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Evaluation of Low Tidal Volume During General Anesthesia in Prone Position on Respiratory Functions

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Abstract: *Background:* Surgery is accompanied by postoperative pulmonary functions impairment especially in the prone position. There is evidence suggested that using low tidal volume during general anesthesia may decrease post-operative lung injury. This study aimed to evaluate the effect of low tidal volume on lung functions during mechanical ventilation for general anesthesia while patients lying in the prone position. A prospective clinical trial was performed on 88 patients ASA I&II scheduled for elective surgery while patients lying prone and were randomly assigned to either protective ventilation group A with tidal volume; 5-7 ml/kg, 10 cm H_2O positive end expiratory pressure (PEEP) with recruitment maneuver (RM) or conventional group B with Tidal Volume; 10-12 ml/kg, without both PEEP and RM. The primary efficacy variables were assessed by pulmonary function tests, performed before surgery, and 6, 12 and 24 hours postoperatively. Improvement of lung functions were found in the first post-operative 6 and 12 hours in the low tidal volume group and significant difference was found in all parameters P value 0.001 except PaO_2/FIO_2 ratio P value 0.4. After 24 hours there were significant difference in the FVC, predicted FEV1 and FVC and FEV1/FVC ratio being higher in the low tidal volume group with P value 0.001. Patients in both groups showed similar rates of postoperative chest complications without significant difference. Lung protective ventilation improved lung functions in the first post-operative 24 hours. There was no significant postoperative chest complications difference between the two groups.

Keywords: Respiratory Functions, Prone Position, Tidal Volume

1. Introduction

Postoperative pulmonary complications, especially postoperative respiratory failure, are important causes of preoperative morbidity and mortality. The tidal volume (VT) is considered as one of the main parameters of ventilation settings during general anesthesia (GA). Using lower tidal volume during mechanical ventilation is important to decrease lung injury. [1, 2]

Patients on mechanical ventilation during surgery experience varying degrees of postoperative respiratory function impairment, including various parameters of lung functions which will impact on the patient's outcome. [3]

After induction of general anesthesia, atelectasis develops within minutes and is a direct source of intra-operative gas exchange abnormalities. These areas of atelectasis can be functionally restored by lung recruitment maneuver followed by a substantial level of positive end expiratory pressure (PEEP), which has been known to improve intra-operative oxygenation. [4]

High VT (10-15 ml/kg) over-distends non-atelectatic alveoli, in particular in non dependent lung areas. During surgery this may stress the non-atelectatic lung regions, triggering local inflammation. [4, 5]

The effects of lower VT in patients on short-term mechanical ventilation have been appeared in many researches [6, 7]. These studies discussed these effects on patients lying supine. Alterations in distribution of pulmonary ventilation and perfusion are well known to occur with change in position especially in the lateral and prone positions [8].

In fact we did not find any published studies on the effect of the lung functions during lung protective ventilation in the prone position, and surgery in the prone position is increasing as the global incidence of spine disorders increases [9]. The aim of this study was to evaluate the effect of low VT, high PEEP and recruitment maneuver (RM) on lung functions during mechanical ventilation for GA while patients lying in prone position.

2. Materials and Methods

This prospective randomized controlled study was performed in the department of anesthesia of Qena University Hospitals, South Valley University between August 2015 and August 2017. We studied all consecutive patients undergoing surgical procedure in the prone position under GA. The inclusion criteria were patients aged from 18 to 65 years, body mass index (BMI) < 30, American Society of Anesthesiologists (ASA) score ≤ II and agreement to complete the study requirement.

2.1. Exclusion Criteria Were Patients with Any of the Following Reasons

(i) Impaired mental state, (ii) Pregnancy, (iii) History of chronic obstructive lung disease, acute lung injury, severe cardiac asthma, neuromuscular diseases, or sleep disorders, (iv) History of previous lung surgery, (v) Heavy smokers (vi) Recent immunosuppressive medication (within the last 2 months), or (vii) Patients on medications that affect their respiratory system.

