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Original Paper

The Effect of Aging on the Serum Biochemistry of Rats with a 50% Distal Small Bowel Resection.

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Abstract

The effect of resecting 50% of the distal small intestine on longevity and serum biochemistry was studied in rats. Male Sprague-Dawley rats were divided into two groups. One group underwent a 50% distal small bowel resection (SBR) and the other was kept as controls. The rats were anesthetized with ether and blood was withdrawn from the tail vein prior to the operation and 4, 12, 24, 36, 48, 60 and 72 weeks postoperatively. At 48 weeks after the operation, serum total protein and albumin levels were significantly lower in the SBR rats. Creatinine was significantly lower in the SBR rats at 4, 12, and 48 weeks after the operation when compared to normal rats. Finally, the present study showed that the life span was longer after small bowel resection, but the reasons for this finding are unclear.

Introduction

In several pathological conditions such as Crohn's syndrome and cancer, intestinal resection is the best treatment option, although it affects the rate of nutrient absorption.

If the patient survives the first few weeks after massive resection, the remaining small intestine adapts to facilitate efficient absorption and digestion. This adaptation to resection has been studied extensively in experimental animals, but only to a limited degree in humans.

Various studies have revealed that the adaptive response of the small intestine changes with aging[1)-8)]. However, there is little information on the possible mechanisms responsible for the age-related adaptive changes.

In the present study, the effect of resecting 50% of the distal small intestine on longevity and the serum biochemistry with aging were investigated in rats.

Experimental procedures and materials

1. Animals

Twenty-six male Sprague-Dawley rats were housed, two animals to a cage, in a constant temperature animal room with a 12 hour light-dark cycle. The animals were provided standard lab rat chow (Oriental Yeast Industry., Co, MF) and tap water *ad libitum* and were weighed weekly.

After fasting overnight, the rats were randomly divided into two groups. One group of 16 rats was anesthetized with an intraperitoneal injection of pentobarbital (50mg/kg Body Weight). The abdomen was opened by a midline incision, and the small intestine was carefully measured along the antimesenteric border. The small intestine was resected, leaving 50% of the jejunum distal to the pylorus and 2cm of the ileum proximal to the ileocaecal valve. The vascular arcades of the resected bowel were sequentially ligated with silk sutures. Intestinal continuity was restored by an end-to-end anastomosis with a single layer of inverted silk sutures. The abdomen was closed with layers of running silk suture. Food was withheld from all rats, although they had free access to water, for 48 hours after surgery. They were then allowed access to a 20% casein diet *ad libitum*. The other group of 10 rats was given no treatment (normal group) except for three days of fasting, which was the same treatment the short bowel resection (SBR) group received.

2. Sample collection and analytical methods

After 16 hours of fasting, rats were anesthetized with ether and blood was withdrawn from the tail vein prior to the operation (280 ± 5 g, 8 weeks after birth). Subsequently, blood was taken at 4, 12, 24, 36, 48, 60 and 72 weeks after the operation. Sera were frozen immediately and stored at −40℃ until they were assayed.

Total protein was measured by the Biuret method[9], albumin by the bromcresol green (BCG) method[10], albumin/globulin (A/G) ratio by the BCG/Biuret method[9,10], blood urea nitrogen (BUN) by the urease UV method[11], creatinine by the alkaline picric acid method[12] and glucose by the enzyme method (glucose-dehydrogenase)[13].

3. Statistical analysis

The data were expressed as means ± SEM and differences were evaluated using the Student's t-test. $p<0.05$ was considered significant.

Experimental results and Discussion

It is well known that the residual small intestinal mucosa exhibits proliferation, differentiation, growth, and hyperplasia after small bowel resection [14)-17)]. Some studies have shown that the capacity to achieve intestinal adaptation after small bowel resection decreases with aging[14),17),18)]. In the present study, the effect of resecting 50% of the distal small intestine on serum biochemistry was investigated with respect to aging.

