Palmitoylethanolamide ameliorates development of colitis caused by injection of dinitrobenzene sulfonic acid (DNBS) in mice

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The inflammatory bowel diseases (IBDs) has a worldwide distribution, but its pathogenesis is not clearly understood. A major advance in the study of IBD has been the discovery and subsequent analysis of a number of models of mucosal inflammation that resemble IBD. Dinitrobenzene sulfonic acid (DNBS)—induced colitis in experimental animals has proven to be a useful model of IBD, as it possesses many of the cell and humoral immunity characteristics found in human IBD (Esposito *et al.*, 2010).

N-palmitoylethanolamine (PEA) is an endogenous fatty acid amide belonging to the family of the N-acylethanolamines (NAEs). Recently, several studies demonstrated that PEA is an important analgesic, anti-inflammatory and neuroprotective mediator, acting at several molecular targets in both central and sensory nervous systems as well as immune cells (Esposito *et al.*, 2013). PEA has been proposed to act as a protective endogenous mediator produced during inflammatory conditions to counteract inflammation, neuronal damage and pain. In fact, several studies demonstrate that the tissue concentrations of PEA are altered during different pathological conditions (Re *et al.*, 2007). For its chemical stability, it can be also administered exogenously as the active principle of current anti-inflammatory and analgesic preparations (Balvers *et al.*, 2013).

The aim of the present study was to examine the effects of PEA in mice subjected to experimental colitis. Colitis was induced in mice by intracolonic instillation of DNBS and PEA was administered daily i.p, (10 mg/kg, 10% ethanol). Four days after DNBS administration, colon nuclear factor NF- kB and MAP kinases (p-ERK) expression was increased as well as cytokines TNF-a and IL-1b production. Neutrophil infiltration, by myeloperoxidase (MPO) activity, in the mucosa was associated with up-regulation of adhesion molecules such as ICAM-1 and P-selectin. Immunohistochemistry for inducible nitric oxide synthase (iNOS), nitrotyrosine and poly (ADP-ribose) polymerase (PARP) showed an intense staining in the inflamed colon. Treatment with PEA significantly reduced the appearance of diarrhea and body weight loss. This was associated with a significant reduction in colonic MPO activity. PEA also reduced nuclear translocation of NF-kB and p-ERK activation, the pro-inflammatory cytokines release, the expression of iNOS, nitrotyrosine and PARP in the colon and reduced the up-regulation of ICAM-1 and P-selectin. In addition, PEA treatment reduced apoptosis (Bax and Bcl-2 expression) in the inflamed colon. Thus, the results of this study suggested that administration of PEA may be beneficial for treatment of several inflammatory diseases such as inflammatory bowel disease.

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