Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2016) 46: 1071-1077

doi:10.3906/sag-1505-25

Comparison of the effects of PEEP levels on respiratory mechanics and elimination of volatile anesthetic agents in patients undergoing laparoscopic cholecystectomy; a prospective, randomized, clinical trial

Hüsnü Mert ARINALP[1], **Nurten BAKAN**[2], **Gülşah KARAÖREN**[2,*], **Ömer Torun ŞAHİN**[2], **Emre ÇELİKSOY**[2]
[1]Department of Anesthesiology, Şanlıurfa Harran State Hospital, Şanlıurfa, Turkey
[2]Department of Anesthesiology and Reanimation, İstanbul Ümraniye Training and Research Hospital, İstanbul, Turkey

Received: 07.05.2015 • **Accepted/Published Online:** 05.10.2015 • **Final Version:** 23.06.2016

Background/aim: In laparoscopic procedures, intraabdominal carbon dioxide (CO2) insufflation can cause decreased compliance, increased airway resistance, and impaired ventilation-perfusion ratios. We aimed to investigate the effects of intraoperative positive end-expiratory pressure (PEEP) treatment on respiratory dynamics and elimination time of volatile anesthetic agents.

Materials and methods: In the present study, 75 ASA I-II patients were randomized into 3 groups to receive 0 cmH2O PEEP (group I), 5 cmH2O PEEP (group II), or 8 cmH2O PEEP (group III). Hemodynamic parameters, peak and plateau inspiratory airway pressures (P_{peak}, $P_{plateau}$), compliance values, the ratio of the fractions of inspired and expired concentration of sevoflurane (Fi/Fexp sevoflurane) at 1 MAC, times from 1 to 0.3 and 0.1 MAC and values for pulmonary function tests (PFT) were recorded.

Results: P_{peak} and $P_{plateau}$ in group III were higher; compliance values in group I and the extent of reduction in postoperative forced vital capacity (FVC) in group III were lower than those in the other groups ($P < 0.05$). No significant difference was observed between the groups regarding times from 1 to 0.3 MAC and times from 0.3 to 0.1 MAC.

Conclusion: It was found that 8 cmH2O PEEP increased compliance without clinically significant pulmonary deterioration and that 8 cmH2O PEEP led to less impairment in postoperative PFTs compared to 0 and 5 cmH2O PEEP but had no effect on sevoflurane elimination time.

Key words: Positive end-expiratory pressure, compliance, pulmonary elimination, sevoflurane, laparoscopy

1. Introduction

Although laparoscopy, the gold standard in cholelithiasis surgery, has many advantages (shorter length of hospital stay, minimal postoperative pain, and quick recovery), it also has systemic disadvantages resulting from increased intraabdominal pressure (1,2).

During laparoscopic interventions, carbon dioxide (CO_2) insufflation into the abdominal cavity causes displacement of the diaphragm, thus reducing functional residual capacity (FRC) and compliance, increasing airway resistance, impairing ventilation–perfusion ratio, and leading to atelectasis as a result of these changes (3–5).

Positive end-expiratory pressure (PEEP) is defined as the application of positive pressure to the airway at the end of expiration. PEEP improves pulmonary oxygen exchange through prevention of the collapse of airways, the redistribution of pulmonary blood flow, increased FRC, increased alveolar–capillary oxygen gradient, the recruitment of collapsed or fluid-filled alveoli, and the rearrangement of gas distribution (6,7). In addition, PEEP also improves pulmonary compliance and ventilation–perfusion abnormalities (8).

In inhalation anesthesia, recovery occurs through the elimination of anesthetic agents by 95%–98% via inhalation (alveolar level). This occurs as a result of solubility of an inhaler agent in the blood, alveolar blood flow, alveolar inspired gas mixtures, and partial pressure gradients in pulmonary capillaries. The factors increasing recovery rate include shorter time of surgery, the prevention of re-inhalation, higher rate of fresh gas flow, lower anesthetic circuit volume, lower anesthetic circuit absorption, low solubility, high rate of blood flow, and increased ventilation (9).

