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ORIGINAL CONTRIBUTIONS

Does Lung Compliance Optimization Through PEEP Manipulations Reduce the Incidence of Postoperative Hypoxemia in Laparoscopic Bariatric Surgery? A Randomized Trial

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Abstract

Background In obese patients (OP), the best intraoperative ventilation strategy remains to be defined. Dynamic lung compliance (C_{dyn}) and dead space fraction are indicators of efficient ventilation at an optimal positive end-expiratory pressure (PEEP). Herein, we investigated whether intraoperative dynamic lung compliance optimization through PEEP manipulations affects the incidence of postoperative hypoxemia ($SpO_2 < 90\%$) in OP undergoing laparoscopic bariatric surgery (LBS).

Methods This was a single-center, prospective, randomized controlled study conducted from July 2013 to December 2015. After obtaining institutional review board approval and informed consent, 100 OP undergoing LBS under volume-controlled ventilation (tidal volume 8 mL/kg of ideal body weight) were randomized according to the PEEP level maintained during the surgery. In the control group, a PEEP of 10 cm H_2O was maintained, while in the intervention group, the PEEP was adapted to achieve the best dynamic lung compliance. Anesthesia and analgesia were standardized. The patients received supplemental nasal oxygen on the first postoperative day and were monitored up to the second postoperative day with a portable pulse oximeter.

Results Demographics were similar between groups. There was no difference in the incidence of hypoxemia during the first 2 postoperative days (control: 1.3%; intervention: 2.1%; $p = 0.264$).

Conclusions The incidence of postoperative hypoxemia was not reduced by an open-lung approach with protective ventilation strategy in obese patients undergoing LBS. A pragmatic application of a PEEP level of 10 cm H_2O was comparable to individual PEEP titration in these patients.

Trial Registration Clinicaltrials.gov identifier, NCT02579798; https://clinicaltrials.gov/ct2/show/NCT02579798

Keywords Laparoscopic bariatric surgery · Mechanical ventilation · Anesthetic management · Lung compliance · Positive end-expiratory pressure · Postoperative hypoxemia

Introduction

Pulmonary atelectasis, which occurs in 85–90% of healthy adults within minutes of general anesthesia (GA) induction, remains the main cause of increased intrapulmonary shunt during and after surgery [1, 2]. Compression of lung tissue, absorption of alveolar air, and impairment of surfactant function have all been implicated; however, many other factors can also contribute, such as the increased abdominal pressure during laparoscopic procedures or the supine position [3]. Obese patients (OP) are more likely to develop intraoperative atelectasis [5] as they exhibit a greater decrease in functional residual capacity (FRC) during GA; an exponential relationship between increasing body mass index (BMI) and decreasing FRC has been observed [4, 5].

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Atelectasis is one of the main causes of postoperative hypoxemia (PH) and may predispose to postoperative adverse outcomes, such as respiratory failure, pneumonia, and mortality [6]. Preventing these complications is a recognized measure of any hospital's quality of care [7, 8].

Several strategies have been found to be effective [9–14] in reducing atelectasis during GA in obese patients. Among intraoperative ventilation strategies, the optimal level of PEEP remains controversial. PEEP improves intraoperative lung function (lung compliance, oxygenation), especially in combination with recruitment maneuvers [1–6, 9–20]. However, the use of high levels of PEEP may result in hemodynamic instability [15] and pulmonary overdistension [21–26]. In a recent review, Fernandez-Bustamante et al. suggested to titrate the level of PEEP to maximize dynamic lung compliance (C_{dyn}) [7].

The primary objective of our study was to test the hypothesis that lung compliance optimization through PEEP manipulations could reduce the incidence of postoperative hypoxemia (IPH) in patients undergoing laparoscopic bariatric surgery compared with a pragmatic level of PEEP fixed at 10 cm H_2O.

Methods

Our study was a prospective, randomized controlled study, approved by the Institutional Ethics Committee. Written informed consent was obtained from all participating subjects. This manuscript adheres to the applicable Enhancing the Quality and Transparency of Health Research (EQUATOR) guidelines.

