Background: Modified radical mastectomy is associated with appreciable blood loss, while endotracheal intubation leads to elevated hemodynamic responses. The present study aimed to evaluate the clinical efficacy of dexmedetomidine infusion as an anesthetic adjuvant to general anesthesia during modified radical mastectomy with I-Gel.

Methods: Sixty adult consenting female patients, of American Society of Anesthesiologists physical status 1 to 2 and aged 4-65 years, were blindly randomized into two groups of 30 patients each. The patients in Group I received intravenous dexmedetomidine at a loading dose of 1 µg/kg over 10 min, followed by maintenance infusion of 0.4 to 0.7 µg/kg/h, while patients in Group II were administered an identical amount of saline infusion until 15 min prior to the end of surgery. The primary end point was bleeding at the surgical field and hemodynamic changes; requirement of isoflurane, intraoperative fentanyl consumption and recovery time were assessed as secondary outcomes.

Results: The patients receiving dexmedetomidine infusion showed significantly less bleeding at the surgical field (P < 0.05). A statistically significant reduction was also observed in the percentage of isoflurane required (0.82 ± 0.80%) to maintain the systolic blood pressure between 100 and 110 mmHg in patients receiving dexmedetomidine infusion compared with the Group II (1.50 ± 0.90%). The mean intraoperative fentanyl consumption in patients in the Group I was also significantly lower compared with that of the Group II (38.43 ± 5.40 µg vs. 75.12 ± 4.60 µg). The mean recovery time from anesthesia did not show any clinically significant difference between the groups.

Conclusions: Dexmedetomidine infusion can be used safely to decrease the bleeding at the surgical field with smooth recovery from anesthesia.

Key Words: Dexmedetomidine, i-gel, Modified radical mastectomy, Supraglottic airways, Surgical bleeding, Surgical field.
Dexmedetomidine infusion for mastectomy

Introduction

Modified radical mastectomy is associated with appreciable blood loss at the surgical site. Currently, many inhalational or intravenous anesthesia techniques have been demonstrated to offer ideal intraoperative conditions for modified radical mastectomy, with both advantages and shortcomings.

Direct laryngoscopy and endotracheal intubation (ETT) may not lead to serious complications in healthy patients, but the potential hazards of an upsurge in the sympathetic activity associated with laryngoscopy, as well as with intubation-like hypertension, tachycardia and dysrhythmias, are evident. These accentuated pressor responses to laryngoscopy can be reduced either by pharmacological interventions, or by using alternative devices to secure the airway. Postoperative hoarseness of the voice with an endotracheal tube is also a major concern.

Presently, i-gel® (Intersurgical Ltd., Wokingham, Berkshire, RG41 2RZ, UK) is used to secure the airway, thus obviating the shortcomings of ETT. The lack of distortion of sensitive extraglottic structures by the i-gel® may be responsible for less oropharyngeal-laryngeal stimulation, thus favoring hemodynamic stability during its placement. However, the risk of gastric distension and inadequate ventilation is evident with i-gel®. The drain tube parallel to the ventilation tube permits drainage of regurgitated fluid away from the airway to prevent aspiration.

Dexmedetomidine, a potent selective α2-adrenoreceptor agonist, is used as an adjuvant to anesthesia because of its anesthetic and analgesic sparing effects, with predictable and dose-dependent hemodynamic effects [1-3]. Intraoperative dexmedetomidine infusion minimizes surgical blood loss and provides better visualization of the surgical field [4-6].

The present prospective, randomized double-blind control study was designed to evaluate the clinical efficacy of dexmedetomidine infusion as an anesthetic adjuvant to general anesthesia during modified radical mastectomy with i-gel® placement to secure the airway.

Materials and Methods

After institutional ethical committee approval and written informed consent from each patient, 60 females with American Society of Anesthesiologists (ASA) physical status 1 to 2, aged 4,065 years and who were scheduled for elective modified radical mastectomy under general anesthesia, were enrolled in this prospective, randomized double-blind control study.

After a complete pre-anesthetic check-up and appropriate investigation, the patients with uncontrolled hypertension, severe cardiac or respiratory disease, hepatic or renal dysfunction, a body mass index (BMI) > 26 kg/m², endocrine and metabolic disease, bleeding or coagulation disorders, and anticipated difficult airway, were excluded from the present study. All of the patients were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg on the night before surgery and fasted overnight prior to surgery.

