



Alveolar fluid in acute respiratory distress syndrome promotes fibroblast migration: role of platelet-derived growth factor pathway

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Résumé en
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OBJECTIVES: Fibroblast migration is an initiating step in fibroproliferation; its involvement during acute lung injury and acute respiratory distress syndrome remains poorly understood. The aims of this study were: 1) to determine whether bronchoalveolar lavage fluids from patients with acute lung injury/acute respiratory distress syndrome modulate lung fibroblast migration; 2) to assess lung fibroblast migration's clinical relevance; and 3) to evaluate the role of the platelet-derived growth factor pathway in this effect. **DESIGN:** Prospective cohort study. **SETTING:** Three intensive care units of a large tertiary referral center. **PATIENTS:** Ninety-three ventilated patients requiring bronchoalveolar lavage fluids were enrolled (48 with acute respiratory distress syndrome, 33 with acute lung injury, and 12 ventilated patients without acute lung injury/acute respiratory distress syndrome). **INTERVENTIONS:** After bronchoalveolar lavage fluids collection during standard care, the patients were followed up for 28 days and clinical outcomes were recorded. Migration assays were performed by using a Transwell model; bronchoalveolar lavage fluids platelet-derived growth factor and soluble platelet-derived growth factor receptor-alpha were characterized by Western blot and measured by ELISA. **MEASUREMENTS AND MAIN RESULTS:** Most of the bronchoalveolar lavage fluids inhibited basal fibroblast migration. Bronchoalveolar lavage fluids chemotactic index increased with severity of lung injury (28% in patients without acute lung injury/acute respiratory distress syndrome and with acute lung injury vs. 91% in acute respiratory distress syndrome patients; $p = .016$). In acute lung injury/acute respiratory distress syndrome patients, inhibition of basal fibroblast migration by bronchoalveolar lavage fluids below 52% was independently associated with a lower 28-day mortality (odds ratio [95% confidence interval] 0.313 [0.10-0.98], $p = .046$). Platelet-derived growth factor-related peptides and soluble platelet-derived growth factor-Ralpha were detected in all bronchoalveolar lavage fluids from acute lung injury/acute respiratory distress syndrome patients. The effect of bronchoalveolar lavage fluids stimulating migration was inhibited by a specific platelet-derived growth factor receptor inhibitor (AG1296). Bronchoalveolar lavage fluids inhibiting migration reversed the effect of rh-platelet-derived growth factor-BB and reduced by 40% the binding of 125I-platelet-derived growth factor-BB to fibroblast cell surface in favor of a role for platelet-derived growth factor-sRalpha. **CONCLUSIONS:** Together, our results suggest that during acute lung injury, fibroblast migration is modulated by bronchoalveolar lavage fluids through a platelet-derived growth factor/platelet-derived growth factor-sRalpha balance. Migration is associated with clinical severity and patient 28-day mortality.

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