46. Severe microcirculatory abnormalities elicited by E. coli hemolysin in the rabbit ileum mucosa.

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Abstract
Decreased capillary flow and heterogeneity of microvascular perfusion are hallmarks of septic circulatory disturbances, and the gastrointestinal mucosa is considered to be particularly prone to such abnormalities. We investigated the impact of Escherichia coli hemolysin (HlyA), a medically relevant pore-forming bacterial toxin, on the mucosal microvasculature in a constant-flow blood-perfused rabbit ileum model. Microsensor techniques were employed to assess spatial distribution of mucosal hemoglobin oxygenation and relative mucosal hemoglobin content, as well as mucosal-arterial PCO(2) gap. Administration of low doses of HlyA (0.005 to 0.1 hemolytic units [HU]/ml) into the mesenteric artery provoked a transient vasoconstrictor response. Whereas physiological mucosal oxygenation is homogeneous, severe heterogeneity in capillary blood flow distribution appeared, paralleled by a marked increase in the mucosal-arterial PCO(2) gap. In addition, HlyA provoked a dose-dependent increase in relative hemoglobin concentration (rel Hb(conc)) values and edema formation, suggesting postcapillary vasoconstriction and capillary leakage. The observed changes occurred while fully maintaining mesenteric oxygen delivery. We conclude that low doses of HlyA may elicit severe mucosal microcirculatory disturbances in the rabbit ileum under maintenance of global hemodynamics, reminiscent ofseptic perfusion abnormalities. Pore-forming bacterial toxins may thus be considered as contributors to splanchnic mucosal damage under conditions of severe infection and sepsis.
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