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ORIGINAL ARTICLE

Effects of soluble fiber on matrix metalloproteinase-2 activity and healing of colon anastomosis in rats given radiotherapy

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Summary
Background and aims: Soluble fiber is fermented by colonic microflora yielding short-chain fatty acids (SCFAs) in the colon. We aimed to investigate the effect of oral administration of soluble fiber on healing of anastomosis and matrix metalloproteinase-2 activity in radiotherapy received colonic anastomosis.
Method: Eighty-four Wistar rats were divided into six groups. All rats were performed a left colonic resection with end-to-end anastomosis. Group I received rat cow. Group II received soluble fiber orally for five consecutive days preoperatively as well as 3rd and 6th days postoperatively. Group III received SCFAs via rectum for five consecutive days preoperatively. Group IV received irradiation to the pelvis at a total dose of 24 Gy on the 10th and 5th days before the operation. Group V was exposed to irradiation like the rats in Group IV and oral treatment like the rats in Group II. Group VI received irradiation like the rats in Group IV and transrectal treatment like the rats in Group III. On the 3rd and 7th postoperative days, all the rats were anesthetized to evaluate the anastomosis healing clinically, histologically and biochemically.
Results: Third and 7th day bursting pressures of the rats that were fed with a normal diet and exposed to radiotherapy were significantly decreased ($P<0.001$). Bursting pressures of Groups V and VI on the 7th day were significantly higher than the control group's bursting pressures ($P<0.05$). Hydroxyproline levels of Group IV were significantly decreased ($P<0.001$). Following oral soluble fiber and transrectal

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administration of SCFAs, these low levels reached to the levels of control radiotherapy group. Matrix metalloproteinase-2 activity of all the rats that were exposed to radiotherapy was higher than the control group ($P<0.001$). Matrix metalloproteinase-2 enzyme levels in the Groups V and VI were lower than the ones in the Group IV ($P<0.001$). The histologic parameters of anastomotic healing such as epithelial regeneration, exudate, necrosis, and fibroblast levels were significantly improved by the use of oral soluble fiber and transrectal SCFAs treatment.
Conclusion: Undesirable effects of preoperative radiotherapy on mechanical, histological and biochemical parameters can be overcome by oral soluble fiber. Oral soluble fiber administration has similar positive effects like the transrectal administration of the SCFA's.

Introduction

Neoadjuvant radiotherapy has been widely accepted and frequently used in the treatment of rectal cancer recently. This approach is associated with a significant decrease in local recurrence rate.[1–3] Results from the Dutch Colorectal Group[4] have revealed that complications related to the radiotherapy included intraoperative bleeding possibly induced by hyperemia and increased vascularity and secondly, adverse effects of radiation on wound healing and local infection. The adverse effect on wound healing is reflected by excessive deposition of scar tissue in the anastomotic region leading to the sequential development of stricture. An increasing infective complication rate, including perineal sepsis, has also been observed following the preoperative radiotherapy in colorectal cancer patients.[5,6]

For colonic healing, an organized and complex cascade of cellular and biochemical events have to take place, including degradation of extracellular matrix (ECM). Collagen is the most abundant ECM protein and it has been shown that the content and the ratio of collagen type I and III basically determine the tensile strength and mechanical stability of the connective tissue and scar tissue.[7,8] The matrix metalloproteinases (MMPs) constitute a family of enzymes that are structurally related to neutral proteinases. MMPs can degrade essentially all ECM components and play an important role in wound healing and remodeling of the ECM.[9,10]

Fiber is an important nutritional component of the diet. Dietary fiber is a mixture of fibrous and/or viscous undigested plant cell wall which is a non-starch polysaccharide. Despite resistance to digestion by mammalian enzymes, many dietary fibers (i.e., pectin, guar gum) are metabolized to short-chain fatty acids (SCFAs) by gut anaerobic bacteria in the intestinal lumen.[11,12] Guar gum is a water-soluble polysaccaride found in the seed guar, a plant indigenous to India, Pakistan and the United States. Because guar gum is extremely viscous, it is very difficult to incorporate it in food in large enough quantities to obtain a physiological effect, so a partially hydrolyzed guar gum (PHGG) is used in beverage form.[12] PHGG is produced by controlled partial enzymatic hydrolysis of guar gum. SCFA's are formed by the metabolization of PHGG in the colon. Metabolizable fiber and SCFAs enhance adaptation and healing after intestinal resection.[13–15] It has recently been proved that SCFAs are beneficial in experimental colon anastomosis healing.[15,16] In the study of Terzi et al.,[16] rectal administration of SCFAs after radiotherapy has been shown to have a positive effect on the healing of anastomosis in rats undergoing left colon anastomosis. However, oral administration of soluble fiber has not been investigated in colon anastomosis after radiotherapy. In clinical application; transrectal drug administration may not always be tolerated by the patients and also this method has technical difficulties. Oral soluble fiber can be taken in both the preoperative and postoperative periods as well. Besides, enteral administration of soluble fiber is more physiologic and less harmful.

The aim of this study is to investigate the effects of oral soluble fiber on the healing of colon anastomosis in rats following radiotherapy and to compare the effects over MMP-2 activity between oral and transrectal administration.

Material and method

Animals

In this experimental study, we used 84 Wistar albino rats (Medical Research Laboratory, Gazi University) with a median weight of 274 (260–327) g. All