Patients were included according to the following criteria: age over 18 years, ASA score (American Society of Anesthesiologists) II or III, body mass index (BMI) > 35 kg/m^2, and elective laparoscopic bariatric surgery (gastric bypass or sleeve).

Exclusion criteria were the following: restrictive [total lung capacity (TLC) < 65%] or obstructive [Tiffeneau ratio (FEV_1/FVC ratio) < 69%] pulmonary disease; increased intracranial pressure; active smoking; current pregnancy; history of heart failure (New York Heart Association class III or IV) or coronary artery disease; urgent surgery; allergy to any drug used in the study. Patients with a higher incidence of postoperative atelectasis (i.e., history of obstructive sleep apnea syndrome) were not excluded from the study.

The anesthetic management was standardized for each patient. Drugs were administered according to the ideal body weight [IBW (kg) = height (cm)—100 (for men) and 105 (for women)], except for muscular relaxants for which the corrected IBW (IBW + 40% overweight) was used (see annex 1 for the complete anesthetic protocol).

Preoxygenation was obtained by vital capacity maneuvers with a fraction of inspired oxygen (FiO_2) of 1.0 and a 10 cm H_2O CPAP until an end-tidal SpO_2 > 90% was obtained in Ramp positioned patients. Anesthesia was induced with propofol, sufentanil, and rocuronium and maintained with desflurane (6–8%) to keep entropy values between 40 and 60.

Patients were ventilated in volume control mode with a mixture of 50% oxygen and 50% air, a tidal volume (V_T) of 8 mL/kg IBW, and an inspiratory-expiratory ratio (I/E) of 1:2 [7]. The initial respiratory rate of 10 breaths/min was adjusted to maintain end-tidal carbon dioxide partial pressure between 35 and 45 mmHg. Plateau pressure (P_{plat}) was limited to 30 cm H_2O and inspiratory peak pressure (P_{IP}) to 40 cm H_2O. Recruitment maneuvers (RM) were applied whenever the SpO_2 < 95%, using to the protocol described by Whalen et al. [10].

For the laparoscopic procedure, a carbon dioxide pneumoperitoneum was performed with a maximal intra-abdominal pressure of 15 mmHg.

Lactated Ringer's solution was administered at a rate of 3 mL kg^{-1}(IBW) h^{-1} throughout the procedure. During surgery, hypotension (decrease in MAP greater than 25% from baseline) was treated with a bolus of 250 mL of 3% modified fluid gelatin (Geloplasma, Fresenius Kabi GmbH, Germany) if pulse pressure variation was greater than 13% (*IntelliVue MP40*™, *Philips* Medical Systems, Andover, USA) (fluid challenge) or by intravenous bolus administration of vasoactive drugs (5 mg ephedrine or 50 mcg neosynephrine) if pulse pressure variation was lower than 13%. Urinary losses were compensated with lactated Ringer's solution at a ratio of 1 to 1 and blood losses were compensated with a 3% modified fluid gelatin at a 1:3 ratio.

At the end of surgery, patients' trachea was extubated when the following criteria were met: hemodynamic stability (heart rate and mean arterial pressure; a maximum variation of 20% around the baseline value was accepted); normothermia (temperature > 36 °C); V_T > 5 mL/kg (IBW); and minimal respiratory frequency of 11 breaths/min.

All patients were transferred to the PACU in head-up sitting position with supplemental nasal oxygen (3 L/min). If the SpO_2 was < 90%, a 'Venturi' mask with 35% FiO_2 was applied. For patients using CPAP preoperatively, CPAP was used as soon as they could cooperate. When leaving the PACU, all patients received supplemental nasal oxygen (3 L/min) during the first postoperative day (D1) and were monitored with a portable pulse oximeter (oxytrue®A, Bluepoint medical, Selmsdorf, Germany) up to the second postoperative day (D2). The invasive arterial catheter could not be maintained after the patient had left the recovery room.