2.1.1. The Number of Patients Needed Was Calculated Based on

As previously published data in the literature about change in pulmonary function test results correlated with change in tidal volume [10]. Considering a power of 80% and reliability of 0.05, we found that a minimum of 41 patients should be present in each group.

The study was started with a target of 147 patients for the possible loss of patients and data during the study.

2.1.2. Study Design

Eligible patients (98 patients) were randomly divided into two equal groups (protective ventilation/study group – group A: low VT, high PEEP and RM, conventional ventilation/control group – group B: High VT, no PEEP and no RM) according to a computer generated random numbers. Of the 49 patients allocated to intervention in each group, 6 patients were excluded from the study group, and 4 patients from the control group, and the remaining 43 & 45 patients in

both groups respectively were included in the study. The study was approved by Qena university hospital ethics committee. Written informed consent was obtained from all patients before inclusion.

2.2. Anesthesia

Before induction of GA and for the purpose of postoperative pain relief systemic opioids in the form of repeated doses of 0.5-1 mg/kg pethidine I.V. was used. Induction and maintenance of GA were done by the same drugs in all patients in both groups. We used propofol (1%) in a dose of 2 mg/kg Tracheal intubation was facilitated by using rocuronium 0.4-0.8 mg/kg I.V. Anesthesia was maintained by sevoflurane in 40% oxygen during the whole anesthesia period. We followed a conservative fluid infusion of 12-15 ml/kg/h during the operative time to ensure sufficient fluid replacement.

2.2.1. Positioning

After induction of GA and assuring that monitoring and venous lines are fixed in position; patients were turned to the prone position. Proper position of the head, shoulders, and the endotracheal tube were checked after turning the patient.

2.2.2. Ventilation Protocol

In both groups we applied a volume controlled mechanical ventilation *(Datex Ohmeda A 7100 GE Healthcare, Finland)* at an inspired oxygen fraction (FiO_2) 0.4, inspiratory to expiratory time ratio (I:E ratio) of 1:2 and a respiratory rate was adjusted to keep normocapnia. In study group: VT was adjusted at 5-7 ml/kg of predicted body weight (PBW) with PEEP 10 cm H_2O with RM, while in control group VT was set at 10-12 ml/kg of PBW with no PEEP. The PBW for male patients was calculated as follows: weight in kg=50+0.91*(height in cm-152.4); and for female patients: weight in kg=45.5+0.91*(height in cm-152.4) [11].

2.2.3. Recruitment Maneuver

The RM was performed directly after induction of anesthesia and before extubation.

The RM was performed by raising the limit of peak inspiratory pressure to 45 cm H_2O, the VT at 5-7 ml/kg PBW, the respiratory rate at 6 breaths/min, PEEP at 10 cm H_2O, and the I:E ratio at 3:1; then the VT was increased in steps of 4 ml/kg PBW until plateau pressure reached 30 cm H_2O and three breaths were allowed. Finally, the respiratory rate, the I:E ratio, inspiratory pause, and the VT were set back at values preceding the RM, whereas the PEEP was maintained at 10 cm H_2O. We defined a remarkable reduction in systolic arterial pressure when less than 90 mm Hg and ensured that a mean arterial pressure less than 60 mm Hg was not accepted. We were allowed to change the ventilation protocol at any point on the surgeon's request, or if there was any concern about patient safety.

2.3. Arterial Blood Gas Analysis Was Done Immediately Before and After Each RM

Peripheral oxygen saturation were measured in the sitting

position in room air, after 10 min of adaptation. After surgery, if the patient was using a Venturi oxygen mask, the mask was removed. If peripheral oxygen saturation dropped below 88% during the 10 min of adaptation, the maneuver was stopped and arterial blood gas analysis immediately obtained. Blood was sampled for gas analysis just after each spirometric measurement. If an arterial catheter was in place, blood was withdrawn from it; otherwise, the sample withdrawn from the radial artery after subcutaneous infiltration of 3 ml lidocaine 2%.

