Acute lung injury: what are the causes?

KGF ENHANCES PULMONARY PRODUCTION OF PRO-EPITHELIAL REPAIR FACTORS IN A HUMAN IN VIVO MODEL OF ACUTE LUNG INJURY

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Introduction Keratinocyte Growth Factor (KGF) has been suggested as a possible intervention for acute lung injury. In vitro it enhances epithelial repair. In the human ex vivo perfused lung model KGF supplementation after LPS-induced injury was associated with improved alveolar fluid clearance indicating improved epithelial function. We hypothesised that KGF pre-treatment in the in vivo human LPS model of lung injury would reduce epithelial injury and increase production of mediators that induce epithelial repair.

Methods 36 subjects were randomised to either placebo or recombinant human KGF (Palifermin) 60 µg/kg/day for 3 days prior to inhalation of 50 µg E. Coli LPS. 6 h after LPS inhalation subjects underwent bronchoalveolar lavage (BAL). BAL concentrations of SP-D, RAGE, MMP-9 and CRP were measured by ELISA. Total protein was measured by Bradford assay. Markers of LPS-induced pulmonary inflammation were measured using multiplex bead array (CXCL8, TNFα, MCP-1, IL-6, MMP-7/-8) or ELISA (HMGB1 and Calgranulin C). Permeability was assessed by BAL IgG:total protein ratio.

Results KGF increased BAL SP-D (Abstract S102 Figure 1A) but not RAGE. KGF increased BAL MMP-9 by 77% (p=0.01) and of facial erythema (p=0.005) were observed in the KGF-treated group. There were no serious adverse events.

Abstract S102 Figure 1

Conclusions KGF specifically increased the production of several factors that are key for epithelial migration and wound healing including MMP-9 and IL-6, and increased the production of SP-D, a marker of type II alveolar epithelial cell proliferation. Furthermore it increases the production of BAL CRP which in the pulmonary compartment acts as an opsonin, aiding the clearance of apoptotic cells (or bacteria). However, KGF pre-treatment did not alter the inflammatory infiltrate or permeability change in response to inhaled LPS. Data suggest that KGF may promote a healing environment within the damaged alveoli and support further investigation of KGF as a treatment for lung injury.