Commentary for Critical Care and Shock

Crit Care & Shock (2004) 7: 115 - 116

Re: Surfactant protein-D and polymorphonuclear leukocyte elastase concentrations in patients with septic acute respiratory distress syndrome.

Systemic markers of acute lung injury, smoke of a distant fire?

Michael R. Pinsky

Acute respiratory distress syndrome (ARDS) is a common and severe disease process seen in critically ill patients. ARDS can be separated into those patients who have primary or secondary ARDS. The mechanisms of disease and its outcome can be quite different between these two processes. Relevant to this issue, the data of Nakae et al. reported in this issue are interesting. These investigators extended their previous work by examining the systemic expression lung injury by measuring serum levels of a specific lung protein, surfactant apoprotein D, as well as a marker of leukocyte activation, neutrophil elastase, in the blood of septic patients with or without ARDS. Their data clearly show that both markers are elevated in ARDS patients and the more elevated these levels the greater likelihood of death. We can conclude from these data that lung-specific makers of injury are preferentially elevated in ARDS patients with sepsis.

Primary ARDS etiologies include lung injury coming from the airways (e.g. aspiration, smoke inhalation) or reflect an isolated lung injury (e.g. pneumonia, lung contusion). Compartmentalization of injury in primary ARDS has been previously described and agrees with preconceived notions of an isolated pulmonary injury. Presumably, the lack of a more advanced systemic inflammatory response in primary ARDS is one of the reasons why primary ARDS often enjoys a lower mortality rate. However, do lung-specific mediators of injury leach out of the lung and present in the systemic circulation? We know that translocation of live bacteria from alveoli to blood stream in animals with experimental pneumonia occurs more frequently with tidal volumes are increased and the lung units allowed to collapse with each expiration [1]. Furthermore, ventilation allowing lung collapse causes bacterial endotoxin to rise in the circulation [2] and induces a pro-inflammatory response both locally [3] and in the systemic circulation [4]. The data of Nakae et al. suggest that back diffusion of apo-protein D, and presumably neutrophil elastase, through a permeable alveolar epithelial barrier was the reason for the increased circulating level of apo-protein D in the blood. However, what we do not know is whether the septic patients with ARDS were managed using a lung protective strategy? Similarly, we are not told if patients with sepsis but without ARDS ventilator-dependent? Potentially, differences in ventilator management even if both groups received mechanical ventilation could explain these findings.

Secondary ARDS etiologies reflect systemic processes where in the lung is injured as part of that systemic process (e.g. sepsis, pancreatitis, burns, trauma). Prior clinical studies have uniformly demonstrated that patients with a systemic inflammatory response syndrome (SIRS) associated with organ injury have persistent elevations of pro-inflammatory mediators and their associated pro-inflammatory effector species, including leukotrienes, thromboxane and activate immune effector cells [5]. However, organ injury during sepsis is often progressive, with organs failing over time while others may recover. The lung-specific inflammatory signal is not merely an off or on one for apo-protein D and neutrophils elastase, but a continuous one. It would have been interesting to see if patients with lower blood levels of either apo-protein D or neutrophil elastase resolved their ARDS sooner or if those with higher levels developed further organ failure and death. Such data can be quantified using any of a number of organ failure scoring systems such as the Goris organ failure score or the Brussels SOFA score. If these markers are measures of systemic activation of illness then they should also reflect subsequent remote organ injury. This analysis can be easily performed on retrospective data. Along the same lines, as a clinical tool threshold values rather than mean values reflect useful information for clinical decision-making. The authors should perform a ROC analysis of various apo-protein D and neutrophil elastase levels to define sensitivity and specificity of these measures elative to specific values.

We see smoke on the horizon and assume that there is a fire. As the smoke levels intensity we assume that the fire has increased in size. But it could merely reflect the increased wind blowing more smoke toward us from a constant fire. This data from this paper does not allow us to separate out these two possibilities. But clearly they show that where there is smoke, there is fire.

References

1. Nahum A, Hoyt J, Schmitz L, Moody J, Shapiro R, Marini JJ (1997) Effect of mechanical ventilation strategy on dissemination of intratracheally instilled Escherichia coli in dogs. Crit Care Med 25:1733-1743.
2. Tremblay L, Valenza F, Ribeiro SP, Li J, Slutsky AS (1997) Injurious ventilatory strategies increase cytokines and c-fos m-RNA expression in an isolated rat lung model. J Clin Invest. 99:944-52.
3. Chiumello D, Pristine G, Slutsky AS (1999) Mechanical ventilation affects local and systemic cytokines in an animal model of acute respiratory distress syndrome. Am J Respir Crit Care Med. 160:109-16.
4. Murphy DB, Cregg N, Tremblay L, Engelberts D, Laffey JG, Slutsky AS, Romaschin A, Kavanagh BP (2000) Adverse ventilatory strategy causes pulmonary-to-systemic translocation of endotoxin. Am J Respir Crit Care Med.162:27-33.
5. Pinsky MR, Vincent JL, Deviere J, Alegre M, Kahn RJ, Dupont E (1993) Serum cytokine levels in human septic shock.. Relation to multiple-system organ failure and mortality. Chest.103:565-75.