A Study of Symptom Evaluation after Yogurt Intake for the Remission Period of Ulcerative Colitis.

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Key words : Ulcerative Colitis, probiotics, Visual Analogue Scale

Summary

Increasing number of ulcerative colitis (UC) patients have been shown in Japan during past 50 years. The causes have been discussed as Europeans style foods and mental stress. For the improvement of UC, not only medical treatments but also functional foods are focused. Especially, patients in the remission period of UC are interested in the functional foods to prevent severe symptom and prolong the term of the remission period. To evaluate effects on the improvements in UC patients, Clinical Activity Index (CAI) is generally used. However, since CAI was developed for the symptom in relapse periods, the index does not match to those in the remission period. The purpose for this study is the establishment of suitable evaluation methods for the symptom of UC in the remission period. We performed the general analysis for intestinal regulatory function and Visual Analog Scale (VAS) analysis in an UC patient after the intake of functional foods. We evaluated the effect of yogurts as probiotics, which has reportedly been effective in the improvement of UC symptom. General analysis for the regulatory intestinal function, stool frequency, color, and shape of feces, were not changed after the yogurt intakes. Intestinal transit time of foods was decreased by the yogurt intakes. By VAS analysis, both of abdominal pain and abdominal tenderness were decreased and appetite was increased in the yogurt intake periods. It is suggested that effects of yogurt intakes on the improvement of UC symptom can be evaluated by the combination of general analysis and VAS analysis for intestinal function. Using this evaluation method for functional foods may lead to an improvement in QOL of the patients with UC in the remission period.

Introduction

Inflammatory bowl diseases (IBD) patients have increased in Japan during past 50 years. The IBD consist ulcerative colitis (UC) and Crohn's disease (CD), mainly[1]. The causes of IBD have been discussed as Europeans style foods and mental stress; however, it remained unclear whether particular risk factors can induce these diseases. Since one of serious characteristics of these IBD is the chronic symptom with relapses and remissions, patients need the long-term care for relieving symptom[2,3]. The chronic inflammations in the relapses phase can be treated with medicine, clinically. In contrast, IBD patients in the remission period have been interested in the functional foods, such as probiotics, which are recently focused on the improvement of IBD. Probiotics include live microbiota and have been used to prevent and improve acute intestine diseases, such as diarrhea and constipation.

To evaluate effects on the improvements in IBD patients, Clinical Activity Index (CAI) is generally used[1,3,4]. However, since CAI was developed for the severe cases, the index does not match to those in remission period[5]. The purpose for this study is the establishment of suitable evaluation methods for the functional foods, which is ingested by UC patients in the remission period. As functional foods, we used two kinds of yogurts, yogurt A and yogurt B. And then, we performed the general analysis for regulatory function of intestine and the Visual Analog Scale (VAS) analysis for sensible examinations in an UC patient. Effects of yogurt consumption on the improvement of UC symptom in the remission period can be evaluated by the combination of general analysis and

VAS analysis. Our methods, which were used in this study, could be simple and personalized. Using this evaluation method for the functional foods leads to an improvement in QOL of the patients with UC.

A Subject, Materials, and Methods

A subject

A subject (woman, 35 years old) with UC has attended to Yamashita Hospital (Aiti, Japan) since 20 years old. During past 15 years, the UC symptom has repeated relapses and remissions. During previous two years, the symptom showed the remission period. Medical observation and clinical treatments were not changed during this study.

Test food

We used two kinds of yogurts, yogurt A and yogurt B. Yogurt A was purchased from Meiji Co Ltd. (Tokyo, Japan) and the nutrient content per 100 g of daily intake was as follows: energy, 62 kcal; protein 3.4 g; fats, 3.0 g; carbohydrates, 5.3 g; sodium, 51 mg; and calcium, 109 mg. Yogurt A contains *Lactobacillus delbrueckii subsp. Bulgaricus* 2038 strain and *Streptococcus thermophiles* 1131 strain as prebiotics. Yogurt B was purchased from Morinaga Co Ltd. (Tokyo, Japan) and the nutrient content per 100 g of daily intake was as follows: energy, 65 kcal; protein 3.7 g; fats, 3.1 g; carbohydrates, 5.5 g; sodium, 50 mg; and calcium, 120 mg. Yogurt B contains *Bifidobacterium longum* BB536 strain as prebiotics.