2.4. Measurement of Pulmonary Functions

It was performed using the spirometer *(VIASYS, HEALTH CARE, microlab, England)*. Preoperative spirometry was performed after the patient had received a detailed instruction. Measurements were performed in accordance with the American Thoracic Society's standards [12]. We made all measurements in the supine position with 30° upper body elevation. A clip was placed over the nose and the patient was breath through the mouth into a tube connected to the spirometer.

First, the patient was breath in deeply, and then was exhale as quickly and forcefully as possible into the tube. This was performed three times and the best of the three results was recorded as the measure of lung function and was selected for the analysis. After operation, measurements were taken at 6, 12, and 24 hours after extubation. The FVC and the FEV1 were measured whereas the ratio between the FVC and the FEV1 (FEV1/FVC %) was calculated by the internal algorithm of the spirometer. We also calculated the predicted values of pulmonary functional tests (FEV1 Pred. % & FVC pred. %) according to Quanjer et al. [13]

2.5. Pain Score

Patients were requested to rate their pain at rest in the supine position with 30° upper body elevation on a numeric rating scale of 0-10 (0: no pain - 10: maximum pain). Spirometric testing was only performed if pain score at rest was ≤ 3. If pain score was > 3, the pain therapy was optimized before spirometric test and meperidine 0.5-1 mg/kg was injected intravenously and pain score was reassessed.

2.6. Chest Radiography

Preoperative and postoperative (day 2) chest radiographs were performed. Results were scored by a radiologist using a radiological atelectasis score: 0, clear lung fields; 1, plate like atelectasis or slight infiltration; 2, partial atelectasis; 3, lobar atelectasis; 4, bilateral lobar atelectasis [14]. All patients were followed until discharge from hospital for possible complications.

Pre- and Postoperative Observations: Preoperatively the following measurements were obtained: arterial blood gas analysis in air, pulmonary functional tests, and chest x-ray. The same measurements were performed on postoperative hours 6, 12, and 24 whereas the chest x-ray was calculated only on postoperative day 2.

2.7. Outcomes

The primary outcome was the pre-to postoperative change of pulmonary function parameters while the secondary outcomes were lung injury (PaO$_2$/ FiO$_2$) and atelectasis.

2.8. Statistical Analysis

The data were entered into a database program (Access; Microsoft, USA), and then tabulated with spread-sheet soft ware (Excel; Microsoft, USA) and analyzed with a statistical package (SPSS 15.0, USA). Data were presented as mean ± standard deviation for parametric and continuous data or numbers and percentage for nonparametric and non-continuous data. Baseline comparisons between groups were made with the independent Student *t* test. *P* value less than 0.05 was considered significant.

3. Results

Eighty eight patients were enrolled in the study and stratified randomly to 43 patients for the study group and 45 patients for the control group. There were no statistically significant differences between groups in demographic data (Table 1).

Table 1. Baseline patients' characteristics.

Characteristics	Group A	Group B	*P value*
Age, yr (mean ± SD)	42.9±7.9	43.4± 8	0.89
Sex (M/F)	26/17	25/20	0.78
BMI, kg/m² (mean ± SD)	25.3±2.6	24.8±3.4	0.45
Tobacco smokers, n (%)	17 (39.5%)	14 (31.1%)	0.81
Physical status, n (%) ASA I			
ASA II	39	38	0.94
Operative procedures	14	17	0.73
Lumbar spine surgery	29 (67.5%)	33 (73.3%)	
PCNL	13 (30.2%)	12 (26.7%)	
Back lipoma excision	1 (2.3%)	0 (0%)	

BMI: Body mass index; ASA: American Society of Anesthesiologists; PCNL: Percutaneous nephro-lithotomy

Pulmonary function test: There were no statistically significant differences between the two groups before surgery, regarding all pulmonary function parameters (Table 2).

Table 2. Preoperative pulmonary functions.

Parameters	Group A	Group B	*P value*
FEV1	2.8±0.6	2.9±0.7	0.4
FEV1 Pred.%	79.5±16.6	84.2±16.9	0.39
FVC	3.2±0.7	3.4±0.5	0.48
FVC pred. %	78.7±14.5	79.4±13.6	0.53
FEV1/FVC %	85.8±15	87.3±13.7	0.7
P/F ratio	416.4±57.8	377.1±58.1	0.6

FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; P/F: partial pressure of oxygen/ Fraction of inspired oxygen.

