tr>
<td>White score &gt; 12</td>
<td>19.04 ± 17.7</td>
<td>16.72 ± 15.6</td>
<td>27.44 ± 12.47</td>
<td>25.48 ± 11.71</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Figure 4. Visual analogue scale (VAS) score over time in all four groups (p = 0.873).
pared to propofol, in a certain population: In women, sevoflurane, but not propofol, decreases the capillary flow coefficient, possibly resulting in decreased extravasation of fluid into the interstitial space. This effect may confer advantage to the use of sevoflurane, as it could reduce intraoperative fluid requirements, which could be beneficial in morbidly obese patients undergoing abdominal surgery. However, the true clinical significance of this effect in morbidly obese patients is unknown.

A study utilizing transesophageal echocardiography (TEE) in patients undergoing laparoscopic cholecystectomy showed that compared to propofol, the use of sevoflurane resulted in significantly higher stroke volume and better hemodynamic stability. In addition, sevoflurane (and desflurane) may have a cardioprotective effect, preserving left ventricular function in elderly high risk patients undergoing coronary artery by-pass surgery compared to propofol.

As we showed in our study, sevoflurane offers great analgesic properties and is sufficient for intraoperative analgesia, limiting the need for opioid use. For better postoperative recovery and mobility, postoperative pain management with epidural analgesia is necessary in this unique patient population. The failure of epidural anesthesia and other local anesthesia techniques is higher in obese patients. In our high volume specialized bariatric center a thoracic epidural catheter was placed successfully in all patients with no early or late complications. The epidural catheter was then used effectively for postoperative analgesia.

Anesthesia for morbidly obese patients is a challenge, not only because of the technical difficulties associated with caring for the morbidly obese, but also because of the physiologic abnormalities that render the morbidly obese patient vulnerable to problems from a variety of organ systems, particularly cardiovascular and respiratory systems. A review of the relevant literature indicates that there is no, at the present time, one “ideal” way to provide anesthesia for the morbidly obese. TIVA, inhalational anesthetic agents and combinations have all been used with success, but it is not clear whether one method or agent is superior. Clearly, any anesthetic regime in the morbidly obese should aim at rapid recovery, optimizing respiratory function in the postoperative period, as these patients are especially prone to postoperative atelectasis. Uneventful recovery is crucial in the morbidly obese, because these patients have a significantly higher morbidity and mortality when admitted to the ICU.

Clearly, there is a need for more studies with larger sample size together with other anesthetic agents to fully evaluate the perioperative anesthetic and postoperative analgesic management of this demanding patient population. Also nowadays with more and more patients undergoing elective laparoscopic bariatric surgery with good results, the perioperative anesthetic management of the patients subjected to laparoscopic surgery should be further evaluated.

Conclusions

This study compared the effectiveness and the recovery from anesthesia of two commonly used agents for the anesthesia management of the super obese. The use of sevoflurane in super obese patients undergoing bariatric surgery is an effective alternative to propofol and remifentanil combination, offering excellent hemodynamic stability and pain management intraoperatively and faster recovery from general anesthesia.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

6) De Hert SG, Ten Broecke PW, Mertens E, Van sommeren EW, De Buyer IG, Stockman BA, Rodrigus IE. Sevoflurane but not propofol preserves myocardial function in the morbidly obese.
dial function in coronary surgery patients. Anesthesiology 2002; 97: 42-49.


