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Premenstrual symptoms interference and equol production status in Japanese collegiate athletes: A cross-sectional study

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Abstract

Aim: Consumption of soy isoflavones reduces the risk of estrogen-related diseases, such as menopausal symptoms, osteoporosis, and cardiovascular disease. Equol is metabolized from the isoflavone daidzein by intestinal bacteria and has higher bioavailability than other isoflavones. Equol producers are believed to benefit from soybean consumption to a greater extent than non-producers. Recently, we showed that equol non-producers were at significant risk of premenstrual syndrome (PMS). Previously, we reported that PMS is a common menstrual problem in female athletes, and almost half of the studied athletes felt a negative effect of premenstrual symptoms on their athletic performance. This study was conducted to evaluate the relation between PMS and equol production status in Japanese collegiate athletes.

Methods: This was a cross-sectional, observational study that included 88 Japanese female collegiate athletes. Equol production status was determined using urine samples collected after a soy challenge test. The subjects also completed a questionnaire about their premenstrual symptoms and their competitive career.

Results: The prevalence of equol producers was 29.5% in Japanese collegiate athletes. The athletic performance of 54.5% of athletes was found to suffer in competition or in practice due to premenstrual symptoms. In multivariate analysis, equol non-producers (odds ratio, 3.34; 95% confidence interval, 1.03–12.20) and restriction of bodyweight (odds ratio, 4.94; 95% confidence interval, 1.47–20.00) were shown to be significant risk factors for poor athletic performance.

Conclusion: This study showed a relation between athletic performance and equol production status in Japanese collegiate athletes.

Key words: athletic performance, collegiate athlete, equol, isoflavone, premenstrual syndrome.

Introduction

Premenstrual syndrome (PMS) is a complex disorder characterized by a wide range of mental, behavioral, and physical symptoms that are limited to the late luteal phase of the menstrual cycle.[1] Epidemiological surveys have shown that the prevalence of premenstrual symptoms is high (80–90%).[2] Among about 5% of women, the symptoms are so severe that they interfere with personal or social relationships or work.[3] Such a severe type of PMS is classified as premenstrual dysphoric disorder (PMDD) according to the DSM-5.[4]

Many reports have documented that the premenstrual phase is associated with decreased athletic performance,[5,6] but there are few reports about PMS in athletes. Previously, we reported that PMS is a common menstrual problem in female high school and collegiate athletes, and almost half of them

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reported negative effects of premenstrual symptoms on athletic performance.[7–9]

The precise pathophysiology of PMS remains unknown. The causes of PMS have been suggested to include hormonal changes, serotonergic dysfunction, stress, and poor dietary habits.[10] Among these factors, dietary changes or dietary supplements might be recommended as non-pharmacological medical approaches without serious adverse effects.[11]

Consumption of isoflavones, which are predominantly derived from soybeans, reduces the risk of estrogen-related diseases, such as menopausal symptoms, breast cancer, osteoporosis, and cardiovascular disease.[12–14] Isoflavones act as selective estrogen receptor (ER) modulators (SERM), ER agonists in low-estrogen conditions, and ER antagonists in high-estrogen conditions.[15] Equol is a metabolite of a soy isoflavone, which is metabolized from the soy isoflavone daidzein by specific intestinal bacteria.[16] Only 30–60% of people can produce equol from daidzein after eating soy.[17] The rate of equol producers is higher in vegetarians[18] and Asian populations and is considered to be associated with the amount of soy intake.[19] Equol is more bioavailable than other soy isoflavones, and equol producers are believed to benefit more from soy isoflavones.[20] It is plausible that isoflavones may stabilize hormonal fluctuations of the estrogen cycle through their SERM-like properties and then alleviate premenstrual symptoms.[21] Recently, we reported that equol non-production was a significant risk factor for PMS.[22] However, data about the equol production status in athletes are lacking.

The aim of this study was to investigate the relation between PMS-induced disturbances in athletic performance and equol production status in Japanese collegiate athletes.

Methods

Study design and participants

The study was carried out in accordance with the principles outlined in the Declaration of Helsinki. Our institutional review board at Kindai University approved the study (approval number 24-099). Written informed consent was obtained from all participants.

A school-based cross-sectional survey was conducted in December 2016 using a sample of 189 Japanese female collegiate athletes at Kindai University in Osaka, the largest city in west Japan. All subjects belonged to authorized university clubs, which all have a high ranking in Japanese university sport. All subjects were undergoing intensive training. We recruited female collegiate athletes who had regular menstrual cycles (22–35 days) and were able to provide informed consent. A total of 104 female athletes participated in the soy challenge test and completed the questionnaire. Sixteen were excluded from the analysis because of incomplete data; therefore, we analyzed the data of 88 athletes aged 18–21 years (average $\pm$ standard deviation [SD], 19.8 ± 0.91). None in these subjects had had a prior diagnosis of a psychological disorder, such as depression or panic disorder.

Questionnaire

We used the Premenstrual Symptoms Questionnaire (PSQ), which was developed in our previous study,[23] to screen for premenstrual symptoms. The PSQ translates DSM-IV criteria into a rating scale with degrees of severity described in Japanese and is essentially identical to the Premenstrual Symptoms Screening Tool.[24] The PSQ asked, 'Within the last 3 months, have you experienced the following premenstrual symptoms starting during the week before menses and remitting a few days after the onset of menses?' The premenstrual symptoms listed on the PSQ are 'Depressed mood,' 'Anxiety or tension,' 'Tearfulness,' 'Anger or irritability,' 'Decreased interest in work, home, or social activities,' 'Difficulty concentrating,' 'Fatigue or lack of energy,' 'Overeating or food cravings,' 'Insomnia or hypersomnia,' 'Feeling overwhelmed,' and 'Physical symptoms, such as tender breasts, feeling bloated, headache, joint or muscle pain, weight gain.' The PSQ also asked whether such premenstrual symptoms interfered with 'Work efficiency or productivity, home responsibilities,' 'Social life activities,' or 'Relationships with coworkers or family.' The PSQ asked the athletes to rate the severity of premenstrual symptoms as *not at all*, *mild*, *moderate*, or *severe.* In addition to the PSQ, we asked whether such premenstrual symptoms interfered with 'Athletic performance in training or competition.' This additional question also asked the athletes to rate the severity as *not at all*, *mild*, *moderate*, or *severe.* We further collected additional information about their age, type of sports played, participation in national or international competition, regular player or not, history of stress fracture diagnosed by a medical doctor, restriction of bodyweight, and severity of

