Protective effects of Histidine-rich glycoprotein on human vascular endothelial cells

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Severe sepsis and septic shock is leading major causes of mortality in ICU patients in the world. Pathophysiology of severe sepsis involves a highly complex response that includes the activation of many cell types where as central to this process is an alteration of endothelial cell function. Histidine-rich glycoprotein (HRG) is a 75kDa serum glycoprotein that circulates in plasma at a concentration about 1µM. It is known that HRG binds to variety of ligands and regulates multiple physiological processes. Our previous study confirmed that the supplementary therapy with HRG improved survival of CLP septic mice with strong inhibition of both attachment of neutrophils to pulmonary vasculature and activation of endothelial cells. In the present study, we examined the effects of HRG on vascular endothelial cells in vitro, especially focused on anti-coagulation mechanism. We found that HRG suppressed the expression of adhesion molecules and modulated the expression of tissue factor and maintained the expression of TFPI on human vascular endothelial cells. HRG also regulate excessive inflammation by modulating cytokine release and gene expression, which could influence the activation of cell apoptotic protein like phosphatidylserine and caspase-3. The obtained results provide an evidence for potential protective effects of HRG on vascular endothelial cells.