Inhibition of Shedding of the Endothelial Glycocalyx and Leukocyte Adhesion with Low Molecular Weight Heparin

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AIM: The endothelial cell (EC) glycocalyx, which consists of a layer of proteoglycans and glycosaminoglycans (GAGs), and adsorbed proteins form the endothelial surface layer (ESL). The ESL acts as a barrier between blood and the EC. Shedding of the ESL in response to cytokines (e.g. TNF-alpha) and chemoattractants (e.g. fMLP) exposes ligands for WBC-EC adhesion. Thus, a means of stabilizing the ESL to resist structural changes during inflammation is highly desirable.

METHODS: The infusion of low molecular weight heparin (LMWH) was explored as a means of mitigating shedding of the ESL and leukocyte adhesion during the inflammatory process using techniques of intravital microscopy. WBC-EC adhesion in response to fMLP was observed in post-capillary venules of mesentery (rat) following infusion of varied concentrations of LMWH.

RESULTS: High concentrations of LMWH (1.6 mg/kg) resulted in diminished shedding of glycans and diminished WBC adhesion in response to topical fMLP. Clustering of glycans in the ESL increased with increasing concentration of LMWH, as evidenced by increasing intensity of fluorescently labeled glycans on the EC surface.

CONCLUSIONS: These results appear to result from the ability of LMWH to scavenge heparanase secreted by activated ECs, and ligation of components of the glycocalyx. Thus, the mitigation of pro-inflammatory conditions by LMWH observed in sepsis and ischemia/reperfusion, may be due, in part, to its stabilization of the EC glycocalyx.