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Original Article

Evaluation of the anti-inflammatory and antioxidant effects of the sucralfate in diversion colitis☆

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ABSTRACT

Sucralfate enemas present good results in the treatment of colitis, however the mechanism of action of the drug is not yet fully clarified.

Objective: To evaluate the anti-inflammatory and antioxidant effects of sucralfate enemas in diversion colitis model.

Method: Thirty-six Wistar rats underwent intestinal bypass by end colostomy in the descending colon and distal mucous fistula. The animals were divided into 3 experimental groups according to the daily dose of enemas received containing 0.9% SF, sucralfate enemas or sucralfate enemas 1 g/kg/day or 2 g/kg/day. Each group was divided into two subgroups according to euthanasia to be performed 2–4 weeks after derivation. The tissue grade of inflammation was assessed histologically, and neutrophil infiltration by the tissue expression of myeloperoxidase (MPO) identified by immunohistochemistry and quantified by computerized morphometry. Oxidative stress was measured by tissue levels of malondialdehyde (MDA). To compare the results the Student's t test variance was used, and also the variance by ANOVA test, establishing a level of significance of 5% ($p < 0.05$) for both.

Results: The intervention with sucralfate enemas showed improvement in the intensity of tissue inflammation related to the concentration used and the duration of the intervention. Intervention with sucralfate enemas reduced the tissue levels of MPO, independent of concentration or time of intervention ($p < 0.01$). There was a reduction of MDA levels in animals irrigated with sucralfate enemas, independent of concentration or duration of the intervention ($p < 0.01$).

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Conclusion: Enemas with sucralfate enemas reduce inflammation, neutrophil infiltration and oxidative stress in the excluded colon suggesting topical application of the substance to be a valid therapeutic option for the treatment of diversion colitis.

Avaliação dos efeitos anti-inflamatório e antioxidante do sucralfato na colite de exclusão

Palavras-chave:
Sucralfato
Mieloperoxidase
Malondialdeído
Peroxidação dos lípidos
Estresse Oxidativo
Ácidos graxos de cadeia curta (AGCC)
Ratos

RESUMEN

A aplicação de clisteres com sucralfato (SCF) apresenta bons resultados no tratamento de colites, entretanto seu mecanismo de ação ainda não encontra-se esclarecido.

Objetivo: Avaliar os efeitos anti-inflamatórios e antioxidantes do SCF em modelo de colite de exclusão.

Método: Trinta e seis ratos, foram submetidos a derivação intestinal por colostomia terminal no cólon descendente e fistula mucosa distal. Os animais foram divididos em 3 grupos experimentais segundo receberem clisteres diários com SF 0,9%, SCF 1 g/kg/dia ou SCF 2 g/kg/dia. Cada grupo foi dividido em dois subgrupos segundo a eutanásia ser realizada após 2 ou 4 semanas da derivação. O grau de inflamação tecidual foi avaliado por estudo histológico e a infiltração neutrofílica pela expressão tecidual de mieloperoxidase (MPO) identificada por imunoistoquímica e quantificada por morfometria computadorizada. O estresse oxidativo foi mensurado pelo conteúdo de malondialdeído (MDA). Para análise dos resultados utilizou-se os teste t de Student, e ANOVA, estabelecendo-se para todos os testes nível de significância de 5% ($p < 0,05$).

Resultados: A intervenção com SCF melhorou o grau de inflamação tecidual relacionando-se a concentração utilizada e ao tempo de intervenção. A intervenção com SCF reduziu os níveis teciduais de MPO, independente da concentração ou do tempo de intervenção ($p < 0,01$). Houve redução dos níveis de MDA nos animais irrigados com SCF, independente da concentração ou tempo de intervenção ($p < 0,01$).

Conclusão: Enemas com SCF reduzem o processo inflamatório, infiltrado neutrofílico e estresse oxidativo no cólon excluso sugerindo que a substância possa se tornar uma opção terapêutica válida para o tratamento da colite de exclusão.

Introduction

Sucralfate (SCF) is formed by the association between sucrose octosulphate and polyaluminum hydroxide.[1] For more than three decades SCF has been used as a cytoprotective agent for treatment of gastrointestinal ulcer diseases.[2] Studies have shown that the therapeutic effects of SCF appear to be related to its ability to adhere to erosions and ulcerations in gastrointestinal mucosa, forming a difficult-to-remove mechanical barrier.[2] However, it was demonstrated later that SCF also presents other mechanisms of action.[3,4] This drug stimulates the secretion of prostaglandin E2 (PGE2), thus increasing the production and secretion of mucus by goblet cells of the gastrointestinal epithelium.[2] SCF enhances the production of epidermal growth factor (EGF), which induces cell division and promotes tissue reepithelialization.[3] SCF has antimicrobial activity, acting against the pathogenic bacterial flora present in the colonic lumen.[3] It has been shown also that the SCF molecule has remarkable antioxidant activity, reducing the production and removing oxygen free radicals (OFR) present in inflamed tissues.[4] This antioxidant action protects the epithelial cells of gastrointestinal mucosa against peroxidation of phospholipids, the main constituents of cytoplasmic membranes, thus reducing apoptosis.[3–5] All of these properties have led several authors to use SCF for treatment of colorectal inflammatory diseases.[2,6–11] The results of these studies confirm that the use of SCF enemas was effective in healing ulcers of rectal mucosa, as those found, for example, in actinic rectitis, ulcerative colitis, solitary ulcer of the rectum and, more recently, diversion colitis (DC).[2,6–11]

DC is an inflammatory bowel disease (IBD) that has its onset in colon segments excluded from intestinal transit.[12] It has been shown that epithelial cells of transit-excluded segments, devoid of their primary energy supply, represented by short-chain fatty acids (SCFA), undergo changes in their respiratory metabolism – increasing, as a result, the formation of OFR.[13,14] The resulting oxidative stress causes breakdown of those various defense systems that form the epithelial protective barrier.[15–17] The rupture of these defense mechanisms enables the invasion of sterile layers of the intestinal wall by bacteria from bowel lumen, triggering the inflammatory