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Original article

Effect of yogurt on postprandial blood glucose after steamed rice intake

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Abstract

***Purpose*:** A continuous hyperglycemic state increases glycative stress. Therefore, even if the fasting blood glucose level is within the reference level, an acute postprandial hyperglycemic state leads to glycative stress. The purpose of this research was to verify the effects of yogurt on the blood glucose level after eating steamed rice.

***Method*:** The subjects were 20 healthy males and females (aged 35.8 ± 6.6) and written consent was obtained from all participants. The eating orders of the test food sets were: (**A**) eating steamed rice only as a control food, (**C**) eating steamed rice before eating yogurt and (**D**) eating yogurt before eating steamed rice. The changes in blood glucose levels based on eating order were then verified. For the purpose of comparison of the inhibiting effects on postprandial hyperglycemic state based on these eating orders, another eating order of vegetable salad before eating steamed rice (**B**) was prepared. On the day of the test, after blood glucose level was measured at fasting time, the subjects ate the test foods within a 10 minute time frame. Then, 15, 30, 45, 60, 90 and 120 minutes after they started eating the test food(s), they measured their own blood glucose level using a self-monitoring blood glucose (SMBG) device by puncturing their own fingertip. The evaluations of glycative stress were conducted using rising blood glucose levels, maximum blood glucose level change (ΔCmax) and the area under the incremental blood glucose curve (iAUC).

***Results*:** There were no adverse events and no subjects who fell under the exclusion criteria. Therefore, all subjects were regarded as effective analysis subjects. ΔCmax was smaller in (**B**) ($p < 0.05$) and (**D**) ($p < 0.01$) than in (**A**). iAUC was smaller in (**C**) and (**D**) than in (**A**) ($p < 0.05$). ΔBlood glucose levels were lower in (**B**) and (**D**) ($p < 0.05$) when eating vegetable salad or yogurt before eating steamed rice than that of (**A**) after 30 minutes and 45 minutes, and lower only in (**D**) after 15 minutes and 90 minutes ($p < 0.05$). When comparing the eating orders of steamed rice and yogurt, Δblood glucose levels (**C**) and (**D**) ($p < 0.05$) were lower than that of (**A**) after 30 minutes and 90 minutes, and lower in (**D**) than that of (**A**) after 15 minutes and 45 minutes ($p < 0.05$).

***Conclusion*:** The habit to eat yogurt together with steamed rice inhibited postprandial blood hyperglycemic states. Eating yogurt before steamed rice greatly inhibited postprandial hyperglycemic state and its effect was more than equal to eating vegetable salad before eating steamed rice, which had been reported. Adding yogurt to the meal possibly contributes to the prevention of the progression of aging and diseases.

***KEY WORDS*:** glycative stress, yogurt, protein, lactic acid

Introduction

Reducing sugars including glucose and aldehyde substances generated by the metabolism of alcohol and lipids react with protein and form advanced glycation end products (AGEs) *in vivo*. The transformation of protein to AGEs is often accompanied by cross-link formation, inflammation and browning which cause physical, physiological and visual damage to various tissues and cells. Therefore, the concept of comprehensively integrating biological stress caused by reducing sugars and aldehyde substances and the effects of the generation of AGEs of protein is called glycative stress [1, 2].

Long-term hyperglycemia enhances glycative stress. Therefore, even if fasting blood glucose levels are within the reference level, an acute postprandial hyperglycemic state leads to glycative stress. It is an age-related risk factor and becomes a factor for the progression of skin aging, diabetic

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complications, osteoporosis and cognitive impairment (dementia). As a means to alleviate glycative stress, there is the inhibition of postprandial hyperglycemic states, the inhibition of glycation reaction and the decomposition and excretion AGEs [3].