The measurement of pulmonary functions tests six hours after extubation showed statistically significant difference between the two groups in all parameters except PaO$_2$/FiO$_2$ ratio.

The parameters were better in study group than the control group (Table 3).

Table 3. Postoperative pulmonary functions after 6 hours.

Parameters	Group A	Group B	P value
FEV1	1.6±0.3	1±0.4	0.001
FEV1 Pred.%	41.6±12.4	32.9±10.9	0.002
FVC	1.9±0.5	1.5±0.7	0.001
FVC pred. %	45.7±15.9	33.2±8.4	0.001
FEV1/FVC %	72.2±10.9	55.4±14.3	0.001
P/F ratio	381.1±29.3	367.1± 27.5	0.4

As regards the 12 hours postoperative evaluation, we found statistically significant difference between the two groups in all parameters except PaO_2/FiO_2 ratio (Table 4).

Table 4. Postoperative pulmonary functions after 12 hours.

Parameters	Group A	Group B	P value
FEV1	2.3±0.7	1.8±0.7	0.03
FEV1 Pred.%	57.3±13.8	40.2±12.7	0.001
FVC	2.5±0.5	1.9±0.4	0.001
FVC pred. %	68.7±13.3	53.2±11.1	0.01
FEV1/FVC %	83.4±9.3	61.4±7.8	0.001
P/F ratio	392.3±31.4	387.1± 28.9	0.89

As regards postoperative 24 hours evaluation showed statistically significant difference between the two groups regarding the FVC, predicted FEV1 and FVC, and the FEV1/FVC ratio being better in the low tidal volume group, while the FEV1 and the PaO_2/FiO_2 ratio were statistically insignificantly between both groups (Table 5).

Table 5. Postoperative pulmonary functions after 24 hours.

Parameters	Group A	Group B	P value
FEV1	2.4±0.5	2±0.4	0.11
FEV1 Pred.%	65.1±12.3	43.4±10.2	0.001
FVC	2.9±0.5	2.3±0.4	0.01
FVC pred. %	66.7±10.4	56±10.2	0.001
FEV1/FVC %	82.8±11.1	74.4±7.7	0.001
P/F ratio	421.6±43.7	398.5±33.2	0.45

Although, postoperative complications were higher in the control group, we found no statistically significant differences in morbidity and mortality between the two groups (Table 6).

Table 6. Post-operative data.

Parameters	Group A	Group B	P value
Temp above 38, n (%)	5 (11.6%)	6 (13.3%)	0.82
Cough, dyspnea, n (%)	5 (11.6%)	7 (15.6%)	0.78
VAS (6h), median (IQR)	3.4 (2.7-4.2)	3.9 (3.1-5.1)	0.89
Patient receiving opioid	6 (14%)	7 (15.6%)	0.76
6 hours	2	1	
12 hours	3	6	
24 hours	6	7	
Opioid dose (mg), mean(SD)	162.5± 74.4	178.6±69.9	0.65
Atelectasis on CRX, n (%)	2 (4.7%)	4 (8.9%)	0.76
Death, n (%)	0	0	-

Vas (visual analogue scale)

4. Discussion

This study showed that a lung protective strategy using low VT with 10 cm H2O PEEP and RM improved pulmonary function tests in the first post-operative 24 hours; with no deleterious effect on neither arterial oxygenation level (intra-operative or postoperative); nor on the incidence of postoperative chest complications. Our study revealed no statistically differences between both groups as regard preoperative patient's characteristics.

Mechanical ventilation during anesthesia promotes alveolar collapse, even in patients with healthy lungs [14], and post-operative pulmonary dysfunction is common due to reduced ventilatory muscle activity, diaphragmatic dysfunction and decreased lung compliance. High tidal volume is one of the factors that induced ventilator associated lung injury in healthy patients [15].

