Rev Bras Anestesiol. 2017;67(1):28–34

Sociedade Brasileira de Anestesiologia

REVISTA BRASILEIRA DE ANESTESIOLOGIA

Publicação Oficial da Sociedade Brasileira de Anestesiologia
www.sba.com.br

SCIENTIFIC ARTICLE

Effects of different levels of end-expiratory pressure on hemodynamic, respiratory mechanics and systemic stress response during laparoscopic cholecystectomy

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Received 9 June 2015; accepted 17 August 2015
Available online 12 April 2016

KEYWORDS
PEEP;
Hemodynamic;
Respiratory mechanics and stress response

Abstract
Objective: General anesthesia causes reduction of functional residual capacity. And this decrease can lead to atelectasis and intrapulmonary shunting in the lung. In this study we want to evaluate the effects of 5 and 10 cmH_2O PEEP levels on gas exchange, hemodynamic, respiratory mechanics and systemic stress response in laparoscopic cholecystectomy.
Methods: American Society of Anesthesiologist I–II physical status 43 patients scheduled for laparoscopic cholecystectomy were randomly selected to receive external PEEP of 5 cmH_2O (PEEP 5 group) or 10 cmH_2O PEEP (PEEP 10 group) during pneumoperitoneum. Basal hemodynamic parameters were recorded, and arterial blood gases (ABG) and blood sampling were done for cortisol, insulin and glucose level estimations to assess the systemic stress response before induction of anesthesia. Thirty minutes after the pneumoperitoneum, the respiratory and hemodynamic parameters were recorded again and ABG and sampling for cortisol, insulin, and glucose levels were repeated. Lastly hemodynamic parameters were recorded; ABG analysis and sampling for stress response levels were taken after 60 minutes from extubation.
Results: There were no statistical differences between the two groups about hemodynamic and respiratory parameters except mean airway pressure (P_{mean}). P_{mean}, compliance and PaO_2; pH values were higher in 'PEEP 10 group'. Also, $PaCO_2$ values were lower in 'PEEP 10 group'. No differences were observed between insulin and lactic acid levels in the two groups. But postoperative cortisol level was significantly lower in 'PEEP 10 group'.
Conclusion: Ventilation with 10 cmH_2O PEEP increases compliance and oxygenation, does not cause hemodynamic and respiratory complications and reduces the postoperative stress response.

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http://dx.doi.org/10.1016/j.bjane.2015.08.015

PALAVRAS-CHAVE
PEEP;
Hemodinâmica;
Mecânica respiratória e resposta ao estresse

Efeitos de diferentes níveis de pressão expiratória final sobre a hemodinâmica, mecânica respiratória e resposta sistêmica ao estresse durante colecistectomia laparoscópica

Resumo
Objetivo: A anestesia geral causa a redução da capacidade residual funcional e essa diminuição pode levar à atelectasia pulmonar e *shunt* intrapulmonar. Neste estudo pretendemos avaliar os efeitos de níveis de 5 e 10 cmH_2O de pressão expiratória final positiva (PEEP) sobre as trocas gasosas, hemodinâmica, mecânica respiratória e resposta ao estresse sistêmico em colecistectomia laparoscópica.
Método: Quarenta e três pacientes, estado físico ASA I-II, agendados para colecistectomia laparoscópica, foram selecionados aleatoriamente para receber PEEP a 5 cmH_2O (grupo PEEP-5) ou PEEP de 10 cmH_2O (grupo PEEP-10) durante o pneumoperitônio. Os parâmetros hemodinâmicos foram registrados, gasometria arterial e coleta de sangue foram realizadas para estimativa dos níveis de cortisol, insulina e glicose para avaliar a resposta ao estresse sistêmico antes da indução anestésica. Trinta minutos após o pneumoperitônio, os parâmetros hemodinâmicos e respiratórios foram registrados novamente e gasometria e amostragem para os níveis de cortisol, insulina e glicose foram repetidos. E os últimos parâmetros hemodinâmicos foram registrados, análise e amostragem de gasometria para os níveis de resposta ao estresse foram realizadas após 60 minutos da extubação.
Resultados: Não houve diferença estatística entre dois grupos quanto aos parâmetros hemodinâmicos e respiratórios, exceto pressão média das vias aéreas ($P_{média}$). Os valores de Pmédia, complacência, PaO_2 e do pH foram maiores no grupo PEEP-10. Também os valores de $PaCO_2$ foram menores no grupo PEEP-10. Não foram observadas quaisquer diferenças entre os níveis de insulina e de ácido láctico nos dois grupos. Porém, o nível de cortisol no pós-operatório foi significativamente menor no grupo PEEP-10.
Conclusão: Ventilação com PEEP de 10 cmH_2O aumenta a complacência e a oxigenação, não causa hemodinâmica e complicações respiratórias e reduz a resposta ao estresse no pós-operatório.

