Alteration of visceral sensitivity after induction of colitis in rats: focus on the role of tryptophan in the development of abdominal pain

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The management of abdominal visceral pain is a major problem in patients with inflammatory bowel diseases (IBDs), particularly because it can persist during the remission phase (Giamberardino, 2009). Despite the high prevalence, pharmacological treatments for visceral pain are still limited and ineffective, since suitable animal models to investigate the aetiopathogenesis and mechanisms of this disorder are lacking (Verma-Gandhu, 2007). Colorectal distension (CRD) is a widely accepted method for assessing visceral sensitivity in both clinical and pre-clinical studies (O'Mahony, 2012). Among the various factors putatively involved in the development of visceral pain, acute tryptophan depletion in patients, leading to a decrease in endogenous serotonin levels, has been shown to affect visceral perception (Kilkens et al., 2004). This evidence, in addition to the anti-inflammatory effect of tryptophan on digestive mucosa during colitis (Hashimoto et al., 2012), supports the rationale of modulating the plasma levels of this essential amino acid to control the development of visceral pain in chronic intestinal inflammation. The aims of the present study were: 1) to assess the intensity and duration of visceral hypersensitivity in the animal model of colitis induced by colonic instillation of dinitrobenzene sulfonic acid (DNBS); 2) to evaluate the effect of tryptophan supplementation on the development of visceral sensitivity alteration during colitis. For these purposes, we induced chronic visceral hypersensitivity in rats through the intra-colonic instillation of two different doses of DNBS (15-30 mg, respectively in 0.25 ml EtOH 50%). Visceral pain was assessed by measuring the abdominal Visceral Motor Reflex (VMR) in response to CRD 3, 7, 14 e 21 days after DNBS administration. VMR was quantified by measuring the electromyographic signals generated from oblique abdominal muscle contractions. The histological evaluation of bowel endothelium was consequently performed. The lowest dose of DNBS caused a significant increase in the VMR in response to CRD, but the effect duration was very limited. By contrast, at the highest dose, DNBS induced a significant increase in visceral sensitivity, which lasted until the 14th day after intra-colonic instillation. The animals were administrated with tryptophan twice daily (50 mg kg-1 s.c.), starting three days before DNBS (30 mg) colonic instillation and continuing this treatment for 7 days after colitis induction. In the animals treated with tryptophan, the development of visceral pain was assessed on day 8 after DNBS-induced colitis, since a peak of pain had been observed at this time. The supplementation of tryptophan partially prevented the increase in VMR associated with intra-colonic DNBS instillation.

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