Original Article

Black rice with giant embryo ameliorates serum C-reactive protein in adults with metabolic syndrome

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Metabolic syndrome is well known to increase the risk of cardiovascular diseases. We have reported that phytochemicals rich black rice with giant embryo reduced fat mass and metabolic disorders in an animal model. However, such effects have not been evaluated in humans. Subjects with metabolic syndrome (*n* = 49, 38 male, 44.3 ± 6.1 years) were randomly assigned into two groups and ingested roasted black-rice with giant embryo (BR, *n* = 26, 20 male) or white-rice (WR, *n* = 23, 18 male) powders mixed with water for breakfast for three months. Subjects were evaluated for various metabolic parameters before and after intervention. All parameters were not significantly different between groups before starting the intervention. After three months of consumption of either BR or WR, changes of body weight in BR vs WR groups (–1.54 kg vs –1.29 kg, *p* = 0.649) as well as waist circumference (–1.63 cm vs –1.02 cm, *p* = 0.365) were not significantly different between groups. However, changes in highly-sensitive C reactive proteins in BR vs WR groups (–0.110 mg/dl vs 0.017 mg/dl, *p* = 0.003) had significant differences. Three months of meal replacement with BR had a significant reduction of highly-sensitive C reactive protein compared to those with WR in adults with metabolic syndrome.

***Key Words*: black rice with giant embryo, metabolic syndrome, highly-sensitive C reactive protein**

Metabolic syndrome is a well-known factor for cardiovascular disease.(1) Especially, one of the major factor of metabolic syndrome, central obesity, is reported to be closely related with cardiovascular mortality and morbidity.(2) It has been also reported that increased inflammation in central obesity is the main cause of cardiovascular disease.(3) Therefore, reduction of low-grade inflammation by weight management via exercise and diet is the main strategy for the prevention of cardiovascular disease.

We have previously reported that black rice with giant embryo (BR), which had similar macronutrient contents as white rice,(4) was rich in bioactives such as carotenoids, vitamin E, γ-oryzanols,(5) and anthocyanins.(6) In addition, we have demonstrated antiadipogenic activity of γ-oryzanol(7) in cell model as well as reactive carbonyl species sequestering activities of anthocyanidins in BR.(8) Furthermore, we found that phytochemicals rich BR(4) effectively reduced fat mass and various metabolic disorders in an animal model.(9) Given these studies, it is highly plausible that meal replacement with BR could reduce metabolic derangements by weight control and reduction of vascular inflammation. However, there is no evidence yet to show such effects of BR in humans. Therefore, a randomized intervention study with BR was conducted to evaluate the biological functions of BR against metabolic syndrome.

Materials and Methods

Study design and subjects. A human study was conducted to evaluate the effects of ingesting BR for three months on body weight and metabolic biomarkers in comparison with white rice (WR). Macronutrients(4) and bioactive components(6,7) in BR and WR are shown in Table 1. Adults (*n* = 49, 11 female, 44.3 ± 6.1 years) with metabolic syndrome were randomly assigned into two groups, black rice with giant embryo group and white rice group after stratification of age, gender and body mass index. Subject who signed informed consent forms received one-month supply of roasted BR or WR powder (60 g each) and were instructed to consume the rice power by mixing it with water as a breakfast replacement. The subjects visited the center every month to receive a monthly supply and educational materials. Meal replacement was provided with the same color of powder in disposable, small plastic bag containing BR or WR. The study participants were instructed not to change their daily exercise level and food intake. Subjects, who were allergic to black rice, had type 2 diabetes, knee osteoarthritis, chronic obstructive lung diseases, tuberculosis, recent cardiovascular diseases (myocardial infarction and variant angina), were pregnant or breast feeding, had hypothyroidism, and/or had psychological problems or cancer, were excluded from the study. In addition, subjects taking various steroids were also excluded. Fifty-one adults with metabolic syndrome were recruited for the study and two subjects dropped out from the study due to moving travel-related causes. Finally, forty-nine subjects finished the current study (Fig. 1). Subjects who had metabolic syndrome aged over twenty years joined this study voluntarily. The Institutional Review Board of Ajou University Hospital approved this study (AJIRB-MED-CT3-15-248).

