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Fructooligosaccharide Consumption Improves the Decreased Cortical Bone Following Gastrectomy in Rats

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Abstract: We examined the effects of fructooligosaccharide (FOS) consumption on gastrectomy-evoked osteopenia in rats. Forty-two 35-day-old male Sprague Dawley rats were equally divided into two groups and a sham operation group or a total gastrectomy group was performed. Four weeks after each surgery, 14 rats were killed in each group (BaseSH and BaseGX groups). Thereafter, the remaining rats were equally divided into two sub-groups; with or without 7.5% FOS (1.35 g/day)-feeding (SH, SH+FOS, GX and GX+FOS groups) for six weeks. Backscattered electron images of the tibial cross-sections were taken to calculate the cortical bone area (CBA). The CBA in BaseGX rats was markedly decreased. Thereafter, FOS-feeding significantly counteracted this reduction, but not to the level seen in SH rats. These results suggest that FOS consumption partially restored osteopenia in cortical bone following the gastrectomy.

Key words: fructooligosaccharide, gastrectomy, cortical bone.

The beneficial effects of fructooligosaccharide (FOS), which are indigestible carbohydrates,[1,2] on bone have been extensively examined.[3,4] FOS increases bone mineral density (BMD), mineral concentration and volume in growing intact rats.[5] On the other hand, significant bone loss has been observed experimentally and clinically after a total gastrectomy.[6~9] It has been reported that gastrectomy-evoked osteopenia occurs not only in trabecular but also in cortical bone.[10]

In previous studies FOS consumption completely prevented gastrectomy-evoked osteopenia in rats.[6,8] Therefore, FOS affects bone structure in gastrectomized rats. However, it is not yet clear whether the defective bone following a gastrectomy is improved by FOS consumption. Thus, we used this experimental model to examine the effect of FOS consumption on the cortical bone structure in gastrectomized rats.

Materials and Methods

Forty-two 35-day-old male Sprague Dawley rats (Saitama Experimental Animals Supply Co., Ltd., Saitama, Japan) were equally divided into two groups and a sham operation or total gastrectomy was performed. The initial body weight in each group was 129.0±4.2 g and 130.5±4.5 g, respectively. Four weeks after each surgery, fourteen rats were killed in each group (BaseSH and BaseGX groups). Four weeks after each surgery, the remaining rats were divided into two sub-groups (n=14); with or without 7.5% FOS-feeding (SH, SH+FOS, GX and GX+FOS groups/n=7) for six weeks. FOS consisted of 34% 1-ketose, 53% nystose and 10% 1F-b-fructofuranosyl nystose (Meioligo-P®, Meiji Seika Kaisha, Tokyo, Japan). The rats were given a synthetic diet (18 g a day) containing 0.5% calcium in individual metabolic cages for 10 weeks.

Total gastrectomy was essentially performed as described previously.[6] Briefly, the stomach and duodenum were removed, and the pyloric sides of the duodenum and jejunum were then ligated. The esophagus was anastomosed to the jejunum, end-to-side. The duodenal segment bearing the bilio-pancreatic opening was grafted to a point 10 cm distal from the esophageal

(Received December 17, 2012; Accepted for publication January 7, 2013)

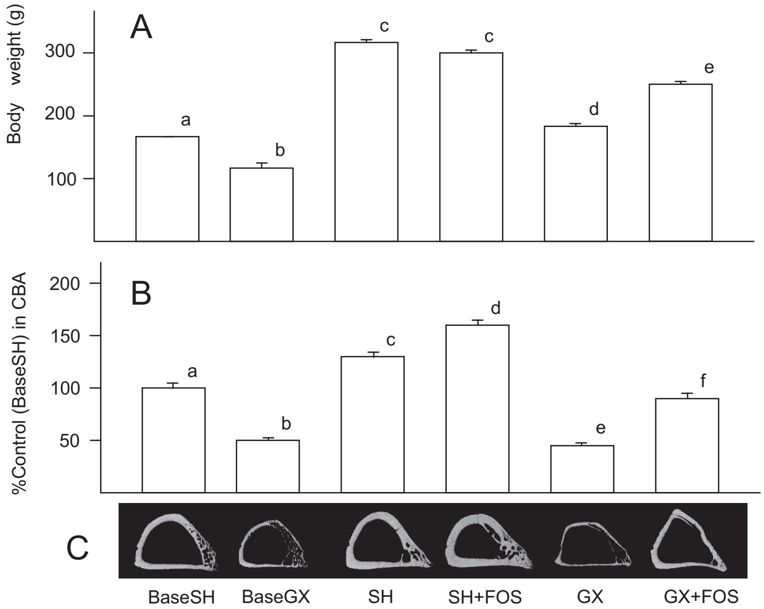

Fig. 1 Final body weight (A), percent value in CBA obtained from tibial cross-sections (B) and backscattered electron images of the cross-sectional surface in the diaphysis (C) in the BaseSH and BaseGX groups at four weeks, and rats fed a diet with (SH+FOS, GX+FOS groups) or without (SH, GX group) FOS at 10 weeks following each operation. Each value represents a mean±SEM, n=7. Means in a panel without a common letter differ, $p<0.01$.

anastomosis to avoid reflux of digestive juice into the esophagus. The abdominal cavity of SH rats was opened for approximately 50 min; i.e., the same length of time needed for the gastrectomy procedure. After each surgery, the rats were deprived of food for 24 h, and then allowed free access to pasteurized cow's milk for two days.