At the 30th postoperative day (POD), the medical record of each patient was reviewed to collect possible postoperative complications.

Study Protocol

In the control group, a 10-cm H_2O level of PEEP was applied throughout the surgical procedure and recruitment maneuvers (RM) were applied whenever SpO_2 < 95% (Fig. 1).

Table 1 Baseline subject characteristics and perioperative data

Characteristics	Control group ($n = 50$)	Study group ($n = 50$)	P value
Age (years)	40 [27–47]	42 [31–48]	0.366
Body mass index (kg/m^2)	42 [39–45]	42 [40–45]	0.588
Male (n)	4	15	0.004
ASA[a] score (n)			0.629
II	40	38	
III	10	12	
Sleep apnea syndrome (n)	8	10	0.602
Carrying CPAP[b] (n)	3	3	1
Procedure duration (min)	88 [65–135]	115 [79–160]	0.163
Hospitalization duration (days)	4 [4–4]	4 [3–4]	0.644

Data presented as median [IQR] or number

[a] American Society of Anesthesiologists (II: mild systemic disease; III: severe systemic disease)

[b] Continuous positive airway pressure

In the study group, starting with the same baseline level (10 cm H_2O), PEEP was adapted to achieve the best C_{dyn} determined by the ventilator (Aisys® CS [2], GE Healthcare, Madison, WI, USA). This maneuver was repeated at 3 time points (Fig. 1: T1, T2, T3). The best C_{dyn} was achieved by first increasing the level of PEEP by 2 cm H_2O. If the C_{dyn} value increased after 6 respiratory cycles, PEEP was further increased by another 2 cm H_2O. Conversely, if the C_{dyn} value decreased after 6 respiratory cycles, PEEP was decreased by 2 cm H_2O. The PEEP levels were limited to the maximum allowed values for the current P_{plat} or P_{ip}. A recruitment maneuver was applied whenever $SpO_2 < 95\%$ [10].

Measurements

Measurements performed preoperatively (ambient air) included heart rate (HR), mean arterial blood pressure (MAP), SpO_2, arterial pH, $PaCO_2$, and PaO_2. Parameters measured intraoperatively were HR, MAP, SpO_2, arterial pH, $PaCO_2$, and PaO_2, end-tidal CO_2, PaO_2/FiO_2 ratio, C_{dyn}, anatomical dead space ratio (V_D/V_T), and the number of recruitment maneuvers (RM). These variables were measured after induction of anesthesia in flat positioning, without pneumoperitoneum (T1), after pneumoperitoneum inflation and anti-Trendelenburg positioning (T2), and after pneumoperitoneum exsufflation, in flat positioning (T3). Volume of fluids administered and the need for fluid challenges and/or vasopressors were also recorded.

Study Outcomes

The primary endpoint was the incidence of postoperative hypoxemia (IPH) defined as the percentage of time spent with a $SpO_2 < 90\%$ during the first (D1) and the second postoperative day (D2). The secondary endpoints included pulmonary dynamic compliance (Vt/Ppeak-PEEP), anatomical dead space ratio ($V_D/V_T = (1\text{-}etCO_2/PaCO_2)$, and PaO_2/FiO_2 ratio. The tertiary endpoints included the number of RM (n), the need for fluid (n), the volume of colloid (mL), the use of vasopressors during surgery (n), and the incidence of complications at the 30th postoperative day (n).

Statistical Analysis

No power analysis was performed, as the incidence of our primary endpoint for the study population was not reported in the literature. We elected to recruit 100 patients and then modify our sample size according to our results if required. Subjects were randomized using a computer-generated random table with block sizes of 10. Patients were blinded to the group allocation. The anesthetist in charge of the patient was not blinded, but data collection and statistical analysis were blinded.

As the distribution of continuous variables was not homogenous (Kolmogorov-Smirnov test), groups were compared with the Mann-Whitney U test and data expressed as median and interquartile range. Categorical variables were compared using Chi-square and data presented as percentage. Two-way analysis of variance for repeated measurements was used to compare PEEP, PaO_2/FiO_2, C_{dyn}, and V_D/V_T between both groups. Statistical programs used were Minitab 16 (Paris, France) and the R version 3.2.1. For all analyses, a p value < 0.05 was considered significant.

