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Fiber enriched diets and radiation induced injury of the gut

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Abstract

The aim of this study was to evaluate the effect of fiber-enriched defined formula diets (DFDs) on radiation-induced enteropathy. Forty-five male Sprague-Dawley rats were assigned randomly after abdominal irradiation to one of three groups (15 in each group): a fiber-free DFD group, a non-soluble fiber-enriched DFD group, and a soluble fiber-enriched DFD group. They kept their diets respectively for seven days. On day eight, the mesenteric lymph nodes were harvested for bacterial translocation, and segments of jejenum and colon were sampled for microscopic examination. The rats in the fiber-enriched DFD groups lost significantly less body weight than the rats in the fiber-free DFD group. The intestinal structure was the worst in the fiber-free DFD group, intermediate in the soluble fiber-enriched DFD group, and the best in the non-soluble fiber-enriched DFD group with significantly higher measures of villous height and jejunal mucosal thickness. These findings suggest that fiber-enriched DFD may effectively protect intestinal structure against radiation-induced damage by improving mucosal integrity. © 2003 Elsevier Science Inc. All rights reserved.

Keywords: Fiber; Radiation; Bacterial translocation; Enteral feeding

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1. Introduction

Radiation therapy has been one of the major factors that might damage intestinal barrier function. The loss of viable regenerating cells of the intestinal epithelium that is the direct effect of intestinal radiation alters the mechanical barrier function [1]. As a result, disruption of the intestinal microflora resulting in bacterial overgrowth and breakdown in peristaltic clearance might result in bacterial translocation [2–5].

Dietary fiber plays a key role in enteral nutrition. The fermentation of fiber by colonic bacteria leads to production of short chain fatty acids (SCFA), which is the primary energy source of colonic mucosa [6]. Over the recent years, the role of dietary fiber in gut barrier function has been emphasized and animal experiments have provided encouraging result [7]. Although, variety of DFDs have been used to eliminate the complications of radiation, and to facilitate bacterial clearance by stimulating the immune system, little has been known about the effects of dietary fiber on radiation-induced enteropathy [4,5].

In our study, we evaluated the potential therapeutic effects of dietary fiber by using liquid formula diets containing either soluble or non-soluble fiber in a rat model of radiation-induced intestinal mucosal injury.

2. Materials and methods

The study protocol was approved by the local ethical committee. All animals received humane care in accordance with the Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH publication No. 85-23, revised 1985).

2.1. Animals and experimental design

Forty-five male Sprague-Dawley rats weighing between 180–260 g were used in the study. During the period of acclimatization to the laboratory conditions, the rats were allowed *ad libitum* intake of standard rat chow and water. At the end of the period, the rats were assigned randomly to one of three groups, with 15 rats in each group. All animals were anesthetized with intramuscular injection of ketamine (10 mg/kg) and subjected to a single dose of abdominal X radiation (cobalt-60, 1100 rad, 116.5 cGy/min, 80 source-skin distance) using a conventional radiation source while the other parts of the body were carefully shielded. Following abdominal irradiation, each group was given individual nutritional schemes including one of the three DFDs (see Table 1 for the contents of each formula). Group I was fed with Nutrodrip Standart-Novartis®, a fiber-free composition. Group II was fed with Nutrodrip Fiber-Novartis® which contained non-soluble fiber, and Group III was fed with Sando Source-Novartis® which contained soluble fiber. All animals had free access to individual DFDs and kept their diets respectively for seven days. The rats were weighed before irradiation and at the end of the post-irradiation nutrition period, respectively, and the body weight changes were recorded. On post-irradiation day 8, all animals underwent

Table 1
Composition of the formulas used in the experiments

	Nutrodrip Standart®	Nutrodrip Fiber®	Sandosource®
Protein (g/500 ml)	20.3	19	21
Lipid (g/500 ml)	17.4	17	18
Carbohydrate (g/500 ml)	70.4	68	72
Soluble fiber (g/500 ml)	—	—	10.8
Non-soluble fiber (g/500 ml)	—	7	—

laparotomy. Under parenteral anesthesia with ketamine (10 mg/kg), a midline incision was performed and mesenteric lymph node samples were immediately recovered using sterile technique. Each sample was incubated for aerobic and anaerobic culture in blood agar. Two-centimeter segments of the jejunum and colon were then resected, opened longitudinally on the paramesenteric side, washed out with saline solution, fixed in 10% buffered formaldehyde, and stained with standard Haematoxylin-Eosin and PAS (Periodic Acid Schiff). Jejunal mucosal thickness (JMT), villous height (VH) from the tip of the villous to the crypt, and colonic mucosal thickness (CMT) were measured and the number of villi per centimeter square of area (VC) was assessed using an ocular micrometer under light microscopy in a blinded fashion.

2.2. Statistical analysis

Paired sample *t*-test, one-way ANOVA and Duncan test were used for statistical analysis of the results. The difference between the groups was considered significant in case the p value was less than 0.05.