The base diets were prepared according to the modified AIN-93G formulation.[11)] Dietary components were purchased from Oriental Yeast Co. (Tokyo, Japan) and Wako Pure Chemical Industries, Ltd. (Tokyo, Japan). Vitamin B_{12} (0.5 mg/kg) was injected intramuscularly every other week in all of the rats. Body weight was recorded every week. This study was approved by the Animal Experiment Ethics Committee of Showa University.

Undecalcified sections of the tibia were prepared and examined. The tibia was cross-sectioned at the center of the diaphysis. Backscattered electron images of the tibial sections were taken with a scanning electron microscope (Hitachi S-2500CX, Tokyo, Japan) after coating with carbon. The cortical bone area (CBA) was calculated using an image processor and analysis software (Ultimage/Pro 2, Graftek, Mirmande, France).

Statistical analyses were performed using the SPSS statistical software package (SPSS version 6.0, SPSS, Chicago, IL, USA). A one-way ANOVA with Tukey's significant difference test was used to evaluate differences in each variable among groups ($p<0.01$). Values are expressed as the mean and standard deviation.

Results

Four weeks after surgery, body weight was significantly reduced in the BaseGX group compared to that in the BaseSH group rats. The body weight and reduction in food consumption in the GX groups were lower than those in SH groups throughout the experiment (data not shown). Food consumption in the GX group was less than 14 g a day. Supplementation with FOS partially counteracted these reductions caused by gastrectomy. Food consumption in the GX + FOS group partially recovered as a consequence of FOS-feeding (range, 16–17 g a day). Meanwhile, the body weight in the GX+FOS group was approximately 60 g greater than that in the GX group at the end of the experiment. A slight but statistically significant reduction was observed in the GX+FOS group compared with the SH group (Fig. 1A) .

In the morphometric analysis of tibial cross-sections, the CBA in the BaseGX group was markedly decreased; these values were less than half of those in the BaseSH group. On the other hand, while FOS-feeding significantly improved this reduction, the level was still lower than that in the BaseSH and SH group. The values in the GX+FOS group were between those in the BaseSH and GX group (Fig. 1B and C).

Discussion

It is well known that gastrectomy is followed by early satiety and body weight loss in most patients.[12] Body weight loss in gastrectomized rats has also been reported.[13] Meanwhile, indigestible carbohydrates such as FOS, in addition to their selective effects on microflora in the large intestine, influence many aspects of bowel function through fermentation.[14] Overall, FOS appears to enhance indices of gut health by positively altering gut microbial ecology.[15] Thus, the effects of FOS on body weight and food consumption might result from the improvement of bowel function in gastrectomized rats.

Marked cortical bone loss was observed in the BaseGX group in this study, as in our previous report.[10] FOS consumption for six weeks partially improved gastrectomy-evoked bone loss (Fig. 1). A reduction in calcium absorption and femoral bone loss in gastrectomized rats has been reported elsewhere.[6,8] In addition, FOS-feeding enhances calcium retention resulting from stimulated calcium absorption.[4] These stimulatory effects of FOS have been explained by the fermentation of FOS in the large intestine to produce short-chain fatty acids, which in turn reduce luminal pH[16] and induce the proliferation of epithelial cells.[17] Considering previous reports, calcium absorbed in the intestine by FOS-feeding is also likely to be retained in the tibia.

The CBA in the GX+FOS group increased compared to that in the GX group. However, these variables did not reach the levels of those in the BaseSH group. It has been reported that BMD is highly correlated with body weight, and weight loss is associated with reduced BMD. Energy restriction reduces body weight and results in a small reduction in tibia density.[18] In young rats, dietary restriction of calcium or energy results in an elevated rate of bone turnover. However, BMD has been shown to be lower in calcium restricted groups, and old rats have a significantly greater BMD than diet-restricted groups.[19] We used growing rats in this experiment. Thus, FOS might help improve bone structure in consequence of the elevated calcium absorption rather than body weight, as we know that gastrectomy produces calcium malabsorption in rats.[20] However, the mechanism of this improvement in osteopenia following gastrectomy at the cellular level is still unclear. Further studies are required to evaluate whether FOS might be useful for osteopenia induced by the malabsorption of calcium.

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