Introduction

General anesthesia causes reduction of functional residual capacity (FRC) due to decreased inspiratory muscle tone, increased abdominal pressure and altered thoracic volume.[1] Changing the erect position to the supine position causes a loss of about 20% FRC, and induction of anesthesia causes a further loss of 10%.[2] Also, the increased abdominal pressure during laparoscopic procedures results in additional loss of FRC. This decrease in FRC can lead to atelectasis and formation of intrapulmonary shunting in the depended lung regions.[3] Perioperative atelectasis affects gas exchange and is accepted as a major cause for development of postoperative hypoxia.[4] Ventilation with lower tidal volume and application of positive end-expiratory pressure (PEEP) improve outcome in acute respiratory distress syndrome (ARDS) and has become a routine strategy for the treatment of the patient with ARDS.[5] However, recent meta-analyses have sustained that ventilation during general anesthesia with lower tidal volumes and PEEP can also benefit patients without ARDS.[6] Also, application of PEEP has been shown to be effective in preventing atelectasis during anesthesia. PEEP is a frequently employed strategy in anesthesiology, but it has capacity to harm as well as to yield beneficial outcomes.[7] Depending on the PEEP level, a decrease in cardiac output (CO) can be induced through increased intrathoracic pressure (ITP) and reduced ventricular preload and systemic venous return pressure gradient.[8]

This study was undertaken to evaluate the effects of different PEEP levels on gas exchange, hemodynamics and stress response in the settings of increased intra-abdominal pressure (IAP) created by CO_2 pneumoperitoneum for laparoscopic cholecystectomy.

Methods

This prospective randomized study was conducted with the approval of the institute's research and ethics committee and after obtaining written informed consent from 43 patients, aged 18–65 years and of American Society of Anesthesiologist (ASA) I–II physical status, scheduled for laparoscopic cholecystectomy. Patients with morbid obesity (BMI more than 30 $kg\,m^{-2}$) or history of diabetes mellitus, endocrine, respiratory, cardiopulmonary and cerebrovascular diseases were excluded from the study. Also, only the cases admitted to the theater until 11:00 A.M. were included in this study. The patients were randomly selected, by opening sealed envelopes, to receive either external PEEP of 5 cmH_2O (PEEP 5 group, $n = 20$) or external PEEP of 10 cmH_2O (PEEP 10 group, $n = 23$) during pneumoperitoneum.

In the operating theater, baseline electrocardiogram (ECG), heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), hemoglobin oxygen saturation (SpO_2) and end-tidal carbon dioxide ($ETCO_2$) were recorded using a multiparameter monitor. Baseline arterial blood gases (ABG) were measured and blood sampling was done for cortisol, insulin and glucose level estimations to assess the systemic stress response. Anesthesia was induced by 2 mg kg^{-1} propofol, 2 μg kg^{-1} fentanyl citrate, and 0.6 mg kg^{-1} rocuronium bromide. Anesthesia was maintained with 1.0 MAC of sevoflurane in a mixture of 50% oxygen and air and the ventilator was set with 8 mL kg^{-1} tidal volume calculated using the predicted body weight and 12 min respiratory rate with an I:E ratio of 1:2 at fresh gas flow 1 L min^{-1}. The 'PEEP 5 group' received 5 cmH_2O PEEP, and the 'PEEP 10 group' received 10 cmH_2O PEEP level. Before pneumoperitoneum, HR, MAP, $ETCO_2$, P_{peak}, P_{plato}, and P_{mean} were recorded. Pneumoperitoneum was created by CO_2 insufflation and IAP was set to be maintained at 14 mm Hg^{-1} by means of an automatic insufflator. Thirty minutes after the pneumoperitoneum, the respiratory and hemodynamic parameters were recorded again and ABG and sampling for cortisol, insulin, glucose levels were repeated. Anesthesia was maintained until the end of surgery, neuromuscular blockade was antagonized with sugammadex and tracheal extubation was carried out when the patient was fully awake. Recording of hemodynamic parameters and ABG, and sampling for cortisol, insulin, glucose levels were repeated for the last time at 60 min after extubation.