Design

The schedule of this study is shown in Figure 1. A cross-over study between yogurt A and yogurt B was designed around the test. During the initial observation period (control, 2 weeks), the subject ingested neither yogurt A nor B. Next, during the 1st intake period (1 week), the subject ingested yogurt A. During the succeeding rest period (1 week), the subject ingested neither yogurt A nor B. During the 2nd intake period (1 week), the subject ingested yogurt B. As shown in Fig.1, the subject ingested yogurt A or B three times for each 1 week. During these intake periods, 150 g of yogurt was ingested daily after dinner.

Evaluation of UC symptom

Stool frequency, color, shapes of feces, and intestinal transit time of foods evaluated regulatory function in the intestine[6]. Briefly, we recorded the stool frequency every day. We classified colors and shapes of feces in six stages as previously reported[6]. For the intestinal transit time of foods, we recorded time that elapsed between the ingestion of color marker and seeing the blue color in the feces. We used 800 mg of food additive blue No. 1 (Kyouritu-Syokuhin, Japan), which was encapsuled with gelatin, as the color marker.

Abdominal pain, abdominal tenderness, and appetite were registered using Visual Analogue Scale (VAS; 0-100mm) in which 0 indicated "none" for the three categories and 100 indicated "the worst". These none and worst could be imagined by a subject.

Statistics

Statistical differences among the groups were determined by a single factor ANOVA, followed by a post-hoc Turkey-Kramer test. Differences were considered statistically significant at $p < 0.01$.

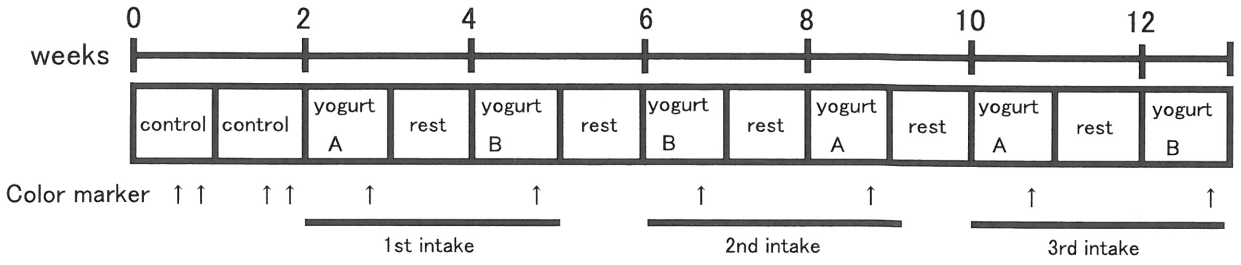

Figure.1 Schedule of the study

Two kinds of yogurt, yogurt A and B, were ingested for 1 week, individually. A cross-over study between yogurt A and B was designed around the test. One set of intake schedule was yogurt A or B-rest-yogurt B or A. Three sets of intake were repeated. Control indicated observation periods.

Results and Discussion

Analysis of general regulatory intestinal function could not evaluate the effects of functional foods in an ulcerative colitis (UC) patient.

It has been previously described that Clinical Activity Index (CAI) is generally used to evaluate the clinical symptom of UC[1,4]. As shown in Table 1, the symptom was categorized into 8 groups, diarrhea, nocturnal diarrhea, visible blood in stool, fecal incontinence, abdominal pain/cramping, general well-being, abdominal tenderness, and need for antidiarrheal drugs. Each symptom was scored and the max score is 21. This CAI was developed for the symptom in relapse priods and used for the evaluation of effects of clinical treatment on severe symptom. A score of less than 10 on two consecutive days was considered to indicate a clinical response. In the case of remission periods, since a CAI score could be maintained less than total 10 during observation times, it was difficult to evaluate the effects of functional foods on the UC symptom in remission period by CAI score.