In laparoscopic surgery, elimination of volatile agents and recovery may be prolonged because of decreased postoperative ventilation caused by atelectasis that may

* Correspondence: drgyilmaz@yahoo.com

result from FRC reduction (9). In the literature, there are studies showing that PEEP accelerated elimination of nitrogen protoxide in patients with chronic obstructive pulmonary disease (COPD) and with FEV1 (forced expiratory volume in 1 s) ≤ 70% (10); however, there is no study about the effects of PEEP on elimination time of volatile agents.

In the present study, we aimed to evaluate the effects of 3 different PEEP levels (0, 5, 8 cmH_2O) on hemodynamics, respiratory dynamics (P_{peak}, $P_{plateau}$, static and dynamic compliance, and PFT) and elimination time of volatile anesthetics in ASA I–II patients scheduled for laparoscopic cholecystectomy.

2. Materials and methods

This was a single-center, balanced, randomized [1:1], and prospective study conducted at the Anesthesia Clinic of Ümraniye Training and Research Hospital. Seventy-five patients aged 30–65 years with ASA physical status I–II and BMI of 25–30 who were undergoing elective laparoscopic cholecystectomy were recruited after approval was obtained from the Ethics Committee and informed consent from the patients.

Patients with ASA III, IV, or V risk; those with comorbid diseases that may increase intraabdominal pressure or pulmonary hypertension; those with renal or hepatic failure; those who were pregnant; and those using a bronchodilator or steroid were excluded. We also planned to exclude patients converted to laparotomy during laparoscopy. All patients were assessed by a chest specialist using PFT.

Randomization was performed by simple randomization procedures using a computerized-random numbers generator. Patients were randomly assigned to 1 of 3 groups according to the PEEP levels used with 1:1:1 allocation using a group size of 25. The preparation of random number list, the assignment of random number list to groups, the application of PEEP levels and the evaluation of respiratory functions and volatile agent elimination were undertaken by different persons.

In addition to routine monitoring (blood pressure, heart rate, and SpO_2), fractional concentration of inspired oxygen (FiO_2), inspired and expired fractional concentration of sevoflurane (F_i/F_{exp} sevoflurane), and minimum alveolar concentration (MAC) levels were also monitored when patients were transferred to the operating room. Isotonic saline infusion (10 mL kg^{-1} h^{-1}) was started for fluid replacement. The patients were intubated following standard anesthesia induction. Anesthesia was maintained by using 1 MAC sevoflurane, 50%–50% O_2–air mixture and remifentanil infusion (0.05–0.01 µg kg^{-1} min^{-1}). Sevoflurane end-tidal concentration was maintained at 1 MAC (adjusted to age) throughout general anesthesia. The patients maintained with pressure controlled ventilation mode (fresh gas flow: 4 L min^{-1}; tidal volume: 6 mL kg^{-1}; respiratory frequency: adjusted to $ETCO_2$ levels between 25 and 35 cmH_2O) were assigned to 3 groups (n = 25) based on PEEP levels (group I: 0 cmH_2O, group II: 5 cmH_2O, and group III: 8 cmH_2O).

During surgery, mean arterial pressure (MAP), heart rate (HR), SpO_2, respiratory dynamics (P_{peak}, $P_{plateau}$, and static–dynamic compliance values) were recorded at 5-min intervals at baseline, insufflation, desufflation, and the end of surgery.

F_i/F_{exp} sevoflurane values were measured just before turning the sevoflurane vaporizer to a sevoflurane value of 1 MAC. Mechanical ventilation was maintained without any change in respiratory parameters, as alterations in alveolar ventilation and fresh gas flow could influence sevoflurane concentration.

Before the withdrawal of inhalational anesthetic, times from 1 to 0.3 MAC and from 0.3 to 0.1 MAC and F_i/F_{exp} sevoflurane rates at 1, 0.3, and 0.1 MAC were recorded.

Remifentanil infusion was maintained until a sevoflurane concentration of 0.1 MAC was reached; then it was withdrawn. All patients were mechanically ventilated until the final measurement. Then the patients were extubated after the reversal of neuromuscular blocker agent.

At postoperative 24 h, the patients were re-evaluated by a chest specialist using PFT.

3. Statistical analysis

Based on power analysis via power and sample size, minimum sample size was calculated as 23 for each group for 80% power at 0.05 level of significance when MAC parameter was 0.1.

