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Original Article

Anti-inflammatory effects of alosetron mediated through 5-HT_3 receptors on experimental colitis

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Abstract

Development of new medicine with fewer deleterious effects and more efficacies for treatment of inflammatory bowel disease is needed. 5-Hydroxytryptamine 3 receptor (5-HT_3R) antagonists have exhibited analgesic and anti-inflammatory features *in vitro* and *in vivo*. The present study was designed to evaluate the anti-inflammatory effect of alosetron, a 5-HT_3R antagonist, on trinitrobenzenesulfonic acid (TNBS)-induced ulcerative colitis in rats. Two h subsequent to induce colitis (intracolonic instillation of TNBS, 50 mg/kg) in male Wistar rats, alosetron (1 mg/kg), dexamethasone (1 mg/kg), meta-chlorophenylbiguanide (mCPBG, a 5-HT_3R agonist, 5 mg/kg), or alosetron + mCPBG were administrated intraperitoneally for 6 days. Animals were thereafter sacrificed and the efficacy of drugs was evaluated macroscopically, histologically, and biochemically (myeloperoxidase, tumor necrosis factor-alpha, interleukin-6, and interleukin-1 beta) on distal colon samples. Treatment with alosetron and dexamethasone improved macroscopic and microscopic colonic damages significantly and decreased myeloperoxidase activity and colonic levels of inflammatory cytokines. The profitable effects of alosetron were antagonized by concurrent administration of mCPBG. Our data provided evidence that the protective effects of alosetron on TNBS-induced colitis can be mediated by 5-HT3R.

Keywords: Alosetron; Inflammatory bowel disease; Colitis; 5-HT3 receptor; TNBS.

INTRODUCTION

Inflammatory bowel disease (IBD), comprising ulcerative colitis (UC) and Crohn's disease, is a chronic relapsing intestinal disorder that influence the patients' quality of life (1). In spite of the fact that immunologic mechanisms are said to serve a crucial role in IBD pathogenesis, the etiology is not well undrestood (2). Many investigations have illustrated that the pathogenesis of IBD is multifactorial. In fact, genetic, immune, and environmental factors have important roles in IBD pathogenesis (1,2,3). Massive cellular infiltration and immune system abnormalities involving heightened number of $CD4^+$ T lymphocytes, mast cells, neutrophils, and eosinophils are observed in IBD (3).

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