Butyrate inhibits NF-kappaB activation in lamina propria macrophages of patients with ulcerative colitis.

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BACKGROUND: In ulcerative colitis (UC) the activation (i.e. nuclear translocation) of nuclear factor kappa B (NF-kappaB) is an important step in the regulation of cytokines secreted by lamina propria macrophages. Clinical trials suggest anti-inflammatory effects of locally administered butyrate in UC. The potential effects of butyrate on NF-kappaB activation in lamina propria macrophages of UC patients were investigated. METHODS: Eleven patients with distal UC were treated for up to 8 weeks with butyrate at 100 mM (n = 6) or placebo (n = 5) enemas. At entry and after 4 and 8 weeks, clinical status was noted and intestinal inflammation was graded endoscopically and histologically. Double-staining with antibodies against NF-kappaB (p65) and CD68 was employed to detect NF-kappaB and macrophages, respectively. RESULTS: In untreated patients, nuclear translocation of NF-kappaB was detectable in virtually all macrophages. Butyrate treatment for 4 and 8 weeks resulted in a significant reduction in the number of macrophages being positive for nuclear translocated NF-kappaB. In addition, butyrate significantly reduced both the number of neutrophils in crypt and surface epithelia and of the lamina propria lymphocytes/plasma cells. These findings correlated with a significant decrease in the Disease Activity Index (DAI). CONCLUSIONS: The decrease in DAI and mucosal inflammation in butyrate-treated patients is associated with a reduction of NF-kappaB translocation in lamina propria macrophages. Since the inflammatory process in UC is mainly sustained by macrophage-derived cytokines, the known anti-inflammatory effects of butyrate may in part be mediated by an inhibition of NF-kappaB activation in these macrophages.