Measurements. Metabolic parameters such as fasting glucose, insulin, lipids (Toshiba 200FR automatic analyzer, Tokyo, Japan), cortisol, highly sensitive c-reactive protein (hs-CRP, Dade Behring Marburg GMBH, Marburg, Germany), thyroid hormones (TSH and free T4), and body proportion via Dual-X ray-Energy-Absorptiometry (DXA, DISCOVERY-W fan-beam densitometry; Hologic Inc., Marlborough, MA) were determined before and after intervention (at baseline and at three months). Body weight, waist circumference, blood pressure (standard mercury manometer with

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Table 1. Macronutrients and bioactives in black rice with giant embryo vs white rice

	Black rice with giant embryo	White rice	Reference
Calorie (kcal/100 g)	312	355	(4)
Carbohydrate(g/100 g)	75.3	79.3	(4)
Protein (g/100 g)	7.6	7.7	(4)
Fat (g/100 g)	2.3	1	(4)
Vitamin E (mg/100 g)	2.8	—	(4)
Lutein (μg/100 g)	243.7	—	(4, 5)
β-carotene[2] (μg/100 g)	24.6	—	(4, 5)
Anthocyanins (mg/100 g)	76.7	—	(6)

—, not detected.

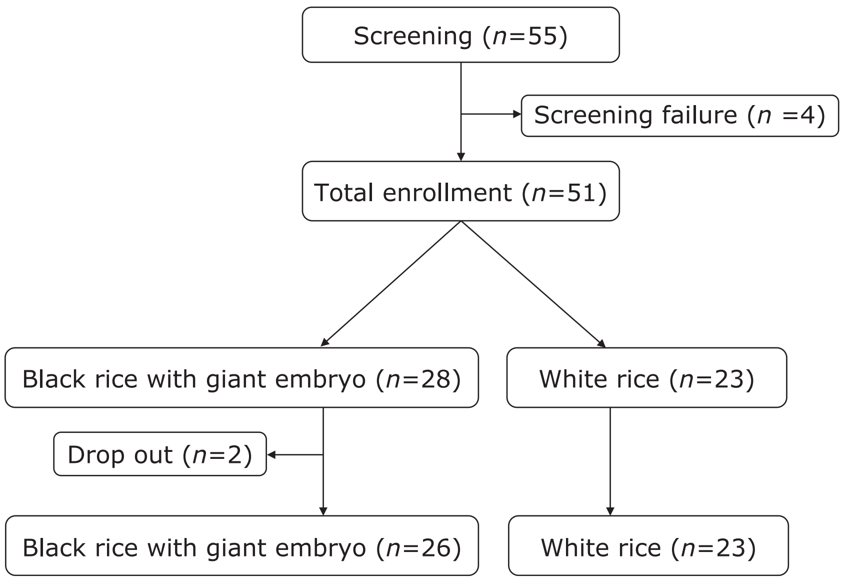

Fig. 1. Study scheme.

the participant in a sitting position for 5 min prior to measurement) as well as any adverse events were recorded by a registered research nurse at every visit. Total calorie intake was assessed with a 24-h food diary by a trained dietitian at every month. Metabolic syndrome (NCEP-ATP III) was defined as follows; over three indications including central obesity (>90 cm in men, >85 cm in women), high blood glucose (>100 mg/dl), high blood pressure (>130/85 mmHg) at rest, high blood triglyceride (>150 mg/dl), or low high-density lipoprotein cholesterol (<40 mg/dl in men, <50 mg/dl in women).[(10)] Blood tests were done after overnight with at least 8 h fasting prior to the blood draw.

Statistics. All values were represented by mean and the SD or error. The baseline data of metabolic parameters and body proportion in both groups (BR vs WR) were determined by independent *t* test. In addition, the changes of all parameters of study subjects before and after intervention were compared by paired *t* test. We also evaluated the mean changes of all parameters between two groups by independent *t* test and further compared the significance of parameter after adjustments with age, sex, smoking, alcohol intake, and moderate intensity exercise that showing the significant difference between the two groups. A *p* value was considered as statistically significant with $p<0.05$. Data were analyzed using SPSS 19.0 (SPSS Inc., Chicago, IL).