It has been reported that eating vegetable salad [4, 5] and vinegar [6] before eating steamed rice can inhibit a postprandial hyperglycemic state. We have studied the effects of the kinds of carbohydrates as stable food and others eaten together on postprandial hyperglycemic states and, as a result, reported that for the purpose of inhibiting a postprandial hyperglycemic state, the following eating styles are recommended: Eat grapefruit before eating bread [7], add dietary fibers to udon noodles [8], eat udon noodles or steamed rice together with side dishes such as eggs, vegetable salad, mabo nasu (eggplant stir-fry recipe) [9] and gyudon (boiled beef and onions) toppings [10] rather than eating noodles or steamed rice only.

In order to verify the effects of yogurt on hyperglycemic state after eating steamed rice in this research, the glucose level transitions were investigated in the cases of eating steamed rice only as a reference diet, eating steamed rice before eating yogurt and eating yogurt before eating steamed rice. For the purpose of comparison of inhibiting actions on postprandial hyperglycemic states, the case of eating vegetable salad before eating steamed rice was verified as a positive control.

Methods

Subjects

The subjects met the following inclusion criteria: those who are fully informed of the purpose and contents of the research, and have the ability to understand and agree with it, applied to participate in this research of their own will and submitted consent in writing, healthy Japanese aged 20 years or older and younger than 50 years old and whose body mass index (BMI) is 30 or less, those who have had no abnormal glucose tolerance for the past a year based on physical checkup, those who are not taking blood pressure lowering medication and those who eat yogurt less than twice a week.

The subjects did not fall under the following exclusion criteria: those who have food and other allergies to these test foods, those who participated in other tests during the month prior to the start of this research, those who are scheduled to participate in another test after they consent to participate in this research, those who are breastfeeding or those who are scheduled to be pregnant or desire to become pregnant during the period of research.

The number of subjects was calculated by two-tailed test, at effect size = 0.8, significance level = 0.05 and power = 0.8, using G*Power 3, version 3.1.9.2 as power analysis software [11]. As a result, the number of subjects satisfying scientific rationality was determined to be 15, so the number of subjects was decided to be 20 by adding extra number (10 males and 10 females).

Test Items and Their Contents

For the purpose of inspection of the participant's backgrounds, the subjects wrote down their own age, health history and the presence of any food allergy on the survey form by themselves. They collected their blood by puncturing their own fingertip using a medical lancet and measured their own blood glucose level using an instrument for SMBG device (Medisafefit, Terumo Corporation, Shibuya-ku, Tokyo, Japan).

Protocol for Testing

As previously reported [8-11], the test was conducted in accordance with the unified protocol by the Japan Glycemic Index (GI) Study Group [12] in this research.

The subjects should live as usual except for the following restrictions during the test period: Refrain from hard exercise the day before the test and do not eat anything after 8:00 pm; avoid excessive drinking and eating and staying up late at night; abstain from taking any new drugs, including those for general medical use, quasi-drugs, supplements, health foods and foods for specified health uses that might affect the results of the test during the test period; and when visiting doctor during the period, report it immediately to the person in charge (Healthcare Systems Co., Ltd., Chiyoda-ku, Tokyo, Japan).

On the day of test, the participants do not eat breakfast. They participate in the test beginning between 7:00 am and 9:00 am. Before they eat the test foods, they sterilize a fingertip thoroughly with alcohol and dry it. After puncturing it using a lancet, they measure their own blood glucose level (any fingertip will do). They eat the control food and test food in 5-10 minutes from start, chew each bite more than 30 times and swallow. They abstain from smoking and are allowed to do mild standing or sitting tasks.

Blood tests are conducted before eating test food (1st time), 15 minutes after start (2nd time), 30 minutes (3rd time) after start, 45 minutes after start (4th time), 60 minutes after start (5th time), 90 minutes after start (6th time) and 120 minutes after start (7th time). The test is conducted in a day or more after the previous test and the number of tests are four during the test period. The test is not carried out during menstruation.

Test foods

Nutrient components of the test foods used in this research are shown in ***Table 1***. The nutrient components were calculated using the information shown in the nutrient facts label of foods used in this research. Commercially available packed steamed rice, yogurt (plain yogurt) and salad were used. Packed steamed rice was "Sato no gohan," Koshihikari, small serving 150 g (Sato Kogyo Co., Ltd., Niigata, Japan), yogurt was "Meiji Bulgaria Yogurt LB81, Plain" (Meiji Holdings Co., Ltd, Chuo-ku, Tokyo, Japan) and vegetable salad was "a mixed salad of onion and lettuce which can be used without washing" (Aeon Co., Ltd., Chiba, Japan). Vegetable salad was eaten without dressing.