The data were analyzed via SPSS (Statistical Package for the Social Sciences) for Windows version 15.0. In addition to descriptive statistics (mean and standard deviation), one-way ANOVA was used to compare quantitative data with normal distribution among groups, followed by Tukey's HSD test. The paired sample t test was used for comparisons within a group. The chi-squared test was used to compare qualitative data. $P < 0.05$ was considered statistically significant.

4. Results

The study was conducted in 75 patients (in 3 groups, each with 25 patients) who underwent laparoscopic cholecystectomy between 1 October 2013 and 1 October 2014 in our clinic. No patient was converted to open surgery in the present study.

Of the patients, 30.7% (n = 23) were men and 69.3% (n = 52) were women. The mean age was 44.73 ± 10.28 years, ranging from 26 to 60 years.

There was no significant difference in age, BMI, time of surgery, time of insufflation, sex, ASA, or smoking status between the groups ($P > 0.05$) (Table 1).

When the hemodynamic data were evaluated, no significant difference was found in MAP or HR values between the groups although there were significant differences compared to baseline values within the groups ($P > 0.05$). SpO_2 value did not decrease below 94% in any patient.

In all 3 groups, significant increases were detected in P_{peak} and $P_{plateau}$ values during insufflation compared to baseline values ($P < 0.05$). In comparison between the groups, the P_{peak} and $P_{plateau}$ values obtained in group III were significantly higher than those obtained in groups II and I at the 0, 5, 10, desufflation, and end time points ($P < 0.05$, $P < 0.01$) (Figures 1 and 2).

Dynamic and static compliances were significantly lower in group I than they were in groups II and III at all time points ($P < 0.05$, $P < 0.01$). Although there was no significant difference between groups II and III, compliance values were higher in group III throughout surgery (Figures 3 and 4).

No significant difference was observed in F_i/F_{exp} sevoflurane ratio at 1 MAC, times from 1 to 0.3 MAC and from 0.3 to 0.1 MAC, or F_{exp} sevoflurane values between the groups ($P > 0.05$) (Table 2).

In all groups, there were significant decreases in FVC (%), FEV1, and FEF 25–75 (%) values measured after surgery when compared to preoperative values ($P < 0.01$). The extent of the decrease in FVC was smaller in group III when compared to that in the two other groups. The increase in FEV1/FVC (%) in postoperative measurements was significant only in group I ($P < 0.05$) (Table 3).

5. Discussion

There are many studies demonstrating that anesthesia causes increased airway pressure, decreased compliance and FRC, and postoperative atelectasis in laparoscopic surgery (1,2). It was reported that an increase of 46% in P_{peak} values and a decrease of 20%–48% in compliance could be observed after abdominal CO_2 insufflation (2,11).

Different levels of PEEP application is the most commonly used recruitment maneuver; it protects alveoli from atelectasis by using continuous pressure above closing pressure, thus ameliorating intrapulmonary shunts, insufficient V/Q ratios, and impaired oxygenation (12,13).

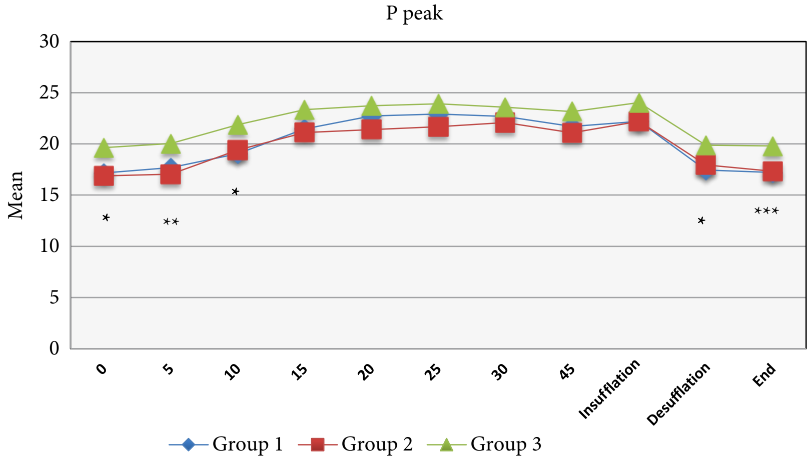
In addition to these advantages, PEEP applications may have adverse effects such as tension injury and barotrauma in some alveolar units by causing excessive tension. Microcirculation can be disrupted and the right ventricle can be affected due to excessive pressure on capillaries. The optimal PEEP value is the lowest value that achieves target oxygenation while causing minimal cardiovascular impairment (14,15).

