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Low tidal volume ventilation for ARDS

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Keywords

ARDS, ALI, ventilation, outcome

Comments

The complete results of this much-talked about study are now in the public domain. It answers an important hypothesis concerning the management of the patient with acute lung insufficiency/acute respiratory distress syndrome (ALI/ARDS), and the results are clearly very impressive. In addition the significant reduction of inflammatory markers seen in the low tidal volume (TV) group support the proposed mechanisms, from animal studies, for protective ventilatory strategies. High respiratory rates and the use of bicarbonate infusions to prevent acidosis in those patients with low TV ventilator strategies are perhaps at odds with present regimes for protective ventilation in the ITU. High respiratory rate (RR) have previously been thought to contribute to stretch injury because of the repeated opening and closing of lung units but perhaps the high positive end expiratory pressure (PEEP) protects against this. Permissive hypercapnia and a moderate acidosis have traditionally been allowed so that low TV strategies can be used to protect against high ventilator inflation pressures. Permissive hypercapnia has been argued to benefit the patient and improve survival ([Paper Report: hypercapnia and the critically ill](#)), and the authors of this study propose that it may in fact be harmful. Consequently our currently adopted protective ventilatory strategies will need to be adapted if this is indeed true.

Introduction

Traditionally, mechanical ventilation in ALI/ARDS has used tidal volumes of 10-15 ml/kg, to maintain normocapnia and pH. This frequently results in high inflation pressures, with the possibility of 'stretch' injury to aerated lung. Animal experiments have also shown that this ventilation strategy results in release of inflammatory mediators and so other organs may become injured. In the human arena to date, protective ventilatory strategies (the use of low tidal volumes) have produced conflicting results.

Aims

To investigate the effectiveness of a low tidal volume (6 ml/kg) ventilator strategy versus the traditional strategy (12 ml/kg) in patients with ALI/ARDS.

Methods

Expected sample size was 1000 patients recruited from hospitals in the ARDS network of the NIH. A full description of the methods has been available at www.ardsnet.org since the initial design of the study. Essentially, randomisation occurred to low or traditional TV ventilator strategies for all patients with ALI/ARDS who met the inclusion/exclusion criteria. Adjustments were then made to achieve specific arterial pH goals, including increasing RR, the infusion of bicarbonate, and if this still failed then increasing TV by 1ml/kg. Adjustments were also made to achieve end-inspiratory pressure goals with ideally 12ml/kg TV at 50 cm H₂O and 6 ml/kg TV at 30 cm H₂O. Oxygenation goals were set, and only prescribed combinations of PEEP/F_iO₂ were to be used. Completion of ventilator procedures occurred either at death, at hospital discharge or if the patient was still alive 28 days after enrollment. Interleukin-6 concentrations were measured on day 0 and 3 in the first 204 patients as a marker of systemic inflammatory response syndrome (SIRS).

Results

Recruitment was stopped early, after 861 patients, when interim analysis revealed mortality of 31.0% in 6ml/kg TV group versus 39.8% in 12 ml/kg ($P = 0.007$), and ventilator free days 10 (11) in 6 ml/kg versus 12 (11) in 12 ml/kg ($P = 0.007$). Secondary endpoints showed significant improvements in weaning in the low TV group [65.7% versus 55% ($P < 0.001$)], and days without organ failure [15 (11) versus 12 (11) ($P = 0.006$)]. Specific ventilator goals were achieved, which explains why no acidosis and only very minor hypercapnia was seen in the low TV group. No differences in the rates of barotrauma were seen between the groups. Interleukin-6 levels were significantly lower at day 3 in the low TV group.

Discussion

The benefits shown are consistent with previous animal data, including the reduction in SIRS response in the low TV group. This translates to a reduced likelihood of other organ failures, which was shown in this study. The authors discuss why the results of this very large study may differ from the previously published randomised controlled trials. A lower TV (6ml/kg) was used in the experiment group resulting in greater differences in TV between groups compared to previous studies, and these studies may also have lacked power to show the moderate benefits in mortality seen in this study. The authors question whether correction of acidosis has a protective role, thus implying that permissive

hypercapnia is harmful. Finally the high PEEP used in this study prevents excessive stretch from repeated opening and closing of lung units.

Additional information

In accordance with policy of the *New Engl J Med*, this [paper](#) is available on the Internet prior to publication in the May 4th issue, because of its importance.

References

1. The Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *New Engl J Med*. 2000, 342: 1301-1308.