Letter

Gene expression changes with a 'non-injurious' ventilation strategy

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See related research by Wolthuis *et al*., http://ccforum.com/content/13/1/R1

We read with interest the article by Wolthuis and coworkers [1], who found that mechanical ventilation initiates ventilator-induced lung injury (VILI), in the absence of a priming pulmonary insult, even with least injurious ventilator settings. Furthermore, high tidal volume was associated with increased histological and biochemical markers of lung injury [1]. The phenomenon of VILI is well recognized, and can be particularly significant in surgical specialties that require large transfusions, cardiopulmonary bypass, and associated lung ischemia-reperfusion injury [2,3]. Counterintuitively, ventilation may be beneficial in specific surgical scenarios in that it may attenuate atelectasis and ischemia-reperfusion injury [4]. Improved understanding of VILI may be gained by studying the response at the genetic level.

Microarray analysis allows one to gain an unbiased view of the gene expression signature at a particular time point. Recent work in animal VILI models revealed that a large number of genes in the lung were markedly upregulated by mechanical ventilation, including genes involved in immunity and inflammation (MIP1, MIP2, IL-1β, and IL-6), stress response (GADD45-γ), and transcription processes (IRF-7, ATF-3) [5]. Previous studies have correlated IL-1β with the process of acute lung injury and lung fibrosis. Furthermore, high tidal volume ventilation caused expression of additional genes, such as Nur77, Btg2, c-Jun, and Egr1; these are early response genes that have been implicated in cell death and protein kinase C-mediated pathways [5].

We recently conducted a microarray study of VILI in rodents utilizing a protective ventilation strategy (room air, 60 breaths/minute, tidal volume 10 ml/kg, and inspiratory and expiratory pressures 5 and 1 cmH_2O) for a short duration of 90 minutes. Expression levels of 64 genes were significantly upregulated in the lungs, including early transcriptional factors ETF, E2F, NRF-1, CRE, and HIF1; inflammatory mediators IL-1β, IL-6, MIP1, MIP2, and GRO1; cell cycle control genes Btg2, Jun, IRF-1, and Atf-3; and others involved in cell signaling and metabolism, consistent with other microarray studies [5]. (The full data are available online [6].)

Current evidence suggests that protective ventilation strategies (in the absence of a priming pulmonary insult) cause significant gene expression in the lung. These changes can be detected after only 90 minutes of ventilation. Indeed, high tidal volume ventilation may cause additional gene expression changes in the lung. Further studies are required to elucidate the role played by these genes in VILI and to devise a superior ventilation strategy.

Competing interests

The authors declare that they have no competing interests. The authors alone are responsible for the content and writing of the paper.

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