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Should we use lung protective ventilation for non-ARDS patients? [version 1; referees: not peer reviewed]

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Abstract

An evaluation of a recent study by Serpa Neto A, Cardoso SO & Manetta JA *et al*: **Association between Uses of Lung-Protective Ventilation with Lower Tidal Volume and Clinical Outcomes among Patients without Acute Respiratory Distress Syndrome a Meta-analysis**. JAMA, October 24/31, 2012—Vol 308, No. 16. PMID: 23093163.

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Critique of:

Citation

Serpa Neto A, Cardoso SO, Manetta JA, Pereira VG, Esposito DC, Pasqualucci Mde O, Damasceno MC, Schultz MJ. Association between Uses of Lung-Protective Ventilation with Lower Tidal Volume and Clinical Outcomes among Patients without Acute Respiratory Distress Syndrome a Meta-analysis. JAMA, October 24/31, 2012—Vol 308, No. 16. PMID: 23093163.

Background

Lung-protective mechanical ventilation with the use of lower tidal volumes has been found to improve outcomes of patients with acute respiratory distress syndrome (ARDS). It has been suggested that use of lower tidal volumes also benefits patients who do not have ARDS.

Methods

Objective

To determine whether use of lower tidal volumes is associated with improved outcomes of patients receiving ventilation who do not have ARDS.

Design

Data Sources. MEDLINE, CINAHL, Web of Science, and Cochrane Central Register of Controlled Trials up to August 2012.

Study Selection. Eligible studies evaluated use of lower vs. higher tidal volumes in patients without ARDS at onset of mechanical ventilation and reported lung injury development, overall mortality, pulmonary infection, atelectasis, and biochemical alterations.

Data Extraction. Three reviewers extracted data on study characteristics, methods and outcomes. Disagreement was resolved by consensus.

Results

Twenty articles (2822 participants) were included. Meta-analysis using a fixed-effects model showed a decrease in lung injury development (risk ratio [RR], 0.33; 95% CI, 0.23 to 0.47; I^2 , 0%; number needed to treat [NNT], 11), and mortality (RR, 0.64; 95% CI, 0.46 to 0.89; I^2 , 0%; NNT, 23) in patients receiving ventilation with lower tidal volumes. The results of lung injury development were similar when stratified by the type of study (randomized vs. nonrandomized) and were significant only in randomized trials for pulmonary infection and only in nonrandomized trials for mortality. The meta-analysis using a random-effects model showed, in protective ventilation groups, a lower incidence of pulmonary infection (RR, 0.45; 95% CI, 0.22 to 0.92; I^2 , 32%; NNT, 26), lower mean (SD) hospital length of stay (6.91 [2.36] vs. 8.87 [2.93] days, respectively; standardized mean difference [SMD], 0.51; 95% CI, 0.20 to 0.82; I^2 , 75%), higher mean (SD) $PaCO_2$ levels (41.05 [3.79] vs. 37.90 [4.19] mmHg, respectively; SMD, 0.51; 95% CI, -0.70 to -0.32; I^2 , 54%), and lower mean (SD) pH values (7.37 [0.03] vs. 7.40 [0.04], respectively; SMD, 1.16; 95% CI, 0.31 to 2.02; I^2 , 96%) but similar mean (SD) ratios of PaO_2 to fraction of inspired oxygen (304.40 [65.7] vs. 312.97 [68.13], respectively; SMD, 0.11; 95% CI, 0.06 to 0.27; I^2 , 60%). Tidal volume gradients between the 2 groupsdid not have a significant influence on the final results.

Conclusions

Among patients without ARDS, protective ventilation with lower tidal volumes was associated with better clinical outcomes. Some of the limitations of the meta-analysis were the mixed setting of mechanical ventilation (intensive care unit or operating room) and the duration of mechanical ventilation.

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Commentary

The use of lower tidal volume (V_T) was shown to reduce morbidity and mortality in patients with ARDS justifying the progressive decrease in V_T used by clinicians over the past decades[1–3]. However, in critically ill patients without ALI, there is limited evidence regarding the benefits of ventilation with lower V_T, partly because of paucity of randomized controlled trials evaluating the best ventilator strategies in these patients[4,5].

It has been suggested that ventilator-induced lung injury (VILI) occurs even in patients without ARDS with an odds ratio of 1.3 for every milliliter above 6 ml/kg[6]. Many RCTs have studied the pattern of inflammatory cytokines in the broncho-alveolar lavage (BAL) and/or blood in patients with non-ARDS, when patients were ventilated at conventional V_T compared to protective V_T of 6 ml/kg PBW, studies showed that these markers had a sustained increase in the former group[7]. Experimentally, inflammatory markers increase as early as 1 hour after initiation of ventilation[8,9]. It has also been shown in animal models that volume and not the high airway pressure is responsible for increasing the alveolar permeability[10]. Overall these studies point to conventional V_T causing a proinflammatory state in otherwise normal lungs. Therefore, ARDS could be an iatrogenic and hence a potentially preventable complication dependent upon how we ventilate our patients. A recent work among patients undergoing elective abdominal surgery suggested that a low V_T approach with intermittent sigh breaths does decrease pulmonary and extra-pulmonary complications within the first 7 days after the surgery[5].

This meta-analysis of 2822 patients consisted of a mixture of operating room and intensive care patients and showed that using lower V_T reduces the risk of developing ARDS by almost three times in patients without lung injury at the onset of ventilation. It also decreases the mortality, incidence of pulmonary infections and atelectasis. Most of the patients were electively intubated for a scheduled surgery and ventilated for a few hours highlighting the importance of the initial set V_T – whether in the operating room or the intensive care unit.

For the reason mentioned above, high tidal volumes elicit an almost immediate increase in the inflammatory markers, even in cases with short duration of mechanical ventilation. The large number of patients analyzed is a major strength of this meta-analysis even though not all the studies were RCTs and the RCTs were of moderate quality.

In the study by Determann *et al*, there were some concerns about the safety of the study in view of the general opinion that lung injury was more likely with the use of conventional tidal volumes necessitating a second interim analysis. The study had to be stopped after the analysis showed a p value of < 0.01 for lung injury using conventional tidal volumes. While not included in the meta-analysis, the work by Futier *et al.* also used relatively high V_T of 10–12 ml/kg without any positive end expiratory pressure (PEEP)[5].

Recommendations

Most patients who need ventilation do not have lung injury and those who develop ARDS do so 48–72 hours after initiation of mechanical ventilation. Studies have shown a large tidal volume set on the first day post intubation is a risk factor for development of lung injury. Some studies point to possible harm by ventilating patients at conventional V_T. Protective ventilation has been proven to be beneficial for lung injury patients and is not associated with an increased use of sedatives or vasopressors[6,7]. Given these facts, and the findings of the impressive reduction in the risk of development of ARDS in this meta-analysis, ventilating all of the ICU patients, ARDS or not, with tidal volumes of 6 ml/kg PBW would seem most desirable. The use of appropriate PEEP needs to be further explored.

Competing interests

The authors declare that they have no competing interests.

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