Table 1 Before and during the pneumoperitoneum time.

	Group				
	PEEP 5		PEEP 10		
	n	%	*n*	%	
Gender					
Men	8	40.0	6	26.1	0.331
Women	12	60.0	17	73.9	
	Mean ± SD	Median	Mean ± SD	Median	*p*
Age (years)	49.0 ± 13.5	49	43.5 ± 12.6	41.5	0.180
Weight (kg)	75.1 ± 11.4	80	72.3 ± 10.6	71	0.416
Heart rate					
1	75.6 ± 5.9	76	83.3 ± 11.5	80	0.090
2	81.9 ± 12.2	84	77.7 ± 15.5	74	0.471
3	84.0	84	78.9 ± 15.0	78.5	–
SAP					
1	131.9 ± 17.1	134	131.2 ± 23.9	128.5	0.941
2	119.2 ± 26.3	119	126.4 ± 14.6	120	0.467
3	142.0	142	119.8 ± 13.4	118.5	–
DAP					
1	82.3 ± 15.1	84.5	84.8 ± 11.7	83	0.651
2	75.4 ± 16.0	79	84.7 ± 8.3	82	0.134
3	89	89	73.3 ± 8.7	73	–
MAP					
1	103.9 ± 13.3	101.5	108.9 ± 15.4	105	0.391
2	96.6 ± 19.3	99	103.3 ± 10.5	103	0.352
3	115	115	90.3 ± 8.2	90	–
P_{peak}					
1	20.7 ± 5.9	18.5	20.6 ± 2.8	20	0.961
2	23.3 ± 3.8	22.5	25.1 ± 2.1	25	0.053
P_{plato}					
1	18.8 ± 4.2	17.5	18.0 ± 5.1	19	0.745
2	21.4 ± 3.7	20.5	23.2 ± 2.1	22	0.054
P_{mean}					
1	9.5 ± 1.4	9	12.4 ± 1.3	13	0.005
2	10.2 ± 1.1	10	13.7 ± 1.3	14	<0.001
Compliance					
1	41.0 ± 10.4	40	60.4 ± 13.1	58	0.009
2	34.7 ± 6.7	34.5	41.4 ± 5.9	41	0.001

DAP, diastolic arterial pressure; MAP, mean arterial pressure; PEEP, positive end-expiratory pressure; SAP, systolic arterial pressure; SD, standard deviation.

Statistical analysis

Windows program SPSS 15.0 was used for the statistical analysis of the results. Descriptive statistics were given in terms of numbers and percentages for categorical variables, and in terms of the mean, standard deviation and the median for the numerical variables. Comparison of two independent groups of variables was carried out using the Student *t* test when meeting the normal distribution criteria, or by the Mann–Whitney *U* test when these criteria were not met. Relationship between numerical variables was assessed by means of the Spearman Correlation Analysis. The differences between categorical variables were evaluated by the Chi-square analysis. Statistical α (alpha) significance level was accepted with the *p*-value below 0.05.

Results

Physical characteristics and demographic parameters of the two patient groups were closely comparable. Also, there were no statistically significant differences between the two groups with respect to the hemodynamic parameters (HR, SAP, DAP, and MAP) and the respiratory parameters of P_{peak} and P_{plato} levels. But the mean airway pressure (P_{mean}) and compliance levels were statistically higher in PEEP 10 group before and during the pneumoperitoneum time (Table 1).

The mean $ETCO_2$ levels were same for the two groups. Although no differences were observed in the PaO_2 values between the two groups preoperatively and in the postoperative period, the values were higher in the 'PEEP 10 group' over the duration of pneumoperitoneum (Table 2, Fig. 1). Before pneumoperitoneum and during pneumoperitoneum

Table 2 Over the duration of pneumoperitoneum.