All of the patients were randomly allocated to two groups in a double-blind manner using a computer-generated randomized number table. Before induction, the patients in Group I received a loading dose of intravenous dexmedetomidine 1 µg/kg over 10 min, followed by a maintenance infusion of 0.4–0.7 µg/kg/h. Patients in Group II were given an identical amount of saline solution. In both groups, infusion was continued until 15 min prior to the end of surgery. The study drug solution was prepared by an anesthesiologist who was blinded to the study protocol and who was not involved in the intraoperative data collection.

The anesthetic technique was standardized, and modified radical mastectomy was performed by the same surgical team to ensure consistency in the estimation of the surgical field. The surgeon and resident anesthetist were also blinded to the treatment regimen.

The patients received lactated Ringer’s solution at a rate of 10 ml/kg through an 18-gauge intravenous cannula, and intramuscular glycopyrrolate (0.2 mg) was given to all of the patients. After arrival at the operation theatre, the basal vital parameters of heart rate (HR), non-invasive blood pressure (NIBP), peripheral oxygen saturation (SpO₂) and continuous electrocardiogram (ECG) were noted, and study drug infusion was started according to the randomization schedule. The patients were premedicated with intravenous palonosetron (75 µg), midazolam (2 mg), and fentanyl (2 µg/kg) before induction of anesthesia.

After preoxygenation for 3 min, anesthesia was induced with propofol (2 mg/kg) along with 50% oxygen in nitrous oxide and isoflurane, in all of the patients, to achieve adequate depth of anesthesia for the placement of appropriately sized and well lubricated i-gel® to secure the airway. The air leak test was performed, the i-gel® position was confirmed, and then the i-gel® was secured in place. All of the patients were maintained on mechanical ventilation after vecuronium bromide 0.08 mg/kg. The patients were initially ventilated at 14 breaths/min, with a tidal volume of 6 ml/kg that was later adjusted to keep the end-tidal carbon dioxide (ETCO₂) level between 35 and 45 mmHg (normocapnia).

Intraoperatively, the HR, NIBP, ECG, ETCO₂, and SpO₂ were monitored and recorded at 5-min intervals until the end of surgery. During the surgery, systolic blood pressure was maintained between 100 and 110 mmHg either by increasing or decreasing the infusion rate of the study solution, or by adjusting the dial concentration of isoflurane (0.8–1.5%). The isoflurane concentration was recorded as a percentage every 15 min until the end of surgery in all of the patients. Any additional fentanyl consumption, given as boluses, was also recorded. The patients...
were observed for bradycardia (HR < 60 beats/min, tachycardia (HR > 100 beats/min), and arrhythmias. All unexpected intraoperative events requiring intervention were recorded and treated according to standard clinical protocols.

During the surgery, bleeding was assessed by the surgeon using the following scoring system: 0 = no bleeding, excellent surgical conditions; 1 = minimum bleeding, sporadic suction; 2 = diffuse bleeding, repeated suction; and 3 = considerable and troublesome bleeding, continuous suction. The ideal value for the surgical conditions was predeterminded to be 1.

All drug infusions were discontinued 15 minutes prior to the end of surgery. Once the surgery was completed, all of the anesthetic agents were withdrawn. When spontaneous breathing movements began, the residual neuromuscular blockade was reversed with neostigmine (2.5 mg) and glycopyrrolate (0.5 mg). Gentle oro-pharyngeal suctioning was performed, and the i-gel® was removed after observing adequate motor recovery and tidal volume during spontaneous breathing. The recovery time, defined as the interval between the discontinuation of anesthetics and eye opening to verbal commands, was recorded.

After full recovery, the patients were transferred to the postanesthesia care unit (PACU) and monitored for respiratory depression, hemodynamic changes, nausea/vomiting, shivering or any other drug-induced side effects, which were managed accordingly. The patients were given rescue analgesia (visual analog score > 4) with an intramuscular injection of Diclofenac sodium 75 mg, and were monitored every 10 min until they achieved a postanesthesia discharge scoring system (PADSS) [7] score > 9 (at which point they were declared for discharge from the PACU).