The management of intra-operative airway mechanics as peak airway pressure, plateau pressure, respiratory rate and tidal volume with their impact on lung compliance may not be sufficient to reduce postoperative atelectasis and impaired lung functions [16]. However, it can be prevented by the incorporation of PEEP, and the alveoli can be stabilized with PEEP greater than 5 cm H2O [17].

Previous randomized, controlled trials have already discussed the influence of ventilation settings, and their conclusion was conflicted because recruitment was seldom applied in them [5, 18]. Pi et al., revealed that PEEP combined with recruitment could stop pulmonary compliance from decreasing. [17]

Previously published studies [16, 17, 19, 20] about the use of lung protective ventilation strategy during general anesthesia with mechanical ventilation showed conflicting opinions regarding the beneficial effect of this method on postoperative lung functions. This conflict comes from the fact that these studies were performed on non-homogenous groups of patients, for example cardiothoracic surgery [21], esophagectomy [21], major abdominal surgery [10], and urological surgery [22], with different end points whether pulmonary functions, systemic inflammation, or alveolar coagulopathy. In addition recruitment was slightly applied and PEEP levels were variable.

In our study, the 6 hours postoperative pulmonary functions evaluation revealed statistically significant difference between the two groups in all parameters except PaO_2/FiO_2 ratio which was statistically insignificant.

Our result was nearly comparable with Asida and Badawy [22], who showed statistically significant difference between groups in all the parameters measured being higher in the low tidal volume group FEV1 (2 vs. 1, p<0.000), FEV1 predicted % (36.7 vs. 25.5, p<0.000), FVC (2 vs. 1.2, p<0.016), FVC predicted % (44.2 vs. 24.9, p<0.000), FEV1/FVC (62.2 vs. 43, p<0.000), and PaO2/FiO2 ratio (378 vs. 352.1, p<0.001).

In our study, the 12 hours postoperative pulmonary function parameters was statistically significantly between the two groups except PaO2/FiO2 ratio which was

statistically insignificant. Our results was in agreement with Asida and Badawy [22] regarding all pulmonary function parameters except FEV1 (3.4 vs. 2.8, p=0.29) which showed statistically insignificant difference.

Postoperative 24 hours pulmonary function parameters evaluation revealed statistically significant difference between the two groups regarding the FEV1 predicted %, FVC, FVC predicted %, and the FEV1/FVC ratio being better in the study group, while the FEV1, and the PaO_2/FiO_2 ratio were insignificantly different between both groups. This difference may be explained by the improvement on the respiratory function of the control group after 24 hours postoperative rather than decreased efficacy of the investigated maneuver in the study group with time.

Pi et al., [17] revealed statistically significantly higher FEV1 (1 vs. 1 vs. 1.5, p<0.001), and FVC (1.2 vs. 1.3 vs. 1.8, p<0.001), on the postoperative day 1 in the low volume with PEEP and recruitment group than in the other two groups and insignificant. PaO_2/FiO_2 ratio difference (392 vs. 393 vs. 398, p=0.98) in all groups. Severgnini et al., [19] revealed comparable results regarding (FEV1 predicted %, FVC, FVC predicted %) which were statistically significant higher in the protective ventilation strategy group as compared with the standard ventilation strategy group, and incomparable result regarding FEV1 and FEV1/FVC which was statistically significant and insignificant, respectively on postoperative days 1, 3, and 5 in both groups.

Treschan et al., [10] revealed that FVC and FEV1 did not differ significantly between groups at any postoperative time which was inconsistent with our result, while they revealed that postoperative PaO_2 values for patients' breathing room air were comparable between groups until day 3 which was comparable with our result. Their final conclusion was that intra-operative lung mechanics and gas exchange were better and atelectasis was less with high VT and prolonged impaired lung function after major abdominal surgery is not ameliorated by low VT ventilation, and that in order to improve lung mechanics they should use higher PEEP in the low VT group that may have influenced the results in favour of lower VT [10]. They stated that they did not do so for several reasons. First, differences between groups, if any, could then not be attributed to low VT alone, and their trial was specifically designed to study effects of intra-operative low VT. Secondly, the ideal PEEP is just high enough to keep the lungs open at end-expiration. Individual patients' 'ideal-PEEP' can be identified by PEEP trials. However, they are time-consuming and difficult to implement into the intra-operative setting. Thirdly, the use of high PEEP ($\geq$10 cm H_2O) may be limited in the surgical setting, and fourthly, for fear that higher levels of PEEP may be associated with high levels of pro-inflammatory cytokines and pulmonary coagulation activation. [4]