	Group				*p*
	PEEP 5		PEEP 10		
	Mean ± SD	Median	Mean ± SD	Median	
$ETCO_2$					
1	31.5 ± 4.9	31.5	33.2 ± 2.4	33	0.428
2	33.0 ± 4.2	33	34.8 ± 3.5	34	0.526
PaO_2					–
1	85.0 ± 15.7	80	91.9 ± 14.4	93	0.158
2	135.2 ± 36.9	132	176.1 ± 37.9	172	0.001
3	96.4 ± 22.8	88.5	91.5 ± 12.2	90	0.838
PCO_2					
1	38.5 ± 4.6	39	36.5 ± 4.3	36	0.165
2	41.9 ± 5.5	40	35.9 ± 5.5	35	0.001
3	39.6 ± 4.9	40	35.0 ± 5.2	34.5	0.006
pH					
1	7.40 ± 0.05	7.41	7.40 ± 0.05	7.40	0.650
2	7.35 ± 0.05	7.35	7.39 ± 0.05	7.38	0.008
3	7.37 ± 0.04	7.37	7.41 ± 0.08	7.41	0.081
SpO_2					
1	100	100	98.0 ± 1.1	98	–
2	99	99	99	99	–
Cortisol					–
1	13.1 ± 5.8	12.9	12.1 ± 5.7	12.0	0.573
2	23.4 ± 6.2	22.1	20.5 ± 5.5	21.6	0.115
3	28.3 ± 6.0	26.1	17.3 ± 11.1	15.9	< 0.001
İnsuline					
1	4.6 ± 3.3	5.1	4.5 ± 3.0	4.1	0.880
2	3.8 ± 4.5	2.5	3.4 ± 2.9	2.6	0.830
3	7.4 ± 5.7	6.1	9.1 ± 9.7	5.5	0.980
Glucose					
1	77.5 ± 13.7	77.0	88.1 ± 12.7	89.0	0.012
2	100.3 ± 18.7	98.0	113.7 ± 24.7	110.0	0.088
3	108.8 ± 20.3	102.5	109.0 ± 32.5	98.0	0.342
Laktat					
1	2.8 ± 0.8	2.9	2.2 ± 0.8	2.3	0.206
2	2.9 ± 0.2	3.0	2.6 ± 0.8	2.8	0.351
3	2.5 ± 0.7	2.6	1.5 ± 0.9	1.6	0.084

$ETCO_2$, end-tidal carbon dioxide; PEEP, positive end-expiratory pressure; SD, standard deviation; SpO^2, hemoglobin oxygen saturation.

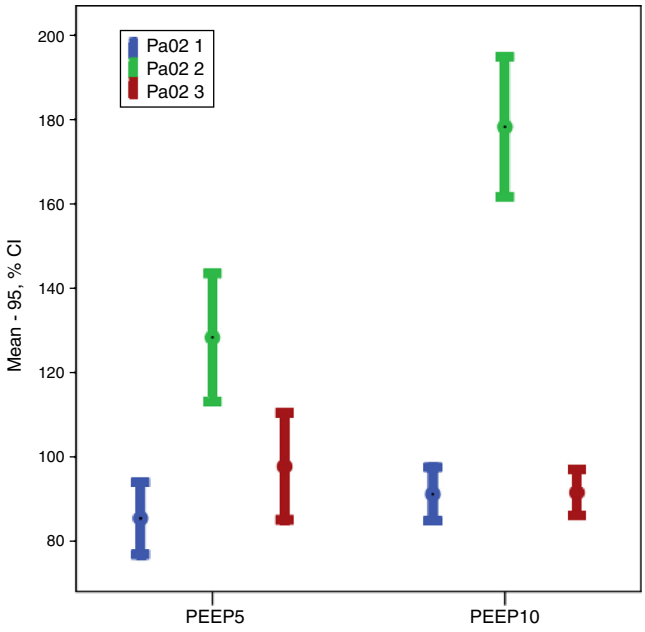

Figure 1 Changes in PaO_2 levels (PaO_2 1, preoperative time; PaO_2 2, peroperative time; PaO_2 3, postoperative time).

time, $PaCO_2$ values were lower in 'PEEP 10 group' (Table 1, Fig. 2). Mean pH values of the 'PEEP 10 group' were higher than those of the 'PEEP 5 group' ($p < 0.01$) (Table 2, Fig. 3). Postoperative mean cortisol level of the 'PEEP 10 group' was significantly lower than that of the other group ($p < 0.001$) (Table 2, Fig. 4). No differences were observed between the insulin and lactic acid levels the two groups. Preoperative glucose level of the 'PEEP 10 group' was higher than that of the 'PEEP 5 group' ($p < 0.05$) (Table 2, Fig. 5).

