Mechanisms of inducible nitric oxide synthase (iNOS) inhibition-related improvement of gut mucosal acidosis during hyperdynamic porcine endotoxemia.


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OBJECTIVE. To determine the mechanisms of improved gut mucosal acidosis associated with selective inducible nitric oxide synthase (iNOS) inhibition.

DESIGN. Prospective, controlled experimental study. SETTING. Animal research laboratory. ANIMALS. Fourteen domestic pigs. INTERVENTIONS. Anesthetized and mechanically ventilated pigs received continuous i.v. endotoxin for 24 h. A selective iNOS-inhibitor (1400W, n=8) or vehicle (control, n=6) was started at 12 h of endotoxin and infused until the end of the experiment. MEASUREMENTS AND RESULTS. Before as well as at 12 and 24 h of endotoxin, portal venous flow (ultrasound probe), intestinal oxygen (O(2)) extraction, portal venous-arterial carbon dioxide (CO(2)) content difference and ileal mucosal-arterial PCO(2) gap (fiberoptic sensor) were assessed together with video recordings of the villous microcirculation (number of perfused/unperfused villi) using orthogonal polarization spectral imaging via an ileostomy. The gut wall microvascular blood flow (units) and hemoglobin O(2) saturation ( micro Hb-O(2)) were assessed with a combined laser Doppler flow and remission spectrophotometry probe. 1400W blunted the otherwise progressive rise in the PCO(2) gap without affecting portal venous flow, regional O(2) and CO(2) exchange or the number of unperfused villi. While endotoxin markedly aggravated the heterogeneity of the microvascular blood flow and oxygenation, 1400W had no further effect.

CONCLUSIONS. Given the uninfluenced parameters of the ileal mucosal microcirculation in our model of long-term porcine endotoxemia, selective iNOS inhibition probably improved the PCO(2) gap due to a redistribution of the microvascular perfusion within the gut wall and/or an amelioration of the cellular respiration.