In our study, 0, 5, and 8 cmH_2O PEEP levels with maximum pneumoperitoneum of 15 mmHg CO_2 were applied under 1 MAC sevoflurane anesthesia in order to avoid barotrauma. Throughout surgery, respiration rate was maintained within the normal range (12–14 min^{-1}) without the need to increase it due to hypercarbia in any patient. No barotrauma was observed in any patient. In

Table 1. Demographic features.

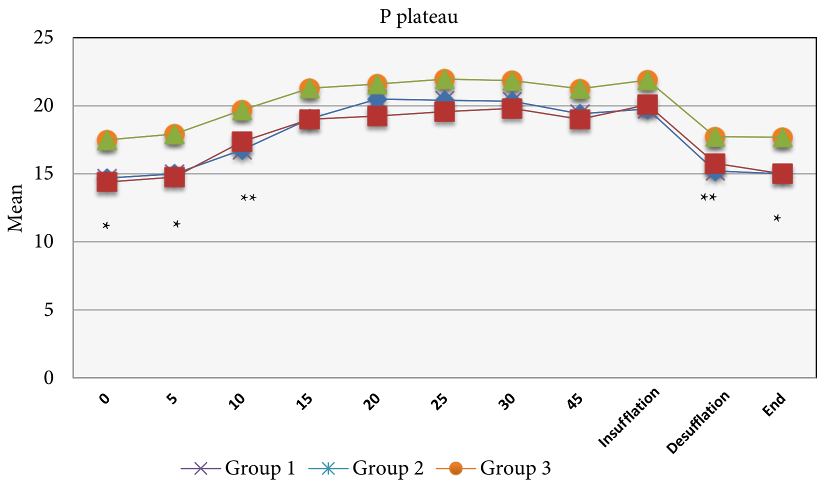
		Group I	Group II	Group III	[1]P
		Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)		44.08 ± 10.74	45.28 ± 10.66	44.84 ± 9.80	0.919
BMI (kg/m^2)		29.36 ± 4.64	27.99 ± 3.97	28.44 ± 3.31	0.475
Operation time (min)		79.60 ± 20.09	74.80 ± 18.96	78.60 ± 35.13	0.787
Insufflation time (min)		55.20 ± 20.89	50.20 ± 17.04	55.60 ± 33.49	0.694
		n (%)	n (%)	n (%)	[2]P
Sex	Male	7 (28)	10 (40)	6 (24)	0.443
	Female	18 (72)	15 (60)	19 (76)	
ASA	I	10 (40)	14 (56)	11 (44)	0.498
	II	15 (60)	11 (44)	14 (56)	
Smoking	Yes	20 (80)	16 (64)	20 (80)	0.324
	No	5 (20)	9 (36)	5 (20)	

Group 1: V (0), Group 2: V (5), Group 3: V (8), [1]One-way ANOVA, [2]Chi-squared test



*p < 0.05 Group III compared to group I (p:0.044, p:0.043, p:0.023)
**p < 0.01 Group III compared to group II (p:0.021)
***p < 0.05 Group III compared to group I (p:0.017) and group II (p:0.024)

Figure 1. Peak airway pressures.



*p < 0.01 Group III compared to group I and group II
**p < 0.05 Group III compared to group I

Figure 2. Plateau airway pressures.

intragroup comparisons, no significant difference was found in MAP or HR values between the groups although there were significant differences compared to baseline values within the groups (P > 0.05), but SpO_2 value did not decrease below 94% in any patient.

In our study, at the 0, 5, 10 min, desufflation, and end time points, P_{peak} and $P_{plateau}$ values were significantly higher in group III, which received 8 cmH_2O PEEP, while compliance values calculated from these values were significantly lower in group I when compared to the two other groups. Although there was no significant difference in compliance between groups II and III at all time points, it was found to be higher in group III (Figures 1–4).

In our study, 5 and 8 cmH_2O PEEP values achieved higher lung compliances without increasing airway pressures to a level that may cause barotrauma when compared to the groups that received no PEEP.