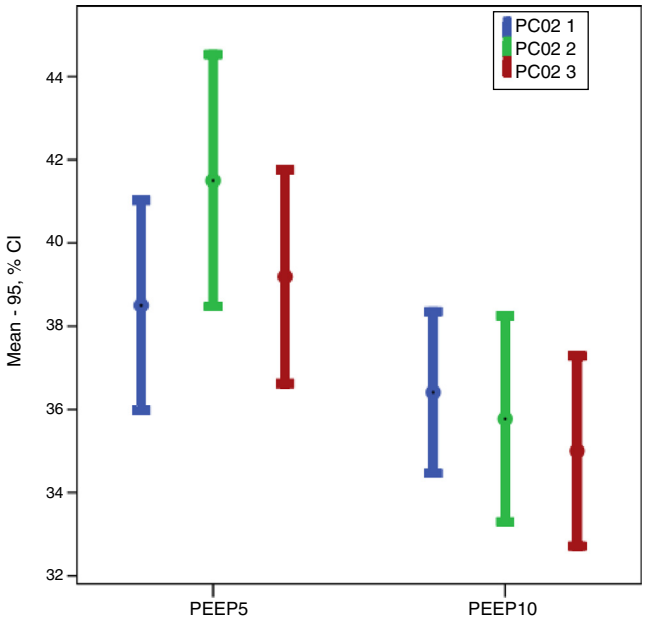

Figure 2 Changes in $PaCO_2$ levels ($PaCO_2$ 1, preoperative time; $PaCO_2$ 2, peroperative time; $PaCO_2$ 3, postoperative time).

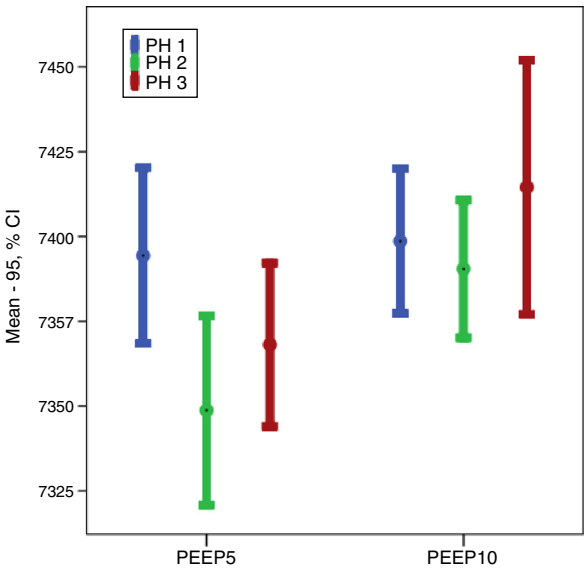

Figure 3 Changes in pH levels (pH 1, preoperative time; pH 2, peroperative time; pH 3, postoperative time).

Discussion

This study aimed to demonstrate the effects of the application of 5 cmH_2O PEEP versus 10 cmH_2O PEEP during pneumoperitoneum in laparoscopic abdominal surgery on any improvement on oxygenation and compliance, prevention of atelectasis and the differences in changes in the respiratory, hemodynamic parameters and the systemic stress response.

Recent reports have demonstrated that application of PEEP during general anesthesia, especially for laparoscopic surgery, improves compliance and oxygenation.[9] In a study