3. Results

All intestinal wall samples showed marked edema and hyperemia. No other special morphologic finding was detected in the abdominal structures of the rats. Fig. 1 shows the microscopic appearances of intestinal specimens in each of the three groups.

Group I (Fiber-free DFD): The mean body weight of this group was 224±16.4 g at the beginning of the experiment, and 182.6 ± 10.9 g at sacrifice. The rate of weight loss was 18.7%, which was the highest among all groups, and the difference was statistically significant ($p < 0.05$). The quantitative mesenteric lymph node culture results of this group indicated translocation of 130.6 ± 203.8 bacteria. The mean CMT and JMT were 609 ± 111 μm and 516 ± 113 μm, respectively, while VH was 216 ± 34 μm, and VC was 7.34 ± 1.3.

Group II (Non-soluble fiber-enriched DFD): At the end of the experiment, the mean weight of the rats decreased from 204.6 ± 9.1 g to 179.3 ± 7.0 g with a 12.2% rate of reduction. The difference was statistically significant ($p < 0.05$). Tissue culture results of mesenteric lymph nodes revealed translocation of 79.6 ± 98.4 bacteria. The mean CMT and JMT were 681 ± 176 μm, and 630 ± 126 μm, respectively, while VH was 255 ± 46 μm, and VC was 8.48 ± 1.3.

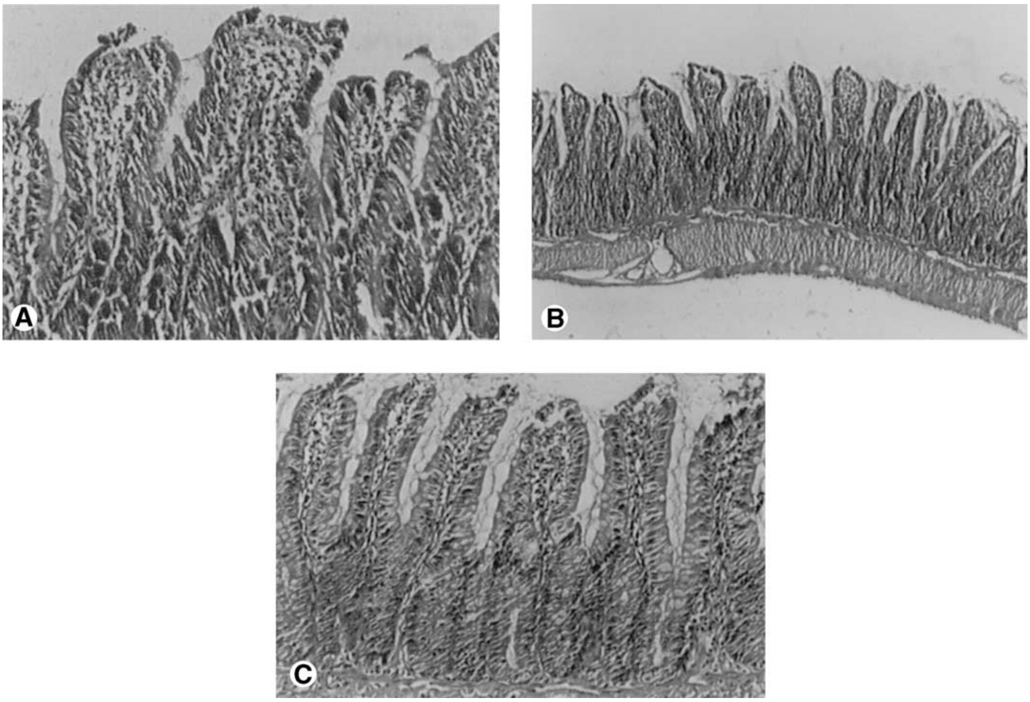

Fig. 1. The microscopic appearance of intestinal specimens from each of the groups. Fig. 1a shows shortening of the villi and a marked reduction in the total epithelial surface area in the fiber-free DFD group. A better intestinal structure was obtained in the soluble fiber-enriched DFD group (Fig. 1b). Mucosal morphometrics was the best in the non-soluble fiber-enriched DFD group with significantly higher measures of villous height and jejunal mucosal thickness (Fig. 1c).

Group III (Soluble fiber-enriched DFD): The mean weight of the rats was 214.6 ± 13.0 g at the beginning and 187.3 ± 10.3 g at the end of the experiment. The rate of weight loss was 12.6% and the difference was statistically significant ($p < 0.05$). Mesenteric lymph node cultures showed translocation of 122.8 ± 143.1 bacteria per gram tissue. The mean CMT and JMT were 717 ± 135 μm and 561 ± 115 μm, respectively, while VH was 233 ± 45 μm and VC was 7.24 ± 1.8.

VH and JMT of Group II were significantly higher than that of the other two groups ($p < 0.05$). The differences between the groups in terms of CMT and VC were not statistically significant ($p > 0.05$). There was also no statistically significant difference between groups in terms of bacterial translocation to the mesenteric lymph nodes ($p > 0.05$). The results of mucosal morphometrics and mesenteric lymph node cultures were shown in Tables 2 and 3.

