Intensive Care Med (2001) 27: 452
DOI 10.1007/s001340000831

CORRESPONDENCE

Frans B. Plötz

Ventilator-induced lung injury

Accepted: 14 November 2000
Published online: 25 January 2001

Sir: I read with great interest the article by Haitsma et al. [1]. Their findings provide useful information about possible pathomechanisms of ventilator-associated systemic inflammation. The authors state that tumor necrosis factor (TNF) α production in response to lipopolysaccharide (LPS) administration is compartimentalized before the start of mechanical ventilation. Loss of compartmentalization occurred by applying a lung-injurious ventilation mode, i.e., ventilation without positive end-expiratory pressure (PEEP). For example, after intratracheal LPS administration the intraalveolar TNF-α levels were higher in animals ventilated with a PEEP level of 10 cmH_2O than those ventilated with zero PEEP, while in the systemic compartment it was the other way around. Based on this observation, it was concluded that ventilation without PEEP results in a loss of compartmentalization of TNF-α.

In their experiments the authors contributed the production of TNF-α solely to the administration of intratracheal or intraperitoneal LPS; the contribution of mechanical ventilation was considered to be unlikely. This is questionable. Several experimental studies have reported that, even after a very short period of time, injurious ventilatory strategies increase TNF-α mRNA expression and lung lavage levels of TNF-α protein [2, 3]. The lung macrophage may be the critical mechanosensor cell capable of producing TNF-α in response to stretching mechanical forces [4], although there is evidence that the pulmonary epithelium may also be a key player in this regard [5]. Pretreatment with intratracheal instillation of anti-TNF-α antibodies improved oxygenation, reduced infiltration of leukocytes, and ameliorated pathological findings [6]. We have recently shown that mechanical ventilation of infants without preexisting lung injury results in a significant increase in TNF-α concentrations in the bronchoalveolar lavage (BAL) [7]. This is a remarkable observation because even a noninjurious ventilatory strategy is capable of inducing intratracheal TNF-α production.

Figure 1a in their article supports the concept that mechanical ventilation itself probably contributed to TNF-α production. In the intratracheally saline-treated animals increased concentration TNF-α was measured in the BAL, which obviously cannot be attributed to LPS. The actual concentrations of TNF-α were of course lower than with the combination of lung injury following intratracheal LPS administration and mechanical ventilation (two-hit model). As the authors state in their "Introduction," ventilation-induced cytokine release may be explained by a two-hit model with ventilation being the second hit to preinjured lungs. A further interesting observation is that the group of intratracheally saline-treated animals ventilated with zero PEEP seem to have higher systemic concentrations and lower BAL concentrations of TNF-α than the group ventilated with a PEEP of 10 cmH_2O (Fig. 1a). This observation is in concert with their concept of compartimentalization loss due to injurious ventilation strategies, thus also in noninjured lungs.

However, if the above is true, i.e., mechanical ventilation also contributes to TNF-α concentrations in the BAL, it remains to be elucidated why in the intraperitoneally saline-treated animals no TNF-α was measured in the BAL despite injurious ventilation strategies (Fig. 1b). Concomitantly, it also remains to be elucidated whether the increased TNF-α concentrations in the BAL of the intraperitoneally LPS-treated animals can be attributed solely to loss of compartmentalization, or whether it is the result of injurious ventilation strategies, or a combination of the two. Further investigations should address this issue.

References

1. Haitsma JJ, Uhlig S, Goggel R, Verbrugge SJ, Lachmann U, Lachmann B (2000) Ventilator-induced lung injury leads to loss of alveolar and systemic compartmentalization of tumor necrosis factor-alpha. Intensive Care Med 26: 1515-1522
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: 944–952
3. Imai Y, Kawano T, Miyasaka K, Takata M, Imai T, Okuyama K (1994) Inflammatory chemical mediators during conventional ventilation and during high frequency oscillatory ventilation. Am J Respir Crit Care Med 150: 1550–1554
4. Tremblay L, Miatto D, Hamid Q, Slutsky AS (1997) Changes in cytokine expression secondary to injurious mechanical ventilation strategies in an ex vivo lung model. Intensive Care Med 23:S3
5. Imai Y, Kawano T, Iwamoto S, Nakagawa S, Takata M, Miyasaka K (1999) Intratracheal anti-tumor necrosis factor-alpha antibody attenuates ventilator induced lung injury in rabbits. J Appl Physiol 87: 510–515
6. Dunn I, Pugin J (1999) Mechanical ventilation of various human lung cells in vitro: identification of the macrophage as the main producer of inflammatory mediators. Chest 116:S95–S97
7. Plötz FB, Vreugdenhil HAE, Zijlstra J, Heijnen CJ, van Vught AJ (2000) Mechanical ventilation induces TNF-alpha production in tracheal aspirates in infants without lung pathology. Intensive Care Med 26:S299

F. B. Plötz
St. Antonius Hospital,
Department of Pediatrics, P. O. Box 2500,
3430 CM Nieuwegein, The Netherlands