Results

Characteristics of the study subjects are shown in Table 1. Study subjects in both groups had elevated blood pressure, triglycerides and fasting glucose levels as expected. There were no significant differences in body mass index, waist and hip circumference and fat mass between subjects consuming BR and WR groups at baseline. In addition, metabolic parameters such as blood pressure, fasting glucose, insulin, total cholesterol, triglyceride, HDL showed no significant difference between two groups (BR vs WR) before starting the intervention (Table 2). When all subjects were pooled together and analyzed for changes of metabolic parameters, body mass index, waist circumference, diastolic blood pressure and triglycerides were significantly reduced after three months of intervention (Table 3). However, when the black rice and white rice ingested groups were separately investigated for the changes of body proportions and metabolic parameters by intervention, there were no significant differences in changes of such parameters. Interestingly, there was a significant decrease in serum concentration of hs-CRP in the group consuming black rice with giant embryo compared to that of white rice group, and the differences remained significant after adjusting for age, sex, smoking, alcohol intake, and exercise (Table 4 and Fig. 2).

Table 2. Characteristics of the study subjects at baseline (n = 49)

Variables	Black rice with giant embryo (n = 26)	White rice (n = 23)	p value
No. of females, n (%)[†]	6 (23.1)	5 (21.7)	0.643
Age (years)	44.3 (3.8)	44.6 (8.3)	0.993
Height (cm)	170.1 (8.5)	169.5 (8.5)	0.823
Weight (kg)	83.2 (11.5)	86.6 (14.8)	0.436
Body mass index (kg/m^2)	28.6 (2.8)	30.1 (4.6)	0.24
Waist circumference (cm)	98.0 (6.8)	100.0 (10.1)	0.473
Hip circumference (cm)	106.0 (6.2)	107.5 (9.3)	0.567
Total fat mass (kg)	28.0 (5.5)	29.6 (9.9)	0.547
Fat free mass (kg)	52.0 (8.7)	54.0 (8.6)	0.491
Daily calorie intake (kcal)	1,988.4 (438.0)	2,128.7 (594.7)	0.434
Systolic BP (mmHg)	135.6 (10.1)	130.6 (13.2)	0.209
Diastolic BP (mmHg)	83.6 (8.0)	85.9 (9.3)	0.434
Heart rate (frequency/min)	78.9 (7.7)	76.3 (8.7)	0.339
Fasting glucose (mg/dl)	109.2 (17.5)	113.5 (13.7)	0.409
Insulin (uIU/ml)	14.6 (5.9)	11.4 (4.1)	0.056
Total cholesterol (mg/dl)	212.0 (34.6)	212.9 (31.7)	0.931
Triglyceride (mg/dl)	208.5 (63.8)	217.4 (106.1)	0.764
HDL (mg/dl)	46.3 (10.1)	46.2 (12.5)	0.979
LDL (mg/dl)	132.7 (34.1)	137.7 (31.2)	0.641
Cortisol (ug/dl)	12.0 (4.8)	12.9 (3.6)	0.512
hs-CRP (mg/dl)	0.205 (0.183)	0.137 (0.165)	0.237
TSH (uIU/ml)	2.51 (1.31)	2.67 (1.37)	0.712
FT4 (ng/dl)	1.33 (0.11)	1.28 (0.11)	0.209

HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TSH, thyroid stimulating hormone; FT4, thyroxin. Values represent mean (SD). P value, independent t test; [†]χ^2 test.