4. Discussion

Radiation has been a major cause of functional impairment on various organs and systems despite the well-known therapeutic effect [2]. Even a single dose of radiation may induce the

Table 2
Mucosal morphometrics

Group	CMT (μm)	JMT (μm)	VH (μm)	VC
I	609 ± 111	516 ± 113	216 ± 34	7.34 ± 1.3
II	681 ± 176	630 ± 126*	255 ± 46*	8.48 ± 1.3
III	717 ± 135	561 ± 115	233 ± 45	7.24 ± 1.8

* Significant ($p < 0.05$) with one-way ANOVA, and Duncan tests.

CMT, colonic mucosal thickness; JMT, jejunal mucosal thickness; VH, villous height; VC, number of villi per centimeter square.

damage to all segments of the alimentary tract [3]. In the intestinal epithelium, which appears to be the most radiosensitive part of the gut, proliferation ceases and progressive cell loss occurs without renewal [8]. Several mechanisms have been described that compensated for this cell loss, such as shortening of the villi, contraction of the crypts, and flattening of mucosal cells to cover basal lamina [2]. Regarding these structural abnormalities, mucosal thickness and villous height have been shown among the most reliable indicators for radiation-induced damage [9]. This study demonstrated that fiber-enriched DFDs might protect the structures of both the small intestine and the colon against radiation-induced damage by improving mucosal morphometrics.

The viability of the gastrointestinal tract is highly dependent on the physical contact of intraluminal nutrients, such as glutamine, nucleotides, and short-chain fatty acids [10]. Although fiber is not a vital component of the diet, the importance of dietary fiber stems from the intraluminal fermentation process. Fermentation of soluble fiber by bacteria, especially in the colon leads to production of short-chain fatty acids, the main fuel for the colonic mucosa [6]. The protective and supporting effects of fiber on the intestinal mucosa have been reported in many clinical and experimental studies [11,12,13,14]. With contribution of other stress factors, which was the intestinal irradiation in the present study, the absence of dietary fiber has caused atrophy of mucosal and Goblet cells, which resulted in a deficient mucus protection layer [7]. On the other hand, some experimental studies postulated that, the atrophy of the intestinal mucosa that has been detected following total parenteral nutrition or fiber-free diet administration was mediated by the reduction of the proliferative activity of the stem cells in the mucosal glands [15,16].

The beneficial effects of commercial diets containing a known formulation of nutrients, known as DFDs, have met wide acceptance in a variety of clinical condition [17]. Specially

Table 3
Bacterial translocation and mesenteric lymph node tissue culture results*

Group	No. of animals with positive culture (percentage)	Quantitative MLN culture (bacteria/g)
I	7 (46.6)	130.6 ± 203.8
II	7 (46.6)	79.6 ± 98.4
III	6 (40)	122.8 ± 143.1

* The differences between the groups were not statistically significant.

enriched formulas have been shown to enhance immunity by providing protection against infectious agents [18]. In radiation-induced intestinal injury models, dietary manipulation with a variety of chemicals and nutrients have been used to stimulate immunity, increase clearance, support mucosal reconditioning, and protect against radiation-induced intestinal epithelial damage and bacterial translocation [4,5,19]. Although, bacterial translocation is a direct reflection of the mucosal integrity and barrier function of the intestines, this study failed to show that fiber-enriched DFDs decreased bacterial translocation in regard to fiber-free formulas. However, recent reports have suggested that bacterial translocation occurred in the early stages of radiation injury, and was not correlated with histological changes of the intestinal mucosa [3].

Diarrhea is the principal symptom of radiation-induced enteropathy and its frequency depends on the severity of malabsorption [20]. In our study, a significant weight loss was evident in all groups, which was the natural outcome of diarrhea caused by radiation-induced enteropathy. However, the fiber-enriched DFDs significantly prevented excessive weight loss in regard to fiber-free formula (12% vs. 18%, $p < 0.05$). The mechanisms by which fiber-enriched DFDs decreased weight loss might be complex. One explanation is that, the short chain fatty acids, which are produced by fermentation of fiber by bacteria, serve as the oxidative fuels for colonic mucosa, thus may improve the intestinal structure and enhance absorption capacity [21,22]. On the other hand, other mechanisms such as stimulation of intestinal mucus secretion, which is an essential component of the host defense system, and absorption and elimination of microorganisms by fecal bulk formation, may be involved [7].

In conclusion, the present study simulates the clinical circumstances of patients receiving intestinal radiation and enteral nutrition, and the results have shown that fiber-enriched DFDs significantly reduced weight loss due to radiation-induced enteropathy and provided a notable improvement in intestinal structure. The results support that, administration of fiber-enriched diets alone or in combination with other DFDs may have potential therapeutic effects in the patients with radiation-induced intestinal injury.

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