To evaluate the effects of functional foods on intestinal general condition in a patient with UC in

Table.1 Clinical Activity Index for the Evaluation of patients with Ulcerative Colitis (CAI score)

score	0	1	2	3	4	5
Diarrhea (no. of daily stools)	0-2	3-4	5-6	7-9	10	
Nocturnal diarrhea	No	Yes				
Visible blood in stool (% of movements)	0	<50	>50	100		
Fecal incontinence	No	Yes				
Abdominal pain/cramping	None	Mild	Moderate	Severe		
General well-being	Perfect	Very good	Good	Average	Poor	Terrible
Abdominal Tenderness	None	Mild and localized	Mild to Moderate and diffuse	Severe on rebound		
Need for antidiarrheal drugs	No	Yes				

The max score is 21. A score of less than 10 on two consecutive days was considered to indicate a clinical response.

Table.2 Effects of yogurts on the regulatory intestine function in UC patients with the remission period.

	frequency		colors		shapes	
yogurt	A	B	A	B	A	B
control	0.57±0.65		5.00±0.53		5.38±1.06	
1st intake	0.43±0.53	0.71±0.95	5.33±0.58	4.60±0.55	6.00±0.00	4.60±0.89
2nd intake	0.57±0.53	0.57±0.53	5.00±0.00	5.00±0.00	5.75±0.50	4.75±0.50
3rd intake	0.71±0.76	0.46±0.53	4.60±0.55	4.33±0.58	5.20±0.84	5.00±1.00

A subject with UC in the remission period ingested 150 g of yogurt A or B three times for each 1 week. A cross-over study between yogurt A and B was designed around the test. Stool frequency per day, color, and shapes of feces evaluated regulatory function in the intestine. Stool frequency per day was recorded every day. Colors and shapes were classified in six stages and recorded once every day.
Value means ±SD, n=7.

remission period, we first examined stool frequencies, color, shapes of feces, and intestinal transit times of foods as the regulatory function in intestine. In this study, two kinds of yogurts, yogurt A and yogurt B, were ingested as prebiotics. A cross-over study between yogurt A and yogurt B was designed around the test as shown in Fig.1. During the 1st, 2nd and 3rd intake periods, stool frequencies, color, and shapes of feces were not changed (Table 2). These scores were not significant in comparison with those in control. As shown in Figure 2, the intestinal transit times of foods were slightly decreased but not significant in the periods of yogurt A intake. Yogurt B did not affect to the times. These results suggested that general analysis for the regulatory intestinal function, stool frequencies, color, shape of feces, and transit times were slightly changed but not significant after the yogurt intake. Since our yogurt intake schedule was shorter than that in previous reports for prebiotics, the regulatory intestinal functions in our study might be not affected. We need further study in which we examine longer terms of yogurt intake.

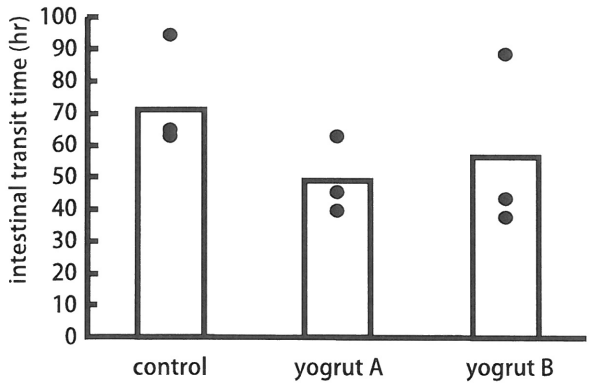

Figure.2 Effect on intestinal transit time

A subject with UC in the remission period ingested two kinds of yogurt, yogurt A and B, individually. The elapsed times between ingestion of color marker and seeing blue color in the feces were recorded as the intestinal transit time. Dots indicate value of the mean. Bar indicates average of the mean.

Analysis of VAS could evaluate the effects of functional foods.

