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Title: Sphingosine 1-phosphate reduces regional alveolar
edema formation in a canine model of LPS-mediated
acute lung injury

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Purpose: High permeability pulmonary edema is a key
feature of acute lung injury (ALI), and a significant
cause of morbidity and mortality in critically ill patients.
We previously demonstrated that sphingosine
1-phosphate (S1P), a biologically active phospholipid,
enhances endothelial layer barrier function in vitro and
attenuates pulmonary vascular permeability in
LPS-injured mice. We hypothesized that S1P would
attenuate regional alveolar edema formation in a canine
model of LPS-induced ALI.

Methods: Eight male beagles (12-18 kg) were
anesthetized and mechanically ventilated (MV). LPS (2
mg/kg in 0.9 NS) was segmentally instilled
intrabronchially via fiberoptic bronchoscope in 4 control
dogs and in 4 dogs treated concomitantly with

intravenous S1P (85 µg/kg). Supportive care including MV ($V_t=17\text{cc/kg}$, $\text{PEEP}=5\text{ cm H}_2\text{O}$, $\text{FiO}_2=30\%$), fluid resuscitation, and hemodynamic monitoring was provided for 8 hours. ALI was quantified by shunt formation (Q_s/Q_t) and bronchoalveolar lavage (BAL) protein concentration. CT quantification of regional lung water/tissue content was performed in two dogs after 6 hours.

Results: All dogs remained hemodynamically stable. Q_s/Q_t increased rapidly following LPS instillation and continued to rise over time in control dogs. S1P attenuated increases in Q_s/Q_t induced by LPS ($p<0.05$ after 5h). BAL protein concentration was lower in S1P-treated dogs compared to controls at all time points. CT-derived lung water content was reduced in S1P-treated dogs compared to LPS controls (35% vs. 57% respectively) and was similar to normal canine lung historical controls (33%).

Conclusions: Intravenous S1P attenuates regional edema formation associated with LPS-induced ALI. These results suggest that vascular leak reduction by S1P may shorten the duration of MV and therefore morbidity associated with ALI in critically ill patients.

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