Sevoflurane is metabolized at a rate of as low as 5% in the human body and it is primarily eliminated via the lungs by exhalation. The determinants of elimination are cardiac output and alveolar ventilation (5). In laparoscopic surgery, it can be proposed that PEEP employed to improve lung capacities can accelerate the elimination of inhalation agents by increasing the number of open alveoli, thus recruiting more lung tissue into ventilation, as demonstrated by preoperative and postoperative PFTs (6,7).

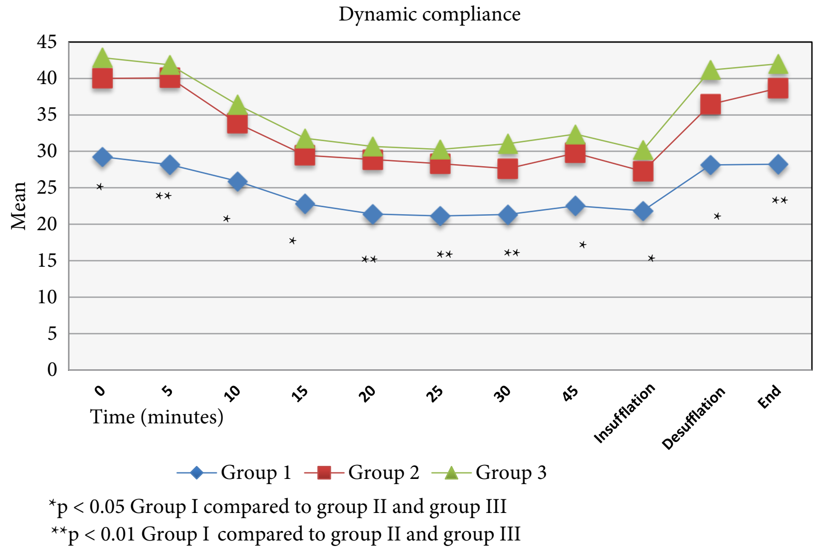


Figure 3. Dynamic compliance.

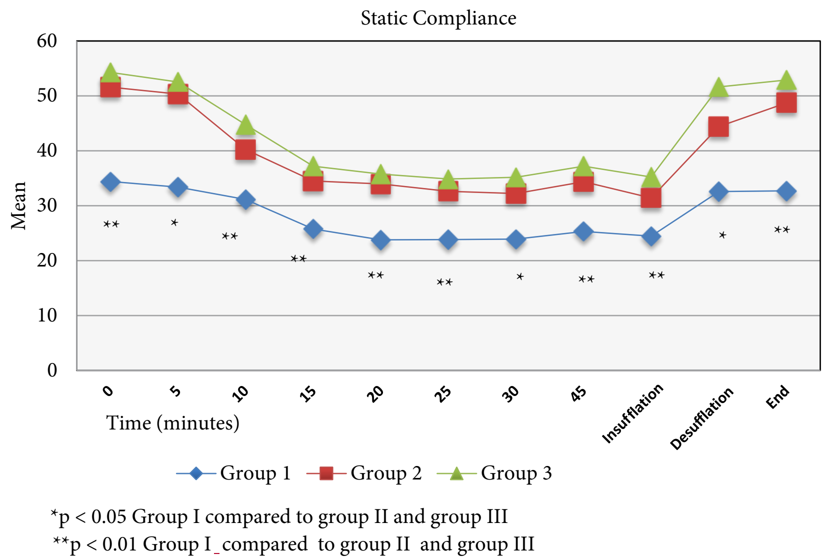


Figure 4. Static compliance.

In a study involving 70 patients in which the relationship between postoperative pulmonary complications and PFT parameters was investigated in laparoscopic upper abdominal surgery, Sen et al. (16) found that the FEV1 value on postoperative day 2 was markedly decreased when compared to the preoperative FEV1 value (P = 0.001), while their FVC and FVC% values were significantly lower on postoperative day 1 when compared to the preoperative values (P = 0.001).

In our study, significant reductions were detected in the postoperative PFT values when compared to the preoperative PFT values in all 3 groups, in agreement with the literature (P < 0.05). However, the extent of FVC reduction was smaller in group III when compared to the two other groups.

Despite the positive effects of PEEP on respiratory dynamics detected in our study, no significant difference was detected in 1 MAC F_i/F_{exp} sevoflurane ratio or times from 1 to 0.3 MAC or from 0.3 to 0.1 MAC between the groups (P > 0.05).