The body weights of normal rats and SBR rats were similar (Fig. 1). The body weights of both groups increased until about 80 weeks after the operation, and then gradually decreased. The median longevity in the normal and SBR groups were 71 and 86 weeks, respectively (Fig. 2). These results suggest that SBR may potentially influence longevity, though there was no effect of SBR on body weight during the experimental period. Weindruch reported that calorie restriction is a well-established intervention for prolonging the life span[19]. In this regard, it could be considered that SBR was similar to calorie restriction because of malabsorption due to

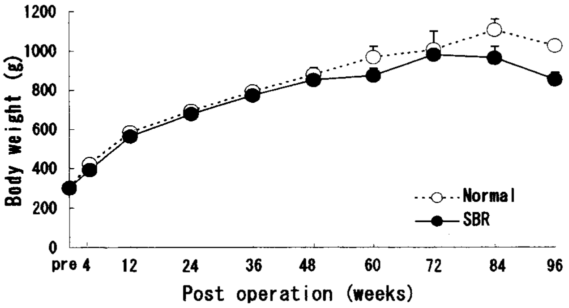

Fig. 1 Effect of 50% distal small bowel resection (SBR) on body weight. Normal group : pre, 4, 12, 24, 36 and 48 weeks, n = 10 ; 60 weeks, n = 7 ; 72 weeks, n = 5 ; 84 weeks, n = 4 ; 96 weeks, n = 2. SBR group : pre, 4, 12, 24, 36 and 48 weeks, n = 16 ; 60 weeks, n = 15 ; 72 weeks, n = 14 ; 84 weeks, n = 9 ; 96 weeks, n = 7. Values are means ± SEM.

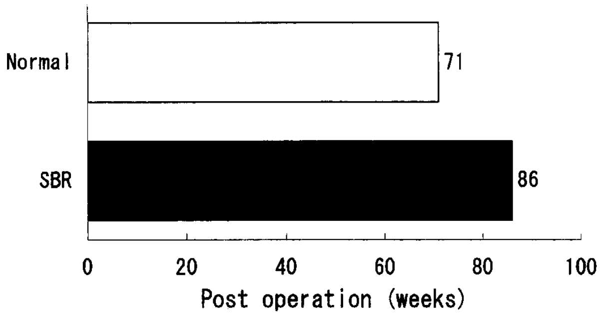

Fig. 2 Effect of 50% distal small bowel resection (SBR) on longevity. Normal group consisted of 10 animals and SBR group consisted of 16 animals.

the fact that the bowel was only half the normal length.

Forty-eight weeks after the operation total protein and albumin levels in the serum were significantly lower in the SBR rats (Fig. 3). Because, the maximum levels of total protein and albumin in the normal group were at 48 weeks after operation, and these in the SBR group were at 24 weeks after operation. It was conceived that the levels of total protein and albumin in the SBR group had already tended to decrease at 48 weeks after operation. The A/G ratio gradually de-

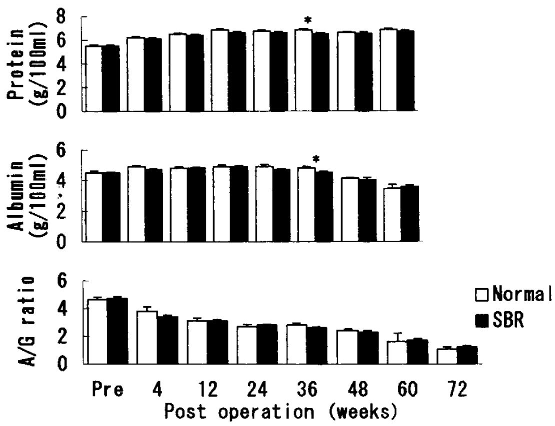

Fig. 3 Effect of 50% distal small bowel resection (SBR) on concentrations of protein, albumin and A/G ratio in the serum. Normal group : pre, 4, 12, 24, 36 and 48 weeks, n = 10 ; 60 weeks, n = 7 ; 72 weeks, n = 5. SBR group : pre, 4, 12, 24, 36 and 48 weeks, n = 16 ; 60 weeks, n = 15 ; 72 weeks, n = 14. Values are means ± SEM.
Statistical significance was evaluated by Student's t-test. *p<0.05, vs. normal.