Results

Of the 208 consecutive OP screened for eligibility, from July 2013 to December 2015, 100 were randomized (50 in the control group, 50 in the intervention group) and included in the analysis (Fig. 2). There was no statistical difference between groups, except for the genre (Table 1).

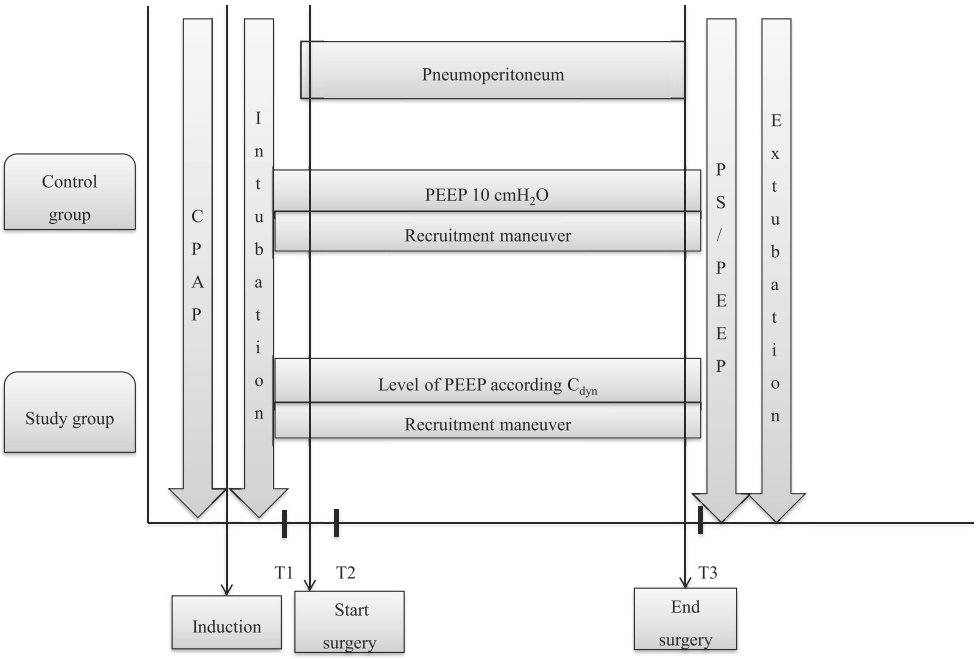

Fig. 1 Study design and three key times: PEEP = positive end-expiratory pressure; CPAP = continuous positive airway pressure; C_{dyn} = dynamic lung compliance; PS = pressure support; T1 = time 1, after induction/intubation, flat patient, without pneumoperitoneum; T2 = time 2, after pneumoperitoneum inflation and implementation anti-Trendelenburg; T3 = time 3, after pneumoperitoneum exsufflation, flat patient

Incidence of postoperative hypoxemia was not different between groups (Table 2). Mean SpO_2 on D2 was not different between groups, although it was higher in the control group on D1. Notably, all but three patients presented with at least one episode of hypoxemia during the study postoperative period.

C_{dyn} was significantly higher in the study group compared to the control group at all time points (Table 3). The level of PEEP and the V_D/V_T ratio was similar between the two groups. The PaO2/FiO2 ratio increased progressively throughout the procedure in both groups, without any significant difference between the groups.

There was no difference in the number of RM at any time point (3 vs 3, 6 vs 2, and 2 vs 0) between the groups. Twenty-two patients in the control group and 27 patients in the study group received a fluid challenge ($p = 0.317$). The total volume of colloid (mL) was 375 mL (250–500) in the control group and 500 mL (250–500) in the study group ($p = 0.613$). Twenty patients in the control group and 23 in the study group received at least one vasopressor bolus ($p = 0.544$).

