The antiprotozoal drug pentamidine ameliorates experimentally-induced acute colitis in mice

E. Capoccia^, C. Cirillo°, R. Cuomo°, L. Steardo^ and G. Esposito^

^Department of Human Physiology and Pharmacology 'V.Erspamer' 00185 Faculty of Pharmacy and medicine, University of Rome La Sapienza P.le A.Moro 5, Rome (Italy)
°Department of Clinical and Experimental Medicine, Faculty of Medicine II Policlinico, University of Naples Federico II, Via Pansini 5 Naples (Italy)

ABSTRACT

Background: Intestinal inflammation is partly driven by enteroglial-derived S100B protein. The antiprotozoal drug pentamidine directly blocks S100B activity. We aimed to investigate the effect of pentamidine on intestinal inflammation using an animal model of dextran sodium sulphate (DSS)-induced acute colitis.

Methods: Mice were divided into: control group, colitis group (4% DSS for 4 days) and 2 pentamidine-treated colitis groups (0.8 mg/kg and 4 mg/kg). Anti-inflammatory effect of pentamidine was assessed in colonic tissue by evaluating the Disease Activity Index and the severity of histological changes. Colonic tissue were also used to evaluate cycloxigenase-2, inducible nitric oxide synthase, S100B, glial fibrillary acidic protein, phospho-p38 MAPkinase, p50, p65 protein expression, malondyaldheyde production, mieloperoxidase activity, and macrophage infiltration. Nitric oxide, prostaglandin E2, interleukin 1-beta, tumor necrosis factoralpha, and S100B levels were detected in plasma samples. Parallel measurements were performed *in vitro* on dissected mucosa and longitudinal muscle myenteric plexus (LMMP) preparations after challenge with LPS+DSS or exogenous S100B protein in the presence or absence of pentamidine.

Results: Pentamidine treatment significantly ameliorated the severity of acute colitis in mice, as showed by macroscopic evaluation and histological/biochemical assays in colonic tissues and in plasma. Pentamidine effect on inflammatory mediators was almost completely abrogated in dissected mucosa but not in LMMP.

Conclusions: Pentamidine exerts a marked anti-inflammatory effect in a mice model of acute colitis, likely targeting S100B activity. Pentamidine might be an innovative molecule to broaden pharmacological tools against colitis.