Although the F_i sevoflurane value at 0.3 MAC was higher in group I when compared to group III, the difference was considered clinically insignificant. It was found that 5 and 8 cmH_2O applications had no effect on the elimination time of sevoflurane, which increased FRC.

In a study on 39 patients, Yamazaki et al. (10) showed

Table 2. Gas concentrations.

Gas concentration		Group I	Group II	Group III	[1]P
		Mean ± SD	Mean ± SD	Mean ± SD	
MAC 1	F_i sevo	2.43 ± 0.13	2.4 ± 0.1	2.4 ± 0.09	0.661
	F_{exp} sevo	2.16 ± 0.09	2.15 ± 0.08	2.14 ± 0.08	0.585
	F_i/F_{exp}	1.12 ± 0.05	1.12 ± 0.02	1.08 ± 0.21	0.501
MAC 0.3	Time (s)	123.2 ± 33.15	139.48 ± 44.25	134.2 ± 37.63	0.320
	F_i sevo	0.31 ± 0.08	0.28 ± 0.09	0.25 ± 0.07	0.023*
	F_{exp} sevo	0.71 ± 0.05	0.7 ± 0.04	0.69 ± 0.06	0.323
MAC 0.1	Time (s)	547.84 ± 156.95	623.4 ± 188.22	560.8 ± 119.72	0.200
	F_i sevo	0 ± 0	0 ± 0	0 ± 0	-
	F_{exp} sevo	0.3 ± 0.01	0.3 ± 0.02	0.3 ± 0.05	0.793

Group I: V (0), Group II: V (5), Group III: V (8), [1]One-way ANOVA
*P < 0.05 (P: 0.018) Group I compared to group III

Table 3. Assessment of PFT.

PFT		Group I	Group II	Group III	[1]P
		Mean ± SD	Mean ± SD	Mean ± SD	
% FVC	Preop	88.52 ± 11.87	90.68 ± 14.61	92.4 ± 10.95	0.552
	Postop	57.88 ± 12.4	57.52 ± 15.88	62.96 ± 8.74	0.244
	[2]In group	0.001**	0.001**	0.001**	
% FEV 1	Preop	91.81 ± 10.73	97.32 ± 14.96	96.24 ± 9.62	0.234
	Postop	64.6 ± 13.05	60.68 ± 17.41	66.76 ± 8.9	0.282
	[2]In group	0.001**	0.001**	0.001**	
% FEV1/FVC	Preop	110.25 ± 12.43	113.2 ± 11.88	110.44 ± 10.14	0.601
	Postop	117.0 ± 8.6	110.56 ± 12.03	112.48 ± 8.16	0.063
	[2]In group	0.015*	0.395	0.487	
% FEF 25–75	Preop	100.4 ± 15.6	103.08 ± 21.42	104.8 ± 16.62	0.687
	Postop	76.76 ± 22.24	69.28 ± 29.87	75.84 ± 17.48	0.482
	[2]In group	0.001**	0.001**	0.001**	

Group I: V (0) Group II: V (5) Group III: V (8) [1]One-way ANOVA [2]Paired samples t test
*P < 0.05 Group I; Preoperative FEV 1/FVC (%) compared to postoperative FEV 1/FVC (%)
**P < 0.01 Group I, II, III; Preoperative FEF 25–75 (%) compared to postoperative FEF 25–75 (%)

that the elimination of nitrous oxide was prolonged significantly in COPD patients with FEV1 < 70% when compared to those with a normal FEV1 (P < 0.05) and that prolonged elimination time in COPD patients with a low FEV1 was preventable by 10 cmH_2O PEEP application.

In line with our study, Adanir et al. (17) showed that smoking did not affect the elimination time of sevoflurane in patients with impaired mucociliary activity due to smoking, which leads to atelectasis.

No adverse effect considered to be related to pneumoperitoneum or PEEP applications such as hemodynamic abnormality, pneumothorax, pneumomediastinum, gas embolism, or subcutaneous emphysema was observed in any of the patients from the 3 groups.

Limitations for this study include the lack of measurement of arterial blood gas values, which is not routinely performed in patients for cholecystectomy surgery. Therefore, further studies are needed to evaluate the elimination time of other volatile agents with different levels of PEEP treatment in laparoscopic procedures.