Incidence of postoperative complications was low (3 in each group). There was no pulmonary complication in both groups.

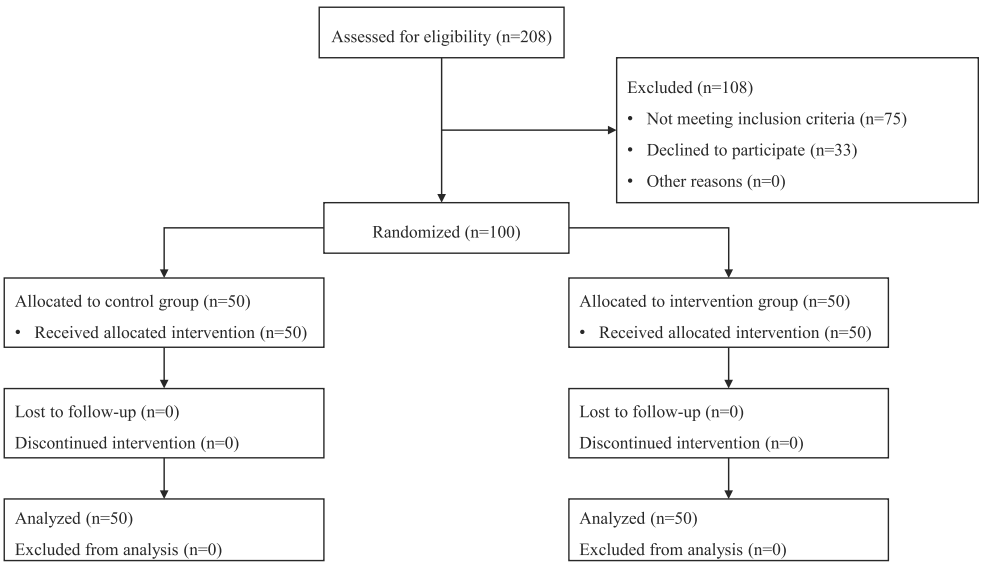

Fig. 2 CONSORT diagram: recruitment, inclusion, exclusion and randomization

Table 2 The percentage of time spent with pulse oximetry oxygen saturation < 90% (hypoxemia time) and overall mean pulse oximetry oxygen saturation

	Control group ($n = 50$)	Study group ($n = 50$)	P value
Total hypoxemia time (%)	1.3 [0.5–3.7]	2.1 [0.8–8.5]	0.264
Hypoxemia time D1[a] (%)	0.6 [0.2–2.0]	0.7 [0.2–3.0]	0.462
Hypoxemia time D2[b] (%)	2.5 [0.6–5.5]	2.6 [0.8–10.0]	0.535
Mean SpO_2[c] D1 (%)	98 [97–99]	97 [95–98]	0.012
Mean SpO_2 D2 (%)	96 [94–97]	96 [93–97]	0.230

Data presented as median [IQR]

[a] First postoperative day

[b] Second postoperative day

[c] Pulse oximetry oxygen saturation

Discussion

In the conditions of our study, C_{dyn} optimization through PEEP manipulations did not reduce the IPH when compared to a fixed 10 cm H_2O PEEP. To our knowledge, this study was the first to assess the effect of C_{dyn} optimization on the IPH up to postoperative day 2.

Although postoperative hypoxemia episodes may have important clinical consequences in obese patients [6], only one study has so far assessed the incidence of postoperative hypoxemia in patients undergoing laparoscopic bariatric surgery during the immediate postoperative period. In this study, Defresne et al. [27] reported IPH on D1 ranging from 2.1 to 2.5%, which is similar to our results. Notably, these authors used a protective ventilation protocol combining 'Ramp' position, recruitment maneuvers using a 10 cm H_2O CPAP, low tidal volume, and 10 cm H_2O PEEP. The observed low IPH might be a result of the beneficial interaction between all the protective strategies used in both studies. Indeed, protective ventilation approaches during general anesthesia could improve postoperative pulmonary function and arterial oxygenation up to 5 days postoperatively [28].