The intake amounts of test foods were determined in accordance with the unified protocol by the Japan Glycemic Index (GI) Study Group so that the total amount of carbohydrate becomes 49.9 ± 0.4 g (mean ± standard deviation [SD]) as follows.

(**A**) Steamed rice 150 g (carbohydrate 49.7 g)
(**B**) Vegetable salad 101 g and steamed rice 138 g (carbohydrate 49.7 g)
(**C, D**) Yoghurt 200 g and steamed rice 120 g (carbohydrate 50.4 g)

For the method of consumption, each test food set was eaten within 10 minutes after the start of test. However, in the cases from (**B**) to (**D**), (**B**) vegetable salad 101 g, (**C**) steamed rice 120 g or (**D**) yoghurt 200 g was eaten first during the first five minutes before eating the second item.

Selection of Safety Analysis Subjects

Safety analysis subjects were those who had experienced eating these foods even once.

Selection of Effective Analysis Subjects

Effective analysis subjects were those who completed all determined test schedules and test contents excluding those falling under the following exclusion criteria: those whose behavior clearly degraded the credibility of test results, those who were clearly proven to have fallen under the exclusion criteria and those who were unable to abide by restrictions after the start of test.

Statistical Analysis

The evaluation and analysis of the safety of the test targeted the safety analysis subjects group. The symptoms, degrees and frequencies of the adverse events and side effects were totaled and evaluated.

The effectiveness analysis of the test targeted the effective analysis subjects group. The blood glucose levels obtained by subtracting the blood glucose levels before the first intake of test foods (1st time, value at 0 minute) from the levels over time after eating test foods were defined as Δblood glucose levels and the maximum blood glucose level change from the start of test to 120 minutes was defined as ΔCmax. Blood glucose incremental area under curve (iAUC) was calculated in accordance with the unified protocol by the Japanese Glycemic Index (GI) Study Group.

IMB SPSS Statistics 24 (IBM Japan, Minato-ku, Tokyo, Japan) was used for statistical analysis. A Friedman test was conducted for the comparison of the test results between the groups and a risk rate of less than 5% by two-sided test was regarded as a significant difference.

Ethical Standard

This research was conducted in compliance with the ethical principles based upon the Declaration of Helsinki (Additional commentary in 2004 General Assembly Tokyo, Japan) and Personal Information Protection Law and in reference to "Standards for the Implementation of Clinical Trials (GCP)), an ordinance of the Ministry of Health, Labour and Welfare No. 28 of March 27, 1997), as well as "Ethical Guidelines for Epidemiology Research" by the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare.

Healthcare Systems Co., Ltd. held an ethical review committee, where the morality and appropriateness of this test were discussed and it was approved (Approval Number: #1701). This test was conducted after being registered in the open database (UMIN) run by National University Hospital Council of Japan (Test ID: #000028061).

Results

Evaluation of Safety

No adverse events concerning this test was reported (data have not been published).

Evaluation of Effectiveness of Subjects

Because there were not any subjects falling under the exclusion criteria, all 20 subjects were effective analysis subjects: 10 males and 10 females; aged 35.8 ± 6.6 (mean ± SD) (male 35.7 ± 6.7, female 35.8 ± 6.9); height 165.3 ± 8.0 cm (male 171.5 ± 5.1, female 159.1 ± 5.), body weight 59.6 ± 12.5 kg (male 69.4 ± 9.0, female 49.9 ± 6.0) and BMI 21.7 ± 3.4 (male 23.7 ± 3.5, female 19.6 ± 1.7).

Evaluation of Effectiveness

Blood glucose level transition after test food intake is shown in ***Table 2***. ΔCmax and iAUC are shown in ***Fig. 1, 2***.