In our study, we found that 8 cmH_2O PEEP increased static and dynamic compliance without clinically significant pulmonary deterioration when compared to 0 and 5 cmH_2O PEEP and that 8 cmH_2O PEEP led to less impairment in postoperative PFTs when compared to preoperative PFTs but had no effect on sevoflurane elimination time.

We think that statistical differences can be established more clearly by further studies with a larger sample size.

Acknowledgment

We wish to thank Ebru Osmanoğlu for her help with the statistical analysis.

References

1. Karsten J, Heinze H, Meier T. Impact of PEEP during laparoscopic surgery on early postoperative ventilation distribution visualized by electrical impedance tomography. Minerva Anestesiol 2014; 80: 158-166.
2. Aydın V, Kabukcu HK, Sahin N, Mesci A, Arici AG, Kahveci G, Ozmete O. Comparison of pressure and volume-controlled ventilation in laparoscopic cholecystectomy operations. Clin Respir J 2016; 3: 342-349.
3. Himal HS. Minimally invasive (laparoscopic) surgery. Surg Endosc 2002; 8: 265-270.
4. Suter M, Meyer A. A 10-year experience with the use of laparoscopic cholecystectomy for acute cholecystitis: is it safe? Surg Endsc 2001; 15: 1187-1192.
5. Dikmen Y, Eminoğlu E, Salihoğlu Z, Demiroluk S. Pulmonary mechanics during isoflurane, sevoflurane and desflurane anaesthesia. Anaesthesia 2003; 58: 745-748.
6. Warner DO. Preventing postoperative pulmonary complications. The role of the anesthesiologist. Anesthesiology 2000; 92: 1467-1472.
7. Salihoglu Z, Demiroluk S, Cakmakkaya S, Gorgun E, Kose Y. Influence of the patient positioning on respiratory mechanics during pneumoperitoneum. Middle East Journal of Anaesthesiology 2002; 16: 521-528.
8. Marini JJ, Hotchkiss JR Jr. PEEP in the prone position: reversing the perfusion imbalance. Crit Care Med 1999; 27: 1-2.
9. Morgan GE, Mikhail MS, Murray MJ, Kleinman W, Nitti GJ, Nitti JT, Raya J. Clinical Pharmacology: Inhalational Anesthetics. In: Morgan GE, Mikhail MS, Murray MJ, editors. Clinical Anesthesiology. New York, NY, USA: McGraw-Hill; 2006. pp. 155-178.
10. Yamazaki Y, Mimura M, Sonoda H, Seki S, Namiki A. Positive end-expiratory pressure facilitates washout of nitrous oxide in patients with obstructive pulmonary disease. The Japanese Journal of Anesthesiology 1998; 47: 404.
11. Oikkonen M, Tallgren M. Changes in respiratory compliance at laparoscopy: measurements using side stream spirometry. Can J Anaesth 1995; 42: 495-497.
12. Whalen FX, Gajic O, Thompson GB. The effects of the alveolar recruitment maneuver and positive end expiratory pressure on arterial oxygenation during laparoscopic bariatric surgery. Anaesth Analg 2006; 102: 298-305.
13. Kim JY, Shin CS, Kim HS, Jung WS, Kwak HJ. Positive end-expiratory pressure in pressure-controlled ventilation improves ventilatory and oxygenation parameters during laparoscopic cholecystectomy. Surg Endosc 2010; 24: 1099-1103.
14. Kundra P, Subramani Y, Ravishankar M, Sistla SC, Nagappa M, Sivashanmugam T. Cardiorespiratory effects of balancing PEEP with intra-abdominal pressures during laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech 2014; 24: 232-239.
15. Russo A, Di Stasio E, Scagliusi A, Bevilacqua F, Isgrò MA, Marana R, Marana E. Positive end-expiratory pressure during laparoscopy: cardiac and respiratory effects. J Clin Anesth 2013; 25: 314-320.
16. Sen M, Ozol D, Bozer M. Influence of preemptive analgesia on pulmonary function and complications for laparoscopic cholecystectomy. Dig Dis Sci 2009; 54: 2742-2747.
17. Adanir T, Atay A, Sencan A, Aksun M, Karahan N. Effect of cigarette smoking on the washout time of sevoflurane anesthesia. BMC Anesthesiology 2010; 10: 8.