Table 3. Changes of anthropometrics and metabolic parameters after 3 months of intervention in all study subjects (n = 49)

Variables	Before	After	p value
No. of females, n (%)	11 (22.4)	—	—
Age (years)	44.3 (6.1)	—	—
Height (cm)	169.8 (8.4)	—	—
Weight (kg)	84.7 (13.0)	83.3 (13.0)	<0.001
Body mass index (kg/m^2)	29.3 (3.7)	28.8 (3.7)	<0.001
Waist circumference (cm)	98.9 (8.3)	97.5 (8.1)	<0.001
Hip circumference (cm)	106.7 (7.6)	105.5 (7.1)	0.002
Total fat mass (kg)	28.7 (7.7)	27.9 (7.1)	0.002
Fat free mass (kg)	52.9 (8.6).	52.4 (8.4)	0.077
Daily calorie intake (kcal)	2,049.0 (508.8)	1,699.7 (288.3)	<0.001
Systolic BP (mmHg)	133.3 (11.7)	128.6 (10.6)	0.002
Diastolic BP (mmHg)	84.6 (8.6)	79.7 (9.4)	<0.001
Heart Rate (frequency/min)	77.7 (8.1)	74.3 (7.7)	0.022
Fasting glucose (mg/dl)	111.1 (15.9)	109.1 (15.3)	0.211
Insulin (uIU/ml)	13.1 (5.3)	12.6 (6.5)	0.62
Total cholesterol (mg/dl)	212.4 (32.9)	209.7 (31.0)	0.58
Triglyceride (mg/dl)	212.4 (84.1)	200.5 (90.8)	0.001
HDL (mg/dl)	46.3 (11.1)	43.7 (10.7)	0.014
LDL (mg/dl)	134.9 (32.5)	145.3 (25.5)	0.05
Cortisol (ug/dl)	12.4 (4.3)	12.3 (4.0)	0.902
hs-CRP (mg/dl)	0.175 (0.177)	0.130 (0.146)	0.095
TSH (uIU/ml)	2.58 (1.32)	2.57 (1.42)	0.925
FT4 (ng/dl)	1.31 (.011)	1.34 (0.6)	0.17

HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TSH, thyroid stimulating hormone; FT4, thyroxin. P values by paired t test.

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Table 4. Changes of anthropometrics and metabolic parameters in black rice with giant embryo vs white rice ingested groups

ΔVariables	Black rice (n = 26)	White rice (n = 23)	p value
ΔWeight (kg)	–1.54 (0.41)	–1.29 (0.37)	0.649
ΔBody mass index (kg/m^2)	–0.42 (0.15)	–0.43 (0.13)	0.948
ΔWaist circumference (cm)	–1.63 (0.55)	–1.02 (0.39)	0.365
ΔHip circumference (cm)	–1.66 (0.61)	–0.68 (0.30)	0.159
ΔTotal fat mass (kg)	–0.92 (0.32)	–0.68 (0.38)	0.627
ΔFat free mass (kg)	–0.33 (0.27)	–0.50 (0.38)	0.714
ΔDaily calorie intake (kcal)	–368.1 (98.2)	–324.7 (112.6)	0.937
ΔSystolic BP (mmHg)	–4.3 (2.0)	–1.46 (2.2)	0.346
ΔDiastolic BP (mmHg)	–5.5 (1.6)	–4.1 (1.5)	0.535
ΔHeart Rate (frequency/min)	–4.9 (1.9)	–1.6 (2.2)	0.255
ΔFasting glucose (mg/dl)	–3.2 (2.7)	–0.6 (1.6)	0.41
ΔInsulin (uIU/ml)	–1.15 (1.70)	0.27 (0.95)	0.472
ΔTotal cholesterol (mg/dl)	–0.3 (7.8)	–5.7 (5.2)	0.567
ΔTriglyceride (mg/dl)	4.4 (19.4)	–32.2 (19.3)	0.19
ΔHDL (mg/dl)	–3.0 (1.5)	–2.1 (1.4)	0.652
ΔLDL (mg/dl)	13.7 (7.1)	6.1 (7.3)	0.462
ΔCortisol (ug/dl)	–0.02 (0.86)	–0.15 (0.90)	0.919
Δhs-CRP (mg/dl)	–0.104 (0.028)	0.017 (0.025)	0.003†
ΔTSH (uIU/ml)	–0.03 (0.21)	0.01 (0.27)	0.917
ΔFT4 (ng/dl)	0.03 (0.15)	0.04 (0.17)	0.871

HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TSH, thyroid stimulating hormone; FT4, thyroxin. Values represent mean (SE). P value, independent t test. $^†p<0.05$, general linear model after adjustments with age, sex, smoking, alcohol intake, and moderate intensity exercise.