Compared with the case of eating steamed rice only (**A**), ΔCmax was significantly lower in the case of eating steamed rice before eating yogurt (**C**) and in the case of eating yogurt before eating steamed rice (**D**) ($p < 0.01$). Similarly, ΔCmax was lower in the case of eating vegetable salad before eating steamed rice (**B**) was lower than the case of (**A**) ($p < 0.05$).

iAUC was smaller in (**C**) and (**D**) than that in (**A**) ($p < 0.01$). Similarly, it tended to be smaller in (**B**) than in (**A**).

ΔBlood glucose level changes (glucose values obtained by subtracting the blood glucose level before the first intake of test foods [1st time, value at 0 minutes]) are shown in ***Table 3***.

Fig. 3 shows Δblood glucose levels in the cases of eating vegetable salad (**B**) or Yogurt (**D**) before eating steamed rice. Compared with (**A**), Δblood glucose levels of (**D**) were lower ($p < 0.05$) after 15 minutes, those of (**B**) and (**D**) were lower ($p < 0.01$) after 30 minutes and those of (**B**) and (**D**) were lower ($p < 0.01$) and ($p < 0.05$), respectively, after 45 minutes. ΔBlood glucose level of (**D**) was lower ($p < 0.05$) than that of (**B**) after 90 minutes.

Fig. 4 shows Δblood glucose levels in the cases of eating steamed rice before eating yogurt (**C**) and eating yogurt before eating steamed rice (**D**). Compared with (**A**), Δblood glucose level in (**D**) was lower ($p < 0.05$) after 15 minutes, (**C**) and (**D**) were lower ($p < 0.05$) and ($p < 0.01$), respectively, after 30 minutes, (**D**) was lower ($p < 0.05$) after 45 minutes and those of (**C**) and (**D**) were lower ($p < 0.05$) after 90 minutes.

Discussion

Inhibitory Effects of Yogurt on Postprandial hyperglycemic state

For the purpose of verifying the effect of yogurt on blood glucose levels after eating steamed rice, the changes in blood glucose level caused by eating only steamed rice as a control food and eating yogurt and steamed rice in different eating orders were compared with those caused by eating vegetable salad before eating steamed rice. The effects on blood glucose were then verified.

Table 1. Nutrition facts of test meal.

Test food	Unit (g)	Energy (kcal)	Protein (g)	Fat (g)	Carbohydrate (g)	Sugar (g)	Fiber (g)
Steamed rice [1)]	150	216	3.2	0.5	49.7	–	–
Yogurt [2)]	100	62	3.4	3.0	5.3	–	–
Vegetable salad [3)] (no dressing)	100	22	0.6	0.1	–	4.0	1.4

1) Sato no gohan, Kodawari Koshihikari, small serve 150 g (Sato Kogyo Co., Ltd.).
2) Meiji Bulgaria Yogurt LB81, plain (Meiji Holdings Co., Ltd.).
3) The mixed salad of the onion and lettuce which can be used without washing (Aeon Co., Ltd.).

Table 2. Blood glucose level transition after intake of the test meal.

Test food	0 min	15 min	30 min	45 min	60 min	90 min	120 min
A	92.3 ± 7.8	103.4 ± 12.3	131.3 ± 20.4	139.6 ± 13.2	135.4 ± 17.3	123.3 ± 20.0	112.9 ± 14.1
B	95.5 ± 7.6	100.9 ± 9.3	114.9 ± 14.7	123.4 ± 16.8	125.7 ± 14.8	122.7 ± 14.0	120.1 ± 12.3
C	96.9 ± 8.6	107.6 ± 11.4	126.1 ± 23.8	129.2 ± 16.0	123.4 ± 15.4	110.3 ± 17.3	105.4 ± 15.5
D	95.1 ± 7.0	97.4 ± 7.0	111.0 ± 12.4	125.4 ± 16.6	124.5 ± 14.2	113.5 ± 10.8	110.7 ± 7.1

Data are expressed as mean ± SD, unit; mg/dL, n = 20. **A**; steamed rice, **B**; vegetable salad (no dressing) before steamed rice, **C**; steamed rice before yogurt, **D**; yogurt before steamed rice.SD, standard deviation.

