474835 - ANTI-INFLAMMATORY EFFECTS OF ANTIBIOTICS WITHIN THE INTESTINAL MICROCIRCULATION IN EXPERIMENTAL SEPSIS IN RATS

Christian Lehmann, MD PhD¹, Sara Whynot, MLT(ASCP)¹, Nancy McGrath, MLT², Crystal Atkinson, BSc³, Orlando Hung, MD¹, Thomas Issekutz, MD PhD³, Michael Murphy, MD¹

1. Department of Anesthesia, Dalhousie University, Halifax, NS, Canada

2. Department of Pharmacology, Dalhousie University, Halifax, NS, Canada

3. Department of Microbiology and Immunology, Dalhousie University, Halifax, NS, Canada

Introduction: Although the benefit of antibiotic therapy in severe sepsis remains unquestioned (1), little is known about the effects of these antibiotics on the inflamed microcirculation independent of their antimicrobial property. Aim of this study was to evaluate acute effects related to antibiotics administration upon the intestinal microcirculation, which may play an important role in the pathogenesis of sepsis and subsequent multi-organ failure (2,3).

Methods: The study was approved by, and carried out according to instructions of the institutional Animal Care Committee. Experimental sepsis was induced in 80 Lewis rats (n=10 per group) using the colon ascendens stent peritonitis model (4). Following 16 hours of observation time, seven frequently used antibiotics (10 mg.kg⁻¹ metronidazol [MET]; 20 mg.kg⁻¹ imipenem/cilastatin [IMI]; 25 mg.kg⁻¹ tobramycin [TOB]; 70 mg.kg⁻¹ vancomycin [VAN]; 5 mg.kg⁻¹ erythromycin [ERY]; 25 mg.kg⁻¹ linezolid [LIN]; mg.kg⁻¹ tigecyclin [TIG]) were then administered as single i.v. bolus. Intestinal functional capillary density and leukocyte-endothelial interactions were evaluated using intravital microscopy one hour following antibiotic treatment. Control experiments with the same antibiotics were performed in 80 animals following two hours of endotoxemia.

Results: Acute IMI or TOB administration, respectively, did not affect the intestinal microcirculation. VAN treatment aggravated leukocyte rolling behavior during experimental sepsis. MET, ERY, LIN and TIG administration significantly reduced leukocyte activation and improved functional capillary density within the intestinal microcirculation both in experimental sepsis and endotoxemia.

Discussion: The data suggest that some of the study antibiotics exert anti-inflammatory effects in addition to their antibacterial action. In conjunction with microbial sensitivity tests, potential beneficial effects of the antibiotics within the intestinal microcirculation should play a role in selecting the appropriate antibiotic therapy for patients with sepsis.

References: (1) Nobre V et al.: Curr Opin Crit Care 2007; 13:586-91 (2) Suliburk J et al.: Eur Surg Res 2007; 40:184-18 (3) Clark JA et al.: Shock 2007; 2 8:384-93 (4) Lustig MK et al.: Shock 2007; 28:59-64