The purpose for this study is the establishment of evaluation methods for the symptom of UC in remission period. In addition to general analysis of intestine function, we performed the sensible examination by Visual Analog Scale (VAS) analysis in an UC patient after the yogurt intakes. Recently, VAS analysis has been used for rheumatoid arthritis disease, because sensible evaluation is also needed to this disease as well as UC[7]. By VAS analysis in our study, we examined abdominal pain, abdominal tenderness, and appetite. For the abdominal pain, sense by the subject recorded using VAS (0-100mm) in which 0 mm indicated no-pain and 100 mm indicated severe pain. For the abdominal tenderness, subject's sense was recorded using VAS in which 0 mm indicated no-intestinal tenderness and 100 mm indicated severe tenderness. For the appetite, 0 mm indicated hypophagia and 100 mm indicated hyperphagia. These scaling might be easy to record the sense of physical condition for the subject, who was an UC patient in the remission period. The abdominal pain and the abdominal tenderness could be reflected in the inflammatory reaction in intestine. The appetite could be reflected in normal and healthy intestinal function. As shown in Figure 3, both of abdominal pain and tenderness were decreased and appetite was increased in the yogurt intake periods. During 2nd and 3rd periods of yogurt A and B intake, abdominal pain was significantly decreased ($p<0.01$). In the case of abdominal tenderness, yogurt A intake at 1st and 3rd periods and yogurt B intake at all of periods significantly decreased VAS in the comparison with control ($p<0.01$). The appetite was significantly increased by yogurt A intake at 2nd and yogurt B intake at 2nd and 3rd ($p<0.01$). It is suggested that VAS analysis could evaluate the effects of yogurt intake on the improvement of UC symptom. Furthermore, the subject convinced VAS analysis in the remission period.

In conclusion, we showed that VAS analysis could evaluate the effects of functional foods in an UC patient at the remission period. Furthermore, we found that the intestinal transit time could also evaluate the effects of functional foods. Combination analysis of VAS and intestinal transit time could be suitable for our subject. We need more analysis by large number of subjects. Using this evaluation method for functional foods may lead to an improvement in QOL of the patients with UC in the remission period.

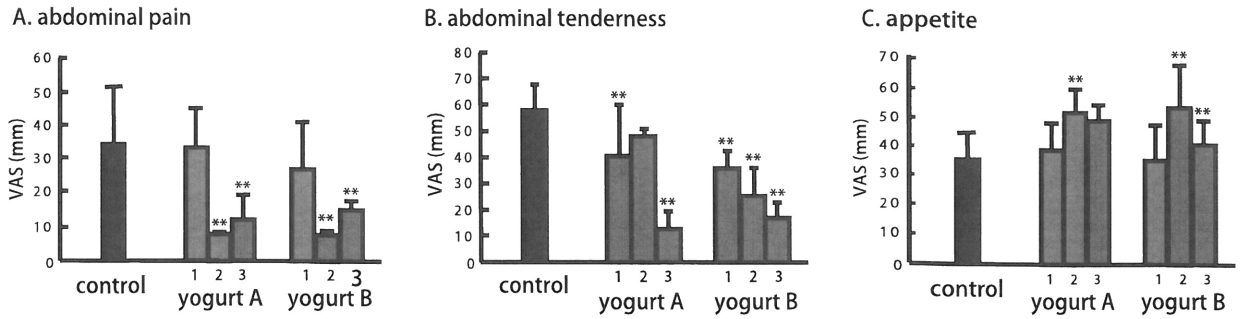

Figure.3 VAS analysis on the abdominal pain, abdominal tenderness, and appetite.

A subject with UC in the remission period ingested 150 g of yogurt A and B individual three times for each 1 week. A cross-over study between yogurt A and B was designed around the test as shown in Figure 1. Abdominal pain, abdominal tenderness, and appetite were recorded by Visual Analogue Scale (VAS; 0-100mm). For these three categories, 0 indicated "none" and 100 mm indicated "the worst". These none and worst could be imagined by a subject. Value means ±SD, n=7. Significantly different from control, **P<0.01.

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