In our study, combining different protective ventilation maneuvers was associated with a low incidence of RM to keep a $SpO_2 > 95\%$. The optimal modalities and systematization of RM remain a matter of debate in the literature [29–31]. Because RM can cause adverse effects including temporary desaturation, decreased preload, hypotension, arrhythmias,

Table 3 Pulmonary dynamic compliance, positive end-expiratory pressure, dead-space ratio (1-$etCO_2/PaCO_2$) at key time points

Parameters	Key time	Control group ($n = 50$) mean ± SD	Study group ($n = 50$) mean ± SD	Group effect P value	Time effect P value
C_{dyn}[a] (mL/cmH_2O)				0.008	< 0.001
	1	38.5 ± 7.0	43.4 ± 10.2		
	2	34.0 ± 6.3	37.0 ± 8.4		
	3	39.2 ± 6.4	43.2 ± 9.5		
PEEP[b] (cmH_2O)				NS[c]	NS[c]
	1	10	9.2 ± 2.6		
	2	10	10.4 ± 2.5		
	3	10	9.6 ± 2.3		
V_D/V_T ratio[d]				NS[c]	NS[c]
	1	0.07 ± 0.07	0.08 ± 0.07		
	2	0.06 ± 0.07	0.09 ± 0.06		
	3	0.07 ± 0.07	0.08 ± 0.07		
PaO_2/FiO_2 (mmHg)[e]				NS[c]	< 0.001
	1	383.5 ± 152.0	368.6 ± 118.6		
	2	408.9 ± 133.6	380.1 ± 121.3		
	3	459.6 ± 129.6	417.3 ± 114.2		

[a] Pulmonary dynamic compliance

[b] Positive end-expiratory pressure

[c] P value ≥ 0.05

[d] Dead-space ratio (1-$etCO_2/PaCO_2$)

[e] 1, after induction of anesthesia; 2, after start of surgery; 3, after the end of surgery

and barotrauma [7], we elected to perform RM only when SpO_2 was < 95%. Defresne et al. [27] showed that when added to a protective mechanical ventilation strategy combining low tidal volume and high PEEP, RM does not improve FRC and arterial oxygenation.

In our study, individual PEEP manipulation to optimize C_{dyn} resulted in a mean level of PEEP of 10 cm H_2O. Interestingly, these results confirm those of Coussa's et al. and Talab's et al. [1, 11] who concluded that 10 cm H_2O was an optimum level of PEEP to reduce atelectasis and maintain oxygenation in obese patients during surgery. This might explain why the level of PEEP manipulated to achieve the best C_{dyn} was similar to that used through a pragmatic approach as recommended by the PROBESE study [32]. Although C_{dyn} was significantly higher in the study group, the difference compared to the control group was probably not clinically relevant.

Individual titration of PEEP to a respiratory mechanical target such as C_{dyn} represents a compromise of regional overdistention and collapsing-reopening of lung units [32]. As such, our methodology is in accordance with Maisch's et al. [23] and Fernandez-Bustamante et al. [7] who suggest that the optimal level of PEEP is the pressure level with the highest compliance value in conjunction with the lowest V_D/V_T ratio [7, 23].

PaO_2/FiO_2 ratios increased throughout the surgery in both groups. This could be the result of a gradual recruitment rather than the consequence of pulmonary overdistension as the C_{dyn} measured before and at the end of surgery was similar.

The need for fluid challenges and the use of vasopressors were not different between groups. Nevertheless, almost half of our patients required a fluid challenge or vasopressors. Our results confirm that the use of high levels of PEEP require more frequent interventions to treat hemodynamic instability [15].

Our study presents several limitations. Firstly, the study was not powered for the primary objective, as the IPH after laparoscopic bariatric surgery was not known when the protocol was designed. However, based on our results, no difference could be expected between both strategies even if a much higher number of patients were recruited.