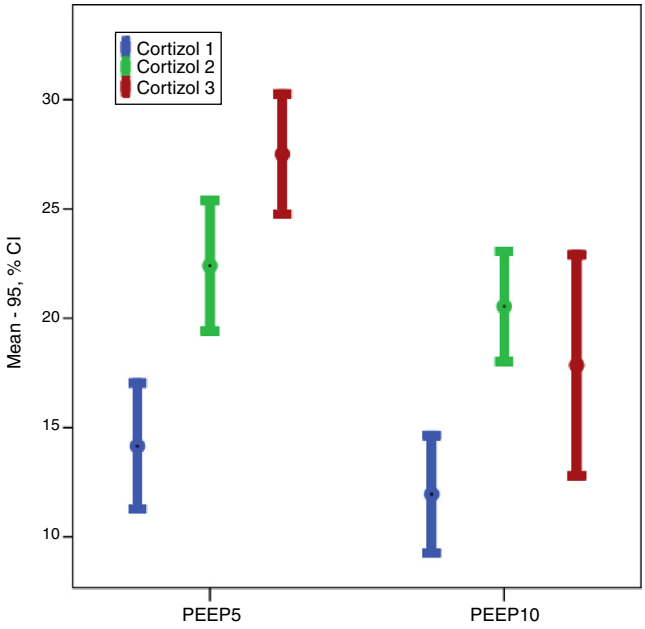

Figure 4 Changes in cortisol levels (Cortisol 1, preoperative time; Cortisol 2, peroperative time; Cortisol 3, postoperative time cortisol values).

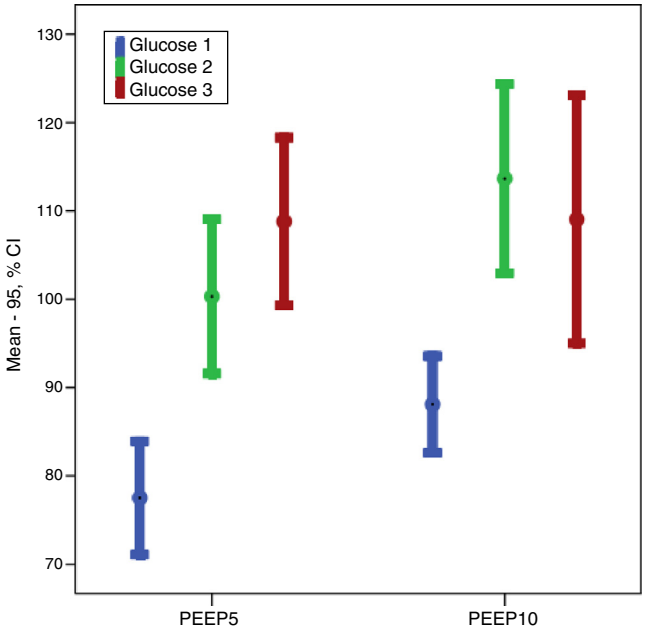

Figure 5 Changes in glucose levels (Glucose 1, preoperative time; Glucose 2, peroperative time; Glucose 3, postoperative time values).

to evaluate the effect on cerebral oxygen saturation of 0 cmH_2O PEEP and of 10 cmH_2O PEEP application during laparoscopic cholecystectomy, Hyun et al. concluded that 10 cmH_2O PEEP usage saved cerebral oxygen saturation without adverse effects on hemodynamic stability.[10] In another study, employing 14, 8 and 14 mm Hg^{-1} IAP pressure, respectively, on groups given 0, 5 and 10 cmH_2O PEEP, they observed that application of PEEP at the corresponding IAP helped maintain CO_2 elimination and improved oxygenation without hemodynamic disturbance.[11] Furthermore, the review by the Cochrane Collaboration group on postoperative mortality and pulmonary complications with and without use of PEEP has suggested, albeit inconclusively, that PEEP improves postoperative atelectasis and oxygenation.[12]

On the other hand, the PROVHILO trial with 900 cases of open abdominal surgery under general anesthesia with 8 mL kg^{-1} tidal volume and recruitment, using either 2 cmH_2O PEEP or 12 cmH_2O PEEP, did not demonstrate significant differences between the two groups with respect to postoperative pulmonary complications despite the higher preoperative oxygenation values in the 12 cmH_2O PEEP group, and the greater need of oxygenation by the 2 cmH_2O PEEP group. They concluded that elevated PEEP and recruitment maneuver in open abdominal surgery did not protect against pulmonary complications and mortality, and defended the ventilation strategy without low tidal volume, low level PEEP and recruitment.[13]

