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SUMMARY OF THESIS*

SPICHLER, Anne Stambovsky - **Leptospirose letal aguda em hamster: caracterização de perfis bioquímicos, histopatológicos e celulares renais, relacionada a ensaios terapêuticos.** São Paulo, 2007. (Tese de Doutoramento - Faculdade de Medicina da Universidade de São Paulo).

REVERSAL OF RENAL TUBULE TRANSPORTER DOWN-REGULATION DURING SEVERE LEPTOSPIROSIS WITH ANTIMICROBIAL THERAPY

Leptospirosis is a zoonosis of worldwide distribution. About 5-10% of all human infections presents with severe forms. Weil's syndrome, the most common presentation of severe forms of leptospirosis, may courses either as a single monophasic disease or as a disease with prolonged course, characterized by a combination of hemorrhage, particularly in the lung, renal failure, and jaundice, with fatality rates ranging from 5 to 15%. The kidney is an important target organ in leptospiral infection. Clinically, renal involvement in leptospirosis occurs in 16% to 40% of cases and is unique because of the atypical presentation of polyuria, hypokalemia, and sodium wasting, suggestive of a special form of tubular dysfunction related to the major renal sodium transporters expressed along the nephron. A wide range of antimicrobial therapy for leptospirosis was described and benefits have been disputed for cases with more than four days of clinical disease, because after a threshold of leptospiremia, the delayed use of antibiotics is unlikely to reduce fatality. Antimicrobial therapy is thought to interfere on fatality, renal involvement, and renal sodium transporters expression during severe disease. The pathogenesis may be related to direct effects of leptospiral compounds or inflammatory response due to oxidative stress. Antioxidant could be considered for adjunctive therapy. We evaluated the expression of proximal tubule type 3 Na^+/H^+ exchanger (NHE3) and thick ascending limb Na^+-K^+-$2Cl^-$ cotransporter (NKCC2) in infected non treated and treated hamsters reproducing the two forms of clinical human presentations of Weil' s syndrome divided in two experiments. Animals were treated or not with ampicillin and/or N-acetyl-cysteine (NAC). Leptospiral antigen/s and expression of renal transporters were evaluated by immunohistochemistry, and serum thiobarbituric acid (TBARS) was quantified. Infected hamsters had high amounts of detectable leptospiral antigen/s in target tissues while renal expression of NHE3 and NKCC2 decreased. Ampicillin treatment was associated with minimal or no detection of leptospiral antigens, normal expression of NHE3 and NKCC2 transporters, and reduced levels of TBARS. Early and late ampicillin treatment rescued tubular defects in leptospirosis severe disease in both experiments, and there was no evidence of benefit from antioxidant therapy.

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