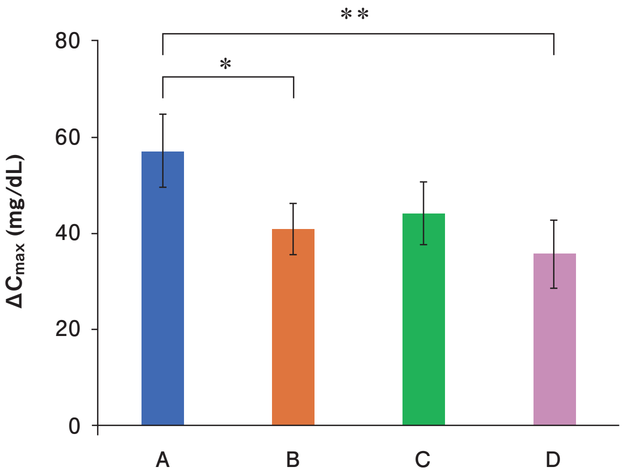

Fig. 1. **The amount of maximum blood glucose level change (ΔCmax) after ingesting test meal.**
Data are expressed as mean ± 95% CI, n = 20. **p < 0.01, *p < 0.05 by Friedman test. **A**; steamed rice, **B**; vegetable salad (nodressing) before steamed rice, **C**; steamed rice before yogurt, **D**; yogurt before steamed rice. CI, confidence interval.

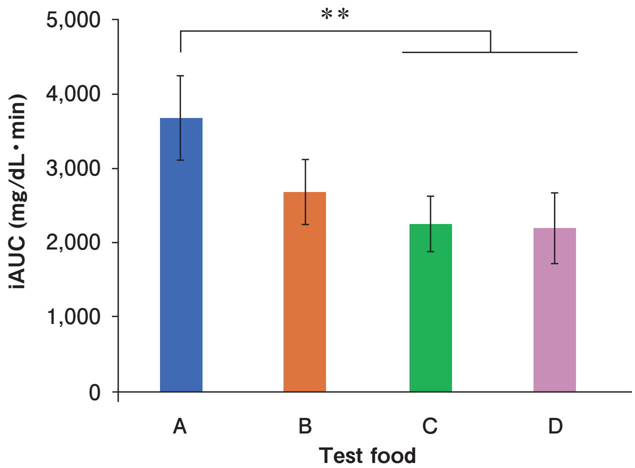

Fig. 2. **The area under curve blood glucose level change (iAUC) after ingesting test meal.**
Data are expressed as mean ± 95% CI, n = 20. **p < 0.01 by Friedman test. **A**; steamed rice, **B**; vegetable salad (no dressing) before steamed rice, **C**; steamed rice before yogurt, **D**; yogurt before steamed rice.

Table 3. The amount of blood glucose level change (Δblood glucose) after ingesting test meal.

Test food	15 min	30 min	45 min	60 min	90 min	120 min
A	11.1 ± 10.6 (5.0)	39.0 ± 19.4 (9.1)	47.3 ± 14.0 (6.6)	43.1 ± 20.5 (9.6)	31.0 ± 21.0 (9.8)	20.7 ± 15.9 (7.4)
B	5.4 ± 7.7 (3.6)	19.4 ± 15.4 (7.2)**	27.9 ± 17.2 (8.0)**	30.2 ± 15.2 (7.1)	27.2 ± 11.9 (5.6)	24.6 ± 14.0 (6.5)
C	10.7 ± 8.8 (4.1)	29.2 ± 23.0 (10.8)*	32.3 ± 14.9 (7.0)	26.5 ± 14.0 (6.6)	13.4 ± 14.0 (6.6)*#	8.5 ± 11.4 (5.4)##
D	2.3 ± 5.3 (2.5)*	16.0 ± 11.2 (5.2)**	30.4 ± 15.0 (7.0)*	29.5 ± 15.5 (7.3)	18.4 ± 11.8 (5.5)*#	15.7 ± 9.1 (4.2)

Data are expressed as mean ± SD, parenthesis indicate 95% CI, unit; mg/dL, n = 20. *p < 0.05, ** p < 0.01 vs **A**, #p < 0.05, ## p < 0.01 vs **B** by Friedman test. **A**; steamed rice, **B**; vegetable salad (no dressing) before steamed rice, **C**; steamed rice before yogurt, **D**; yogurt before steamed rice. SD, standard deviation; CI, confidence interval.