**Sample size and statistical analysis**

The sample size was calculated using standard programs, which showed that approximately 25 to 27 patients should be included in each group for a clinically meaningful reduction in bleeding between the groups, at a type I error of 0.05 and power of 80%. Thus, 60 patients were enrolled to account for a dropout rate of 5%.

All recorded data were tabulated and the results were expressed as means and SD, which was considered the best predictor for the statistical analysis. Statistical analysis was performed using SPSS for Windows software (version 18.0, SPSS Inc., Chicago, IL, USA). The demographic data for the categorical variables were compared using the chi-squared test. Statistical significance, in terms of the mean difference between groups, was assessed using Student’s t-test and repeated measured analysis of variance. A P value less than 0.05 was deemed to indicate statistical significance.

**Results**

The present study was successfully completed by 60 consenting adult female patients, all of whom were included in the analysis to study the ability of dexmedetomidine infusion to provide an appropriate surgical field for modified radical mastectomy.

The demographic profiles of the groups were comparable in terms of age, weight, height, BMI, ASA physical status and duration of surgery (Table 1).

During modified radical mastectomy, the surgeons observed bleeding of grade 1 (minimum bleeding with sporadic suction) at the surgical site in most of the patients who received dexmedetomidine, while no patient in the Group II showed clinically significant reduction in bleeding at the surgical site. Thus, it was evident that the patients who received dexmedetomidine infusion had a significantly better surgical field compared with the Group II (P < 0.05) (Tables 2A and 2B). The baseline value for

| Table 1. Demographic Data |
|---------------------------|
| Parameters                | Group I (n = 30) | Group II (n = 30) | P value |
| Age (yr)                  | 46.1 ± 08.1     | 45.2 ± 7.8        | 0.715   |
| Weight (kg)               | 59.3 ± 11.5     | 61.1 ± 12.5       | 0.803   |
| Height (cm)               | 160.0 ± 3.9     | 159.5 ± 4.3       | 0.662   |
| BMI (kg/m²)               | 23.1 ± 4.3      | 24.2 ± 5.8        | 0.594   |
| ASA (I/II)                | 18/12           | 16/14             | 0.355   |
| Duration of surgery (min) | 129.4 ± 13.0    | 137.1 ± 12.1      | 0.641   |

Data are expressed as mean ± SD. BMI: body mass index, ASA: American Society of Anesthesiologists.

| Table 2. Assessment of Intraoperative Bleeding |
|----------------------------------------------|
| (A) Quality of Field 30 Minutes after the Start of Surgery |
| Grade of surgical field | Group I (n = 30) | Group II (n = 30) | P value |
|-------------------------|------------------|-------------------|--------|
| 0                       | 0                | 0                 | 0      |
| I                       | 11               | 0                 | 0.006* |
| II                      | 17               | 18                | 0.064  |
| III                     | 2                | 12                | <0.001*|

Data are expressed as the number of patients. *P < 0.05 is statistically significant.

| (B) Quality of Field 60 Minutes after the Start of Surgery |
|------------------------------------------------------------|
| Grade of surgical field | Group I (n = 30) | Group II (n = 30) | P value |
|-------------------------|------------------|-------------------|--------|
| 0                       | 0                | 0                 | 0      |
| I                       | 11               | 1                 | 0.004* |
| II                      | 18               | 14                | 0.059  |
| III                     | 1                | 15                | <0.001*|

Data are expressed as the number of patients. *P < 0.05 is statistically significant, †P < 0.001 is highly statistically significant.
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Table 3. Changes in Heart Rate

|                  | Group I (n = 30) | Group II (n = 30) | P value |
|------------------|------------------|-------------------|---------|
| Baseline         | 94.7 ± 12.6      | 93.8 ± 10.7       | 0.738   |
| After induction  | 83.6 ± 12.4      | 87.3 ± 10.0       | 0.938   |
| After i-gel      |                  |                   |         |
| 10 min           | 73.1 ± 9.3       | 84.3 ± 9.7        | 0.683   |
| 30 min           | 71.2 ± 8.8       | 78.2 ± 9.7        | 0.505   |
| 45 min           | 69.1 ± 8.3       | 73.1 ± 7.8        | 0.775   |
| 60 min           | 69.6 ± 8.3       | 71.2 ± 9.6        | 0.798   |
| 90 min           | 70.5 ± 8.5       | 72.5 ± 9.2        | 0.500   |
| 120 min          | 78.3 ± 12.3      | 81.7 ± 10.2       | 0.676   |
| Post-operative   | 87.4 ± 11.4      | 97.1 ± 12.7       | 0.824   |

Data are expressed as mean ± SD.

