Adenosine A2a receptor agonist as a rational treatment for colitis

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Inflammatory bowel diseases (IBDs) are characterized by an overexpression of proinflammatory mediators, leukocyte infiltration and apoptosis. Adenosine by activation of A2A receptor modulate the release of proinflammatory cytokines, such as TNF-α and IL-1β. Therefore, aim of this study was to investigate the effects of PDRN an A2A receptor agonist, in experimental colitis induced with either dinitrobenzenesulfonic acid (DNBS), or dextrane sulphate sodium (DSS). In the DNBS model colitis was induced in 21 rats by a single intra-colonic instillation of DNBS (25mg in 0.8ml 50% ethanol), after 6hrs animals were randomized to receive i.p. either PDRN (8mg/kg), or the A2a receptor antagonist DMPX (10mg/kg), or a combination of both, or vehicle. Animals in the Sham (n=7) or in the DNBS-vehicle (n=7) group received 0.8ml of saline or 50% ethanol, respectively, in a single intra-colonic instillation. In DSS model colitis was induced in 21 animals by the administration of 8% dextran sulfate sodium dissolved in drinking water. After 24hrs animals were randomized to the same above reported treatments. Sham animals (n=7) received standard drinking water. Animals were sacrificed 7 days in the DNBS model and 5 days in the DSS model, after colitis induction, respectively. Colon and blood samples were collected for analysis. PDRN improved weight loss, macroscopic and microscopic damage, and apoptosis. Moreover, reduced IL-1β and TNF-α serum levels, colonic myeloperoxydase activity and malondialdheyde levels. Our research demonstrated a protective effect of PDRN in IBD, suggesting that this agonist of A2A receptor may represent a future treatment for inflammatory bowel diseases.