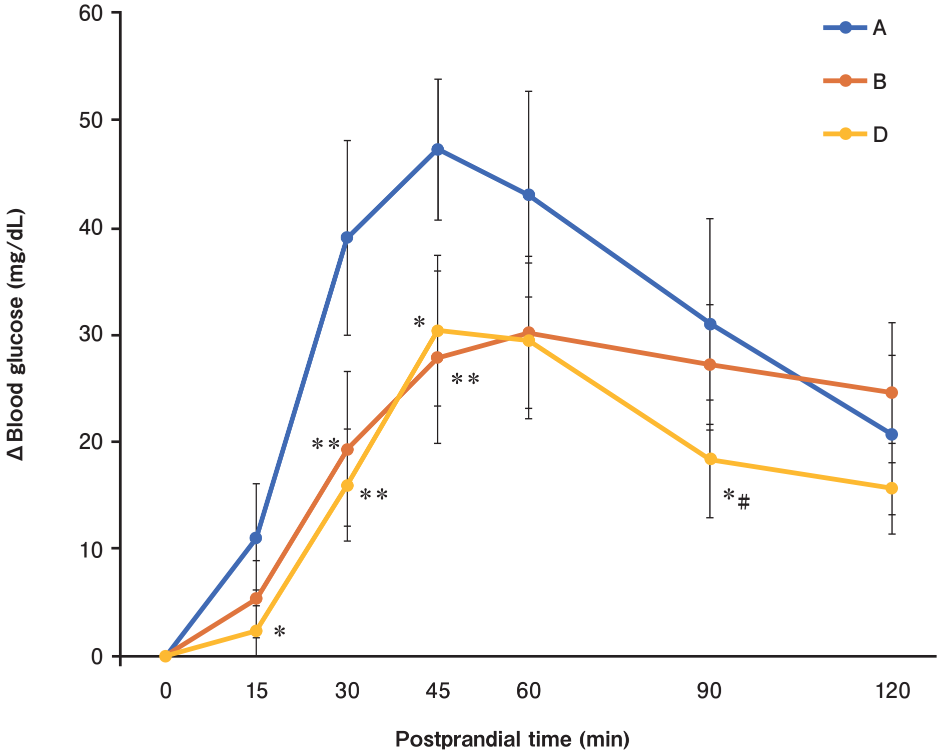

Fig. 3. **Fluctuation of the blood glucose level at the time of ingesting vegetable salad or yogurt ahead of rice.**
Data are expressed as mean ± 95% CI, n = 20. * p < 0.05, ** p < 0.01 vs **A**, # p < 0.05 vs **B** by Friedman test. **A**; steamed rice, **B**; vegetable salad (undressed) before steamed rice, **D**; yogurt before steamed rice. CI, confidence interval.