Table 4. Changes in Systolic Blood Pressure

|                  | Group I          | Group II         | P value |
|------------------|------------------|------------------|---------|
| Baseline         | 123.4 ± 17.3     | 127.2 ± 11.5     | 0.834   |
| After induction  | 102.7 ± 6.5      | 102.5 ± 7.4      | 0.982   |
| After i-gel      |                  |                   |         |
| 10 min           | 105.8 ± 2.8      | 107.4 ± 6.2      | 0.633   |
| 30 min           | 98.7 ± 7.5       | 104.6 ± 4.7      | 0.551   |
| 45 min           | 98.3 ± 8.9       | 106.5 ± 2.7      | 0.573   |
| 60 min           | 97.6 ± 4.8       | 106.8 ± 3.9      | 0.842   |
| 90 min           | 99.6 ± 2.7       | 108.7 ± 6.3      | 0.379   |
| 120 min          | 103.3 ± 1.37     | 112.6 ± 5.6      | 0.167   |
| Post-operative   | 112.4 ± 15.7     | 133.3 ± 14.6     | 0.051   |

Data are expressed as mean ± SD.

The mean HR was comparable between the groups. Intraoperatively, the mean HR values were also comparable between the groups, and the patients did not show much variation. Bradycardia was observed in five patients in Group I, which responded promptly to intravenous atropine (0.6 mg). The mean HR was found to be higher in patients in Group II after removal of the i-gel® (97.1 ± 12.7 vs. 87.4 ± 11.4 beats/min; P = 0.824 ) (Table 3).

The baseline mean systolic blood pressure values were comparable between both groups, but were comparatively lower during surgery in patients of Group I, with no statistically significant difference. Patients did not show much variation in blood pressure, as it was maintained between 100 and 110 mmHg in both groups. After the discontinuation of study drug infusion at the end of surgery and after recovery, the mean systolic blood pressure was significantly lower in patients in Group I (Table 4).

The mean intraoperative fentanyl consumption in patients in Group I was significantly less than that of the Group II (38.43 ± 5.4 µg vs. 75.12 ± 4.6 µg). Patients in Group I required significantly less isoflurane to maintain the desired level of systolic blood pressure than patients in the Group II (0.82 ± 0.8% vs. 1.5 ± 0.9%) (Table 5).

Table 5. Comparison of Fentanyl Consumption and the Isoflurane Requirement

| Groups       | Isoflurane requirement (%) | Fentanyl consumption (µg) | P value |
|--------------|---------------------------|---------------------------|---------|
| Group I      | 0.82 ± 0.80               | 38.43 ± 5.40              |         |
| Group II     | 1.50 ± 0.90               | 75.12 ± 4.60              |         |
| P value      | 0.023*                    | 0.017*                    |         |

Data are expressed as mean ± SD. *P < 0.05 is statistically significant.

All of the patients could obey verbal commands. The duration of recovery was 6.78 ± 3.29 min in patients in Group I and 5.57 ± 1.63 min in patients in Group II, and the difference in recovery time was not clinically significant between the groups.

Postoperatively, the respiratory rate and SpO2 were comparable, with no episode of desaturation in any patient. None of the patients complained of discomfort or recall of awareness when interviewed after surgery. No adverse effects were observed due to the intraoperative infusion of dexmedetomidine in any patient. Only seven patients in Group I, and 18 in Group II, required rescue analgesia, with a statistically significant difference between the groups. The time to discharge from the post-anaesthesia room, as assessed by PADSS, was comparable between the groups.

