Possible involvement of VEGF in sepsis-associated lung vascular hyperpermeability

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Acute lung injury is one of the common lethal complications in sepsis. It is clinically characterized by refractory hypoxemia, diffuse pulmonary infiltrates, and high permeability pulmonary edema. Several molecules could contribute to increased vascular permeability during sepsis. In this study, we investigated whether VEGF, originally known as a vascular permeability factor, plays a possible role in sepsis-associated lung vascular hyperpermeability. Initially, we examined time-dependent expression of VEGF and its receptors, Flt1 and KDR, in human pulmonary endothelial cells (HPMEC-ST1.6R) when stimulated with LPS + INFγ. Following stimulation, VEGF expression was significantly increased, but Flt1 and KDR remained unchanged. VEGF release by HPMEC-ST1.6R after stimulation was significantly increased, and it was suppressed by JNK, MEK, and p38 MAPK inhibitors. Next, when experimental mouse models of sepsis were used, septic conditions resulted in enhanced lung vascular permeability, as assessed by IgM concentrations in bronchoalveolar lavage fluid, and led to a significant increase in blood VEGF concentrations. Bevacizumab, an anti-VEGF antibody, significantly suppressed pulmonary hyperpermeability in sepsis. These results suggest that VEGF is involved as one of the factors that increase lung vascular permeability in sepsis.

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