Treschan et al., [10] used a minimum PEEP of 5 cm H_2O in both groups in order to counterbalance this component of cyclic airway opening and closing. This was not the case in our study as we did not apply PEEP in the high VT group which may affect lung mechanics differently [23], second we used PEEP levels higher than 5 cm water in the low VT

group while monitoring heart rate and arterial blood pressure not to impair these parameters, but we did not measure pro-inflammatory cytokines to assess the effects of low VT with PEEP and RM on the inflammatory response to this technique.

Koner et al., [24] revealed no statistically significant difference regarding FEV1 (1.9 vs. 1.9 vs. 2.1, P>0.05) and FVC (2.1 vs. 2.3 vs. 2.4, p>0.5) among the groups. During general anesthesia, atelectasis is potentiated by anesthesia and muscle relaxants altering diaphragmatic position [26]. Some research has reported that pain could decrease indices of pulmonary function [27, 28]. Our study was different from most published studies regarding low VT effect on postoperative pulmonary functions in that we evaluated potential complications of higher PEEP levels and RMs during general anesthesia not in the intensive care setting; again we evaluated the effect of this technique in the prone position which was not done before.

In our study we investigated major postoperative complications with relevant clinical parameters associated with alterations in the pulmonary function. The study revealed no statistically significant differences between the two study groups regarding the incidence of fever (>38° C), cough and dyspnea, pain score, number of patients receiving opioid, total opioid analgesic consumption, and X-ray changes, although they were higher in the control group. This may be attributed to the use of the same general anesthesia protocol regardless of the tidal volume.

Atelectasis develops within minutes after the induction of general anesthesia, and is a significant source of intra-operative gas exchange abnormalities [29]. These areas of atelectasis can be ameliorated in part by a lung recruitment maneuver followed by a substantial level of PEEP which has been demonstrated to improve intra-operative oxygenation in morbidly obese patients [30].

Many studies [17, 22, 25] revealed that in protective compared with standard ventilation group fever, cough and dyspnea, chest X-ray abnormalities including atelectasis, the quality of analgesia and hospital length of stay were not statistically different between groups and they were lower in the protective ventilation group compared with standard ventilation group on postoperative day 1. Similarly, Cai et al., [31] concluded that ventilation using low VT does not cause more pulmonary atelectasis than mechanical ventilation using standard VT.

Treschan et al., [10] comparably to our results revealed that pain score, fever, cough, dyspnea, hospital stay and death was insignificantly different between both groups and incomparably to our results revealed statistically significant more patients with atelectasis in the low tidal volume group (88% vs. 68%, p=0.017). While in contrast to our result, Severgnini et al., [19] reported statistically significant chest X ray alterations in the high tidal volume group at day 1 and 3 which was explained by gross atelectasis and potential peripheral airway injury, caused by tidal airway closure, which was maintained in the postoperative period. Also, Yang et al., [24] revealed a statistically significant difference

of lung infiltration and atelectasis (2 vs. 10, P <0.03) being low in the protective ventilation.

We present a single-centre trial with a specific group of patients undergoing surgery under general anesthesia in prone position. Thus, our data cannot be generalized to other groups of patients or types of surgery. Larger trials are still warranted to determine whether intra-operative protective mechanical ventilation improves major outcome parameters.

Limitations of our study: First, we did not titrate PEEP levels individually. Second, chest x-ray may underestimate the presence of atelectasis and lung morphology alterations as compared with computed tomography [32].

5. Conclusion

A lung protective strategy using low VT with 10 cm H_2O PEEP and RM showed improved pulmonary function tests in the first post-operative 24 hours; with no deleterious effect on neither arterial oxygenation level (intra-operative or postoperative); nor the incidence of postoperative chest complications.

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