Discussion

Modified radical mastectomy surgery required appropriate surgical field visibility with steady intraoperative hemodynamics, and the present study aimed to minimize the bleeding at the surgical site by dexmedetomidine infusion. It is evident from the results that the patients receiving dexmedetomidine infusion showed an appropriate surgical field due to minimum bleeding, with better visibility at the surgical site compared with patients receiving normal saline. The findings of present study can be attributed to dexmedetomidine reducing sympathetic activity, resulting in lower blood pressure and a reduced HR, thereby decreasing bleeding at the surgical site and thus improving the quality of the surgical field. Dexmedetomidine infusion was well-tolerated, and no drug-related side effects were observed during the study period.

Direct laryngoscopy plus tracheal intubation is the most well-established method of securing the airway and achieving positive pressure ventilation, but it stimulates pharyngeal tissues, leading to a hypertensive pressor response due to an appreciable increase in sympathetic outflow. Although these hemodynamic changes are short-lived, they are undesirable in patients with pre-existing myocardial or cerebral insufficiency. Such elevated pressure responses were not observed with i-gel® placement.

Dexmedetomidine is a highly selective α2-adrenergic agonist,
which is used as adjuvant in anesthesia to reduce the intraoperative anesthetic and analgesic requirement due to its sedative, analgesic and hypnotic effects [8,9]. It regulates the autonomic and cardiovascular system by acting on blood vessels, thus mediating vasoconstriction, and on sympathetic terminals to inhibit norepinephrine release, thus attenuating the elevated pressor responses to stressful events [10]. Dexmedetomidine effectively minimizes surgical blood loss, thereby improving surgical field visibility.

Conventional techniques for electively lowering the blood pressure include positive pressure ventilation and the administration of hypotensive drugs. Although controlled hypotension represents the conventional method to reduce surgical bleeding, it may lead to complications such as compromised perfusion of other vital organs and rebound hypertension. Almost the same result can be achieved by maintaining systolic blood pressure on the lower side. There are many drugs available to perform this task, but intraoperative dexmedetomidine infusion showed the best pharmacological profile, with stable hemodynamics and improved surgical field visibility [8]. The same results were observed in the present study.

The efficacy of dexmedetomidine, in terms of providing an ideal surgical field during control hypotension, was previously reported during middle ear surgery and maxillofacial surgery with predictable hemodynamic effects [11,12]. Many studies have investigated the effects of dexmedetomidine during extubation and reported a significant reduction in the HR, blood pressure and awareness [13-15]. The results of the present study showed the same results.

The optimal anesthetic technique to reduce blood loss at the surgical field seems to cause relative bradycardia and associated hypotension. Ulger et al. [16] compared dexmedetomidine with nitroglycerine to achieve controlled hypotension in patients scheduled for middle ear surgery. The infusion rate of drugs was titrated to maintain a mean arterial pressure between 65 and 75 mmHg. They concluded that dexmedetomidine was better for maintaining hemodynamic stability and a drier surgical field, and was devoid of reflex tachycardia and rebound hypertension. The results of the present study are in accordance with these data.

Guven et al. [17] and Goksu et al. [18] reported better hemodynamic stability and visual analog scale pain scores, as well as a clear surgical field and few side effects, with dexmedetomidine infusion for functional endoscopic sinus surgery. In the present study, there was significant improvement in the quality of the surgical field with little bleeding, which did not hamper the radical mastectomy surgery in patients receiving dexmedetomidine infusion.

The results of the present study indicated that the use of dexmedetomidine infusion reduces the isoflurane concentration to maintain the systolic blood pressure at a lower level. These findings are in accordance with those of a previous study done by Khan et al. [1], which also showed that dexmedetomidine infusion reduces the requirement of an inhalational anesthetic. Aantaa et al. [2] also reported a reduction in the isoflurane requirement in their study, confirming the synergism between isoflurane and dexmedetomidine.

Dexmedetomidine has sedative and analgesic-sparing effects thus, it may be associated with a longer emergence time and recovery time from anesthesia [14]. Richa et al. [12] reported a significantly slower extubation time in patients receiving dexmedetomidine compared with those receiving remifentanil for controlled hypotension. In the present study, patients in the Group I showed slower but smooth recovery from anesthesia, although there was no clinically significant difference between the groups in recovery time.

Dexmedetomidine infusion as an anesthetic adjuvant with isoflurane was effective in reducing bleeding at the surgical site and provides appropriate surgical field visibility during modified radical mastectomy. The lack of complications, coupled with a good success rate due to analgesia, sedation and an analgesic-sparing effect, makes dexmedetomidine infusion suitable for obtaining a clear surgical field.