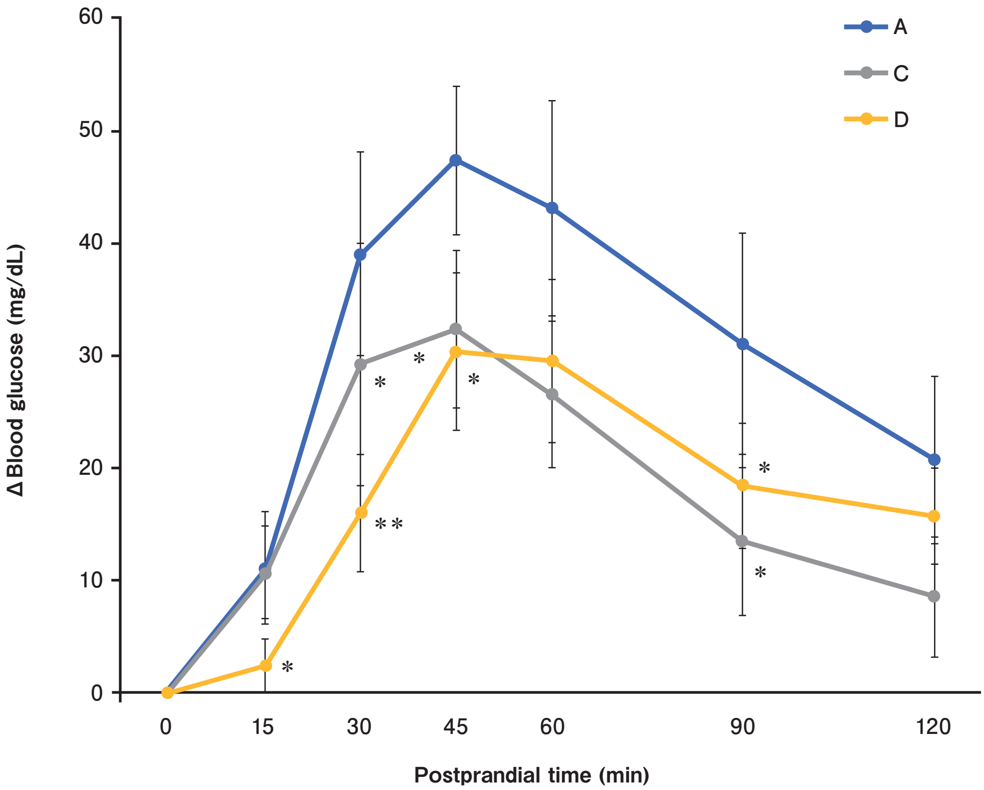

Fig. 4. **Fluctuation of the blood glucose level at the time of changing thesequence of ingesting yogurt and rice.**
Data are expressed as mean ± 95% CI, n = 20. * p < 0.05, ** p < 0.01 vs A by Friedman test. **A**; steamed rice, **C**; steamed rice before yogurt, **D**; yogurt before steamed rice.

ΔCmax was smaller in (**B**) and (**D**) than in (**A**). iAUC was smaller at the time when eating yogurt in (**C**) and (**D**) than in (**A**). ΔBlood glucose levels by measuring time when eating vegetable salad (**B**) or yogurt (**D**) before eating steamed rice were smaller in both (**B**) and (**D**) than in (**A**) after 30 minutes and 45 minutes; however, that of (**D**) only was smaller after 15 minutes and 90 minutes. Therefore, it was verified that the diet of eating vegetable salad or yogurt before eating steamed rice inhibited postprandial hyperglycemic state to a greater extent than eating steamed rice only.

It has been reported that the diet of eating vegetable salad before eating steamed rice inhibits postprandial hyperglycemic state [4, 5]. There are some examples of clinical experiments on the effect of yogurt to inhibit hyperglycemia using animals including rats and mice [13, 14] as well as human clinical tests [15].

It was reported that the amino acids included in milk whey promote the secretion of incretin which causes an inhibitory action on postprandial hyperglycemic states [16]. It is known that lactic acid has the effect of promoting the gelation of digesta in digestive organs [17], and the inhibitory action on digestion rate by the gastrin secretion inhibition is known [18]. Furthermore, mono carboxylic acid, including lactic acid, promotes the generation of energy in mitochondria in muscle tissues through monocarboxylate transporter (MCT) existing on cell membranes [19]. According to the results of an investigation into 19 kinds of commercially available plain yogurt, the amount of protein in yogurt was 3-4 g/100 g (shown on the nutrient facts label) and the amount of lactic acid was 90-900 mg/100 g (data is not shown). It has been reported that a plasma concentration of lactic acid rises 30 minutes after eating yogurt and it is maintained for the following three hours [20]. Therefore, it is possible that the inhibitory effect on postprandial hyperglycemic state at the time when eating yogurt and steamed rice together is caused by secretion of incretin promoted by amino acids associated with the digestion of milk protein in yogurt, the delay of digestion rate by lactic acid in the stomach, promotion of the gelation of digesta in digestive organs and the promotion of carbohydrate metabolism caused by absorbed lactic acid.

