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## Role of Dopamine and D2 Dopamine Receptor in the Pathogenesis of Inflammatory Bowel Disease.

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### Abstract

#### BACKGROUND:

VEGF-induced vascular permeability and blood vessels remodeling are key features of inflammatory bowel disease (IBD) pathogenesis. Dopamine through D2 receptor (D2R) inhibits VEGF/VPF-mediated vascular permeability and angiogenesis in tumor models. In this study, we tested the hypothesis that pathogenesis of IBD is characterized by the disturbance of dopaminergic system and D2R activity.

#### METHODS:

IL-10 knockout (KO) mice and rats with iodoacetamide-induced ulcerative colitis (UC) were treated intragastrically with D2R agonists quinpirole (1 mg/100 g) or cabergoline (1 or 5 µg/100 g). Macroscopic, histologic, and clinical features of IBD, colonic vascular permeability, and angiogenesis were examined.

#### RESULTS:

Although colonic D2R protein increased, levels of tyrosine hydroxylase and dopamine transporter DAT decreased in both models of IBD. Treatment with quinpirole decreased the size of colonic lesions in rats with iodoacetamide-induced UC ( $p < 0.01$ ) and reduced colon wet weight in IL-10 KO mice ( $p < 0.05$ ). Quinpirole decreased colonic vascular permeability ( $p < 0.001$ ) via downregulation of c-Src and Akt phosphorylation. Cabergoline (5 µg/100 g) reduced vascular permeability but did not affect angiogenesis and improved signs of iodoacetamide-induced UC in rats ( $p < 0.05$ ).

#### CONCLUSIONS:

Treatment with D2R agonists decreased the severity of UC in two animal models, in part, by attenuation of enhanced vascular permeability and prevention of excessive vascular leakage. Hence, the impairment dopaminergic system seems to be a feature of IBD pathogenesis.

#### KEYWORDS:

Animal models; D2 dopamine receptor; Dopamine; Inflammatory bowel disease; Vascular permeability

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