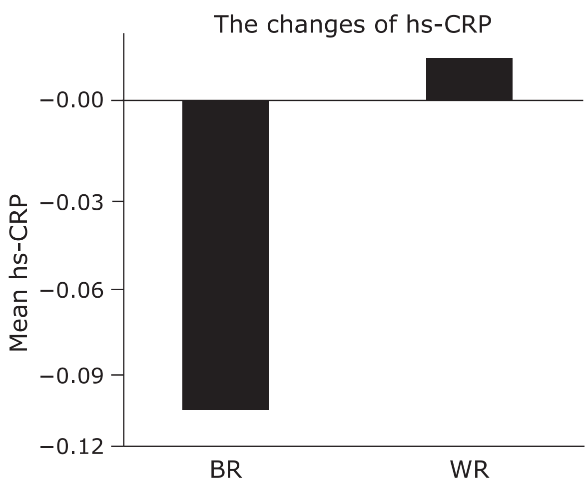

Fig. 2. Changes of serum hs-CRP concentrations in black rice with giant embryo vs white rice groups after 3 months of intervention. Subjects consumed roasted powder of black rice with giant embryo or white rice mixed with water as a breakfast replacement. BR, black rice with giant embryo; WR, white rice.

Discussion

The current study was conducted to evaluate the effect of BR that is rich in phytochemicals such as anthocyanins and carotenoids against metabolic syndrome when compared to conventional WR. Even though there was no significant difference in changes of body proportion and other metabolic parameters between BR and WR after three months of intervention, the inflammation marker, hs-CRP, showed significant reduction in serum concentration for the BR group only.

Considering that weight loss is one of the most critical factors for reducing chronic inflammation[11] and various cytokines such as hs-CRP are associated with cardiovascular events depending on body mass index,[12,13] prevention of inflammation by weight reduction can be an important strategy for reducing cardiovascular morbidity and mortality. Various dietary approaches have been conducted to reduce the inflammation in obese or prediabetic subjects using either whey protein,[14] whole grain,[15] or high-protein diet[16,17] and showed significant reduction of inflammatory markers regardless of body weight changes. In the same line with these studies, the current study indicated that meal replacement with BR significantly reduced hs-CRP as compared with that of WR without significant difference in changes of body weight. Previously we have reported that the phytochemicals in BR can be an important contributing factor for beneficial changes of metabolic parameters in obese animal model.[9]

Meal replacement for controlling body weight has long been studied. The current study utilized a roasted powder of black rice with giant embryo and white rice as meal replacements that could be mixed with water and consumed as breakfast for three months. Even though there was no significant difference in the changes of body weight between groups, study subjects in both groups had a reduction of body weight of 1.54 kg and 1.29 kg by BR and WR meal replacement, respectively. In accordance with the current study, dinner meal replacement with reduced calories equaling 388 kcal for twelve weeks was reported improve the body composition and metabolic parameters in obese patients.[18] It is interesting to note that a relatively short period of intervention for two weeks with portion controlled meal replacement with cereal also resulted in effective weight loss in obese/overweight females (BMI 29.2 ± 2.4 kg/m^2).[19] In addition, treatment option with meal replacement in combination with drug therapy[20] can also be considered for longer-term treatment or in the management of morbid obese patients.

Chronic low-grade inflammation, which is common in subjects with obesity and metabolic syndrome, can lead to development of chronic diseases such as cardiovascular diseases. Therefore, amelioration of such systemic inflammation by simple meal replacement can be a good strategy for preventing chronic diseases as shown in the current study. Larger scale of longer-term intervention studies warrants for the development of dietary strategy to reduce the systemic inflammation in subjects with metabolic disorders.

Author Contributions

K-JY, S-IH, S-JN designed & conducted the study and wrote the initial draft of the manuscript. K-NK, K-MK, B-TK, S-BP conducted study, contributed to interpretation of data and assisted in the preparation of the manuscript.

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Conflict of Interest

No potential conflicts of interest were disclosed.

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