Meanwhile, in this research, iAUC was further decreased by eating yogurt rather than eating vegetable salad. In a preceding research on a vegetable salad eating experiment, olive oil and vinegar were used as dressing and eaten together with a vegetable salad [4, 5]. It has been reported that vinegar and olive oil have an inhibitory action on postprandial hyperglycemic states [21]. It was also reported that the inhibitory action of dressing on postprandial hyperglycemic states differ based on different compositions [22]. It is possible that because no dressing was used for the vegetable salad in this research, the inhibitory action of vegetable salad on postprandial hyperglycemic state was weaker.

Eating Order of Yogurt and Steamed Rice

The effects of eating orders of both (**C**) and (**D**) were smaller than (**A**) after 30 minutes and 90 minutes, disregarding eating order. However, the effect of eating yogurt before steamed rice (**D**) was small after 15 minutes and after 45 minutes. The difference in Δblood glucose after 15 minutes is possibly caused by the time allocation for carbohydrate intake in 10 minutes. However, because the time when both (**C**) and (**D**) become ΔCmax was after 45 minutes, the diet of eating yogurt before steamed rice was considered to possibly increase the inhibitory action on the postprandial hyperglycemic state. This phenomenon is considered to be similar to the diet of eating grapefruits before eating bread [7] and that of taking vinegar [6] and a vinegar drink [23] before eating steamed rice can inhibit a postprandial hyperglycemic state.

It has already been reported that in order to inhibit a postprandial hyperglycemic state, it is recommended to add dietary fibers to udon noodles [8] and eat udon noodles or steamed rice together with side dishes such as egg, vegetable salad, mabo nasu [9] and gyudon topping [10], rather than eating noodles or steamed rice only. However, eating yogurt after eating steamed rice shows a greater inhibitory effect on postprandial hyperglycemia state than eating noodles or steamed rice only. Therefore, as far as yogurt is concerned, the difference in effect based ondifferent eating order is possibly small. The reason is considered to be that the time difference of eating order was only five minutes and the lactic acid in yogurt was promptly absorbed and the concentration of lactic acid in the blood is maintained. As a result, the carbohydrate metabolism was promoted and continued through MCT.

Inhibition on Glycative Stress by Inhibition of Postprandial Hyperglycemic State

A postprandial hyperglycemic state leads to excess secretion of insulin [24]. Therefore, the repetition of extreme postprandial hyperglycemic states is involved in causing insulin resistance. It has been reported that responding to a rise in postprandial blood glucose, the concentrations of 3-deoxyglucosone, glyoxal and methylglyoxal, which are glycation reaction intermediates in blood [25], increased. It is known that methylglyoxal in blood damages vascular endothelial cells [26]. Therefore, the inhibition of a postprandial hyperglycemic state prevents damage to tissues and organs caused by the injuries of small blood vessels. The continued dietary guidance for 1-2.5 years to eat vegetables before staple foods has led to the decrease of HbA1c in patients with diabetes and the prevention of the progression of diabetic complications [27]. There is a result of a meta-analysis that the dietary habit of eating a portion of yogurt everyday reduces the risk of type 2 diabetes [28]. Therefore, the dietary habit to continuously eat yogurt together with a meal possibly alleviates glycative stress by inhibiting a postprandial hyperglycemic state and contributes to the prevention of aging and the progression of age-related diseases.

Conclusion

The dietary habit of eating yogurt together with a meal inhibited postprandial hyperglycemic states and eating yogurt before eating steamed rice contributed to the inhibitory action to a greater extent. This diet exhibits the same inhibitory action or more as that of eating a vegetable salad before eating steamed rice, which has been reported. It is possible that eating yogurt together with a meal contributes to the prevention of progression of aging and age-related diseases.

Declaration of Conflict of Interest

This research received support from Ez Es Company Ltd. (Tokyo, Japan).

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