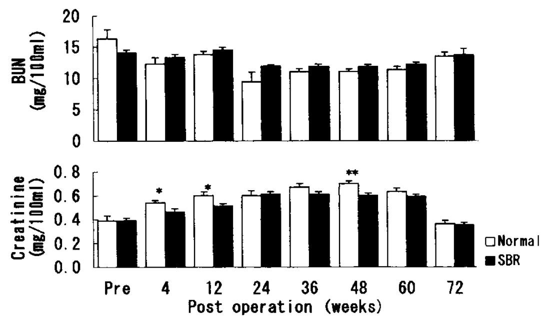

Fig. 4 Effect of 50% distal small bowel resection (SBR) on concentrations of urea nitrogen and creatinine in the blood. Normal group : pre, 4, 12, 24, 36 and 48 weeks, n = 10 ; 60 weeks, n = 7 ; 72 weeks. SBR group : pre, 4, 12, 24, 36 and 48 weeks, n = 16 ; 60 weeks, n = 15 ; 72 weeks, n = 14. Values are means ± SEM.
Statistical significance was evaluated by Student's t-test. *p<0.05, **p<0.01, vs. normal.

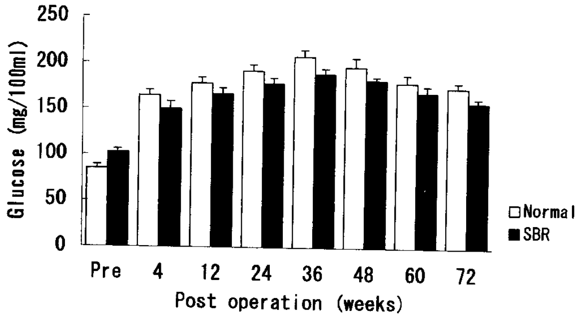

Fig. 5 Effect of 50% distal small bowel resection (SBR) on concentrations of glucose in the blood. Normal group : pre, 4, 12, 24, 36 and 48 weeks, n = 10 ; 60 weeks, n = 7 ; 72 weeks, n = 5. SBR group : pre, 4, 12, 24, 36 and 48 weeks, n = 16 ; 60 weeks, n = 15 ; 72 weeks, n = 14 ; 84 weeks, n = 9 ; 96 weeks, n = 7. Values are means ± SEM.
Statistical significance was evaluated by Student's t-test.

creased with time in both groups (Fig. 3). These results showed that 50% small bowel resection did not have an effect on these values that are used to assess the nutritional state of the animal. BUN was higher in the SBR rats (Fig. 4), but the difference was not statistically significant. Creatinine was lower in the SBR rats (Fig. 4). These results suggest that 50% small bowel resection may influence renal function. In this study, urinary creatinine was not measured. The decrease of serum creatinine may indicate that the muscle mass may have decreased in the SBR rats. Glucose increased until 36 weeks and then gradually decreased in both groups (Fig. 5). Blood glucose levels in the SBR group were lower than those of the normal group throughout the experimental period, but the difference was not significant. Various studies have showed that the adaptive response of the small intestine changes with aging[1)-8)]. Furthermore, Sakamoto reported that a decrease in ornithine decarboxylase is involved in the decreased adaptive response that occurs with aging[20)]. In this study, serum values also changed in response to aging.

In conclusion, these results showed that intestinal function was sufficient, even though 50% of the small bowel was resected. Furthermore, the SBR group rats had greater longevity. However, this finding could not be explained by the serum biochemical values in this study. In any case, further studies are required to investigate the cause of the prolonged life span after small bowel resection.

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