When levels of 0, 5, 10 and 15 cmH_2O PEEP were applied in cardiac surgery, it was reported that as the PEEP level was increased, respiratory system total resistance and elastic recoil were decreased; oxygenation and CO_2 elimination increased; dead space and shunting were decreased; arterial oxygen content, oxygen consumption and the oxygen extraction rate were increased despite the progressive reduction in the cardiac index; and no differences in the mean arterial blood pressure was demonstrable between the different PEEP groups. It was concluded that although application of PEEP above the 10 cmH_2O PEEP level increased oxygenation, it should be cautiously applied especially in patients with marginal cardiac function due to contractility disturbances or hypovolemia.[14] Daniel et al., after evaluating the effects of 5, 8 and 10 cmH_2O PEEP applications on the duration of mechanical ventilation after coronary artery bypass grafting surgery, reported a significantly shortened ventilation time in the 10 cmH_2O PEEP group.[15] Karsten et al. evaluated regional ventilation using electrical impedance tomography on 32 patients undergoing laparoscopic cholecystectomy either with 0 (zero) cmH_2O PEEP (the ZEEP application) or 10 cmH_2O PEEP. They reported that recruitment maneuver and 10 cmH_2O PEEP application in laparoscopic surgery improved oxygenation and corrected compliance.[9] The same group of authors investigated the effects of 0, 3, 5, 7 and 10 cmH_2O PEEP application during robot-assisted laparoscopic radical prostate surgery on the hemodynamic and respiratory parameters. They reported that HR and MAP values did not vary with the PEEP level, but the PaO_2 level was significantly low in the ZEEP group of patients and most elevated in the 10 cmH_2O PEEP group. One patient in the 10 PEEP group had subcutaneous emphysema resolved after cessation of the insufflation. They concluded that application of 7 cmH_2O PEEP resulted in significant oxygenation augmentation without excessive peak airway pressure or depression of hemodynamic parameters during prolonged laparoscopic surgery.[16]

In our study, we observed that during the pneumoperitoneum period, PaO_2, compliance, P_{mean}, and pH levels were higher in the 10 cmH_2O PEEP group as compared to the 5 cmH_2O PEEP group. Although 5 cmH_2O PEEP preserved oxygenation during pneumoperitoneum, 10 cmH_2O PEEP produced a significant improvement in oxygenation. Similar observations were made by Andrea et al. during laparoscopic gynecological surgery. PEEP application resulted in recruitment in the alveoli, improving cardiac and pulmonary functions and thereby improving oxygenation, enhancing CO_2 washout and inhibition of the vasoconstrictor reflex.

It was argued that while 5 cmH_2O of PEEP acted as a shield against the negative cardiopulmonary effects induced by pneumoperitoneum, 10 cmH_2O of PEEP actually improved the effects.[17] Although the most common complications of high PEEP application are observed in the hemodynamic parameters, especially in hypovolemic patients, on including respiratory effects such as barotrauma, we did not encounter hemodynamic or respiratory complications in our series of patients. In patients undergoing laparoscopic inguinal hernia surgery with application of 8 mL kg^{-1} tidal volume with 0, 5 and 10 cmH_2O PEEP, end-expiratory lung volume (EELV), measured with the nitrogen wash-out/wash-in method using electrical impedance tomography, was increased during application of 10 cmH_2O PEEP which also homogenized ventilation distribution.[18]

We observed, when evaluating the effects of 5 and 10 cmH_2O PEEP application on the systemic stress response, that preoperative blood glucose levels, although significantly elevated, were still within the physiological limits in the 10 cmH_2O PEEP group, while the cortisol level was significantly lower in postoperative time and the insulin level was unmodified as compared to the 5 cmH_2O PEEP group. We

could not find another study in the literature on the effects of PEEP level on the systemic stress response parameters to be able to make direct comparisons on the results.

However, in studies evaluating the inflammatory response, it was found out that PEEP was beneficial at high inspiratory pressure and caused some stress, but imposed only moderate stress at low inspiratory pressure.[19] Weingarten et al. compared the effects of 'low tidal volume with high (12 cmH_2O) PEEP' application versus 'high tidal volume with ZEEP (0 cmH_2O PEEP) application' on the systemic inflammatory response parameters IL-6 and IL-8, and found no differences between the two groups. But the perioperative oxygenation of the 'low tidal volume and 12 cmH_2O PEEP' group was increased and lung mechanics were much better.[20] In our study, the observation of low postoperative cortisol levels with 10 cmH_2O PEEP application may be related to better peroperative oxygenation and compliance.

Conclusion

We believe that during laparoscopic cholecystectomy surgery, ventilation with 10 cmH_2O PEEP increases compliance and oxygenation does not cause hemodynamic and respiratory complications and reduces the postoperative stress response with this study.

Conflicts of interest

The authors declare no conflicts of interest.

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