Secondly, evaluation of hypoxemia episodes through portable oximeter was performed during a relatively short postoperative period. The incidence of postoperative hypoxemia tended to be higher on D2 than on D1, but it should be noted that the patients did not receive supplemental oxygen up to D1 according to our institutional practices. The mean hospitalization duration was short in our population (4 days).

Thirdly, our results are limited to laparoscopic bariatric surgery in obese patients and may not apply to other surgical procedures and populations. Such ventilatory approach required the use of an anesthetic machine allowing the determination of C_{dyn} which is the case for most modern ventilators.

In conclusion, IPH was not reduced by an open lung approach with protective ventilation strategy aiming at optimizing C_{dyn} in obese patients undergoing laparoscopic bariatric surgery. A pragmatic application of a PEEP level of 10 cm H_2O was comparable to an individual PEEP titration in these patients.

Presentation: Preliminary data for this study were presented as a poster presentation at the Euroanaesthesia meeting, 28–30 May 2016, London.

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Data Availability *Data are available upon reasonable request to the corresponding author.*

Compliance with Ethical Standards

Our study was a prospective, randomized controlled study, approved by the Institutional Ethics Committee. Written informed consent was obtained from all participating subjects. This manuscript adheres to the applicable Enhancing the Quality and Transparency of Health Research (EQUATOR) guidelines.

Conflicts of Interest The authors declare that they have no conflict of interest.

Ethical and Consent Statement Ethical and consent statement provided by the Institutional Ethics Committee. Written informed consent was obtained from all participating subjects.

Annex 1: anesthetic protocol

All subjects stopped consuming solid food from 6 h and clear liquids from 2 h before the elective surgery, and received 0.5–1 mg alprazolam and 150 mg ranitidine perorally, 1 h before the procedure as premedication.

Before induction, each patient was placed in 'Ramp' position. Basic monitoring was undertaken, including: electrocardiogram, non-invasive blood pressure (NIBP), and pulse oximetry oxygen saturation (SpO_2).

An 18-gauge catheter was placed in a vein and a 20-gauge catheter in a radial artery. Further monitoring included entropy, thumb's adductor neuromuscular monitor, nasopharyngeal temperature probe, and urinary catheter.

Anesthesia was induced by intravenous administration of propofol (2–3 mg/kg IBW) and sufentanil (GEPS model with target concentration of 0.3 ng/mL based on IBW: discontinued 1 h before the end of surgery). The intubation (tube size 8 for women and 8.5 for men) was facilitated by the administration of intravenous rocuronium (0.6 mg/kg corrected IBW). Antibiotic prophylaxis (cefazolin 2 g and metronidazole 500 mg) was also given at the induction.

Anesthesia was maintained with desflurane (6–8%) to keep entropy values between 40 and 60. Every 30 min, a train of 4 (TOF 50 Hz) was performed and a rocuronium bolus (0.15 mg/kg IBW) was administered as needed to maintain a TOF ratio of 0:4.

At the end of surgery, all patients received paracetamol (1 g). Neuromuscular blockade was checked at the thumb's adductor. The neuromuscular blockade was reversed with 4 mg/kg (corrected IBW) sugammadex when the train-of-four (TOF) ratio reached 2:4.

After attaining a TOF ratio of 4:4 with a sustained tetanic stimulation at 100 Hz over 5 s, patients were placed in 'Ramp' position and the administration of desflurane and mechanical ventilation with volume control mode was discontinued in order to switch to mechanical ventilation with pressure support [PEEP of 5 cm H_2O and 100% inspired fraction of oxygen (FiO_2)].

Anti-emetic prophylaxis was administered to all patients as follows: 40 mg methylprednisolone at the induction and 4 mg ondansetron at the end of the intervention.

Thromboprophylaxis included intermittent pneumatic compression device beginning before surgery and low molecular weight heparin (80 mg/day) beginning 6 h after the procedure.

In the postoperative period, each patient received paracetamol 1 g every 6 h and patient-controlled intravenous analgesia with piritramide was started at the post-anesthesia care unit (PACU) (2-mg bolus every 7 min with a maximum of 30 mg in 4 h).

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