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References

1. Khan ZP, Munday IT, Jones RM, Thornton C, Mant TG, Amin D. Effects of dexmedetomidine on isoflurane requirements in healthy volunteers. 1: Pharmacodynamic and pharmacokinetic interactions. Br J Anaesth 1999; 83: 372-80.
2. Aantaa R, Jaakola ML, Kallio A, Kanto J. Reduction of the minimum alveolar concentration of isoflurane by dexmedetomidine. Anesthesiology 1997; 86: 1055-60.
3. Jaakola ML, Salonen M, Lehtinen R, Scheinin H. The analgesic action of dexmedetomidine--a novel alpha 2-adrenoceptor agonist--in healthy volunteers. Pain 1991; 46: 281-5.
4. Shams T, El Bahnasawe NS, Abu-Samra M, El-Masry R. Induced hypotension for functional endoscopic sinus surgery: A comparative study.

Online access in http://ekja.org
of dexmedetomidine versus esmolol. Saudi J Anaesth 2013; 7: 175-80.
5. Özcan AA, Özyurt Y, Saraçoglu A, Erkal H, Süslü H, Arslan G, et al. Dexmedetomidine versus remifentanil for controlled hypotensive anesthesia in functional endoscopic sinus surgery. Turk J Anaesthesiol Reanim 2012; 40: 257-61.
6. Lee J, Kim Y, Park C, Jeon Y, Kim D, Joo J, et al. Comparison between dexmedetomidine and remifentanil for controlled hypotension and recovery in endoscopic sinus surgery. Ann Otol Rhinol Laryngol 2013; 122: 421-6.
7. Palumbo P, Tellan G, Perotti B, Pacilè MA, Vietri F, Illuminati G. Modified PADSS (Post Anaesthetic Discharge Scoring System) for monitoring outpatients discharge. Ann Ital Chir 2013; 84: 661-5.
8. Sudheesh K, Harsoor S. Dexmedetomidine in anaesthesia practice: A wonder drug? Indian J Anaesth 2011; 55: 323-4.
9. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN, Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can J Anaesth 2006; 53: 646-52.
10. Gupta K, Bansal M, Gupta PK, Pandey M, Agarwal S. Dexmedetomidine infusion during middle ear surgery under general anaesthesia to provide oligaemic surgical field: a prospective study. Indian J Anaesth 2015; 59: 26-30.
11. Richa F, Yazigi A, Sleilaty G, Yazbeck P. Comparison between dexmedetomidine and remifentanil for controlled hypotension during tympanoplasty. Eur J Anaesthesiol 2008; 25: 369-74.
12. Turan G, Ozgultekin A, Turan C, Dincer E, Yüksel G. Advantageous effects of dexmedetomidine on haemodynamic and recovery responses during extubation for intracranial surgery. Eur J Anaesthesiol 2008; 25: 816-20.
13. Güler G, Akin A, Tosun Z, Esiktoğlu E. During the extubation the effects of dexmedetomidine on cardiovascular changes and quality of extubation in the old patients undergoing cataract surgery. Turk J Anaesth 2005; 33: 18-23.
14. Pollard RJ, Coyle JP, Gilbert RL, Beck JE. Intraoperative awareness in a regional medical system: a review of 3 years’ data. Anesthesiology 2007; 106: 269-74.
15. Bajwa SJ, Kaur J, Kulshrestha A, Haldar R, Sethi R, Singh A. Nitroglycerine, esmolol and dexmedetomidine for induced hypotension during functional endoscopic sinus surgery: a comparative evaluation. J Anaesthesiol Clin Pharmacol 2016; 32: 192-7.
16. Guven DG, Demiraran Y, Sezen G, Kepek O, Iskender A. Evaluation of outcomes in patients given dexmedetomidine in functional endoscopic sinus surgery. Ann Otol Rhinol Laryngol 2011; 120: 586-92.
17. Goksu S, Arik H, Demiriyurek S, Mumbuc S, Oner U, Demiriyurek AT. Effects of dexmedetomidine infusion in patients undergoing functional endoscopic sinus surgery under local anaesthesia. Eur J Anaesthesiol 2008; 25: 22-8.