dysmenorrhea. Athletes were grouped into six groups: ball games, track, swimming, fighting sports, archery, and other sports. We asked the athletes about the severity of their pain during menses with the categories of *not at all*, *mild*, *moderate*, and *severe.*

Before this survey, the athletes received an educational program on PMS in June 2016 consisting of a 30-min health education session. An outline of the content was as follows: (i) Physiology of female reproductive systems; (ii) Prevalence of PMS/PMDD; and (iii) Symptoms and self-care treatments of PMS/PMDD. Because students' attendance was voluntary, we asked the athletes about their attendance at this lecture.

Soy challenge

To determine the equol production status, participants underwent a soy challenge in accordance with the procedure described previously.[25] Participants were instructed to eat soy food containing approximately 50 mg isoflavones twice a day, and then first morning urine samples were collected the next morning. To avoid the influence of antibiotic use on enterobacterial flora, the soy challenge was scheduled at least 1 week after discontinuation of any antibiotic treatment. These samples were transported by mail to Saga Nutraceuticals Research Institute of Otsuka Pharmaceutical Co., Ltd. Then, the equol concentration was measured by high-performance liquid chromatography using a modified method of Lundh *et al*.[26] The detection limit of equol in this assay was 0.85 nmoL/mL. The participants in whose urine equol was detected were classified as equol producers.

Statistical analyses

Statistical analysis was performed using JMP 11.2.1 (SAS). Data are expressed as the means ± SD. Statistical significance was set at $P < 0.05$. Fisher's exact test was applied to compare the prevalence of equol producers between athletes and young adult women in general. Multivariate analysis was applied to analyze factors that were significantly associated with reduced athletic performance. We selected age, equol non-producers, severe menstrual pain, participation in national or international competition, regular player, restriction of bodyweight, and attendance of the lecture and put these variables into the model.

Results

The characteristics of the study population are presented in Table 1. Considering that 83% of the athletes participated in national or international competitions, these clubs have a high ranking in Japanese college sport. We had previously given a lecture for female athletes to help raise awareness about the management of PMS. In total, 25% of the athletes had attended this lecture. The prevalence of equol producers was 29.5%. This rate is statistically the same as that reported previously in young adult female Japanese (mean age ± SD, 20.1 ± 0.5 years;[27] 14 out of 68; $P = 0.139$ by Fisher's exact test).

The prevalence of menstrual pain and each premenstrual symptom is shown in Table 2. The athletic performance of 54.5% of athletes was found to suffer in competition or in practice due to premenstrual symptoms. Next we compared the severity of premenstrual symptoms as to whether or not they disturbed athletic performance (Table 3). Most of the symptoms – besides 'Decreased interest in work, home, or social activities' – were more serous in those who suffered athletic disturbance. The severities of 'Work efficiency or productivity, home responsibilities' and 'Relationships with coworkers or family' in athletes who suffered premenstrual symptoms were much higher than those who did not.

To analyze the relation between interference by premenstrual symptoms and equol production in more detail, we analyzed the factors that were significantly associated with interference by premenstrual symptoms. Multivariate analysis was performed using

Table 1 Characteristics of study participants (N = 88)

Characteristics	
Age (years), mean ± SD	19.8 ± 0.91
Type of sport, *n* (%)	
Ball games	13 (14.8)
Track	3 (3.4)
Swimming	15 (17.0)
Fighting sports	35 (39.8)
Archery	20 (22.7)
Others	2 (2.3)
Participation in national or international competition, *n* (%)	73 (83.0)
Regular players, *n* (%)	58 (65.9)
Restriction of bodyweight, *n* (%)	24 (27.3)
Stress fracture, *n* (%)	8 (9.1)
Attended the lecture, *n* (%)	22 (25.0)
Equol producers, *n* (%)	26 (29.5)

SD, standard deviation.

Table 2 Prevalence of menstrual pain, premenstrual symptoms, and interference with work, usual activities, or relationships with degrees of severity (N = 88)

Symptoms	Not at all		Mild		Moderate		Severe	
	n	%	*n*	%	*n*	%	*n*	%
Menstrual pain	10	11.4	35	39.8	32	36.4	11	12.5
Premenstrual symptoms								
Depressed mood	34	38.6	31	35.2	18	20.5	5	5.7
Anxiety or tension	22	25.0	36	40.9	24	27.3	6	6.8
Tearfulness	32	36.4	25	28.4	27	30.7	4	4.5
Anger or irritability	25	28.4	33	37.5	22	25.0	8	9.1
Decreased interest in work, home, or social activities	44	50.0	28	31.8	13	14.8	3	3.4
Difficulty concentrating	35	39.8	37	42.0	15	17.0	1	1.1
Fatigue or lack of energy	24	27.3	33	37.5	25	28.4	6	6.8
Overeating or food cravings	26	29.5	19	21.6	28	31.8	15	17.0
Insomnia or hypersomnia	35	39.8	29	33.0	19	21.6	5	5.7
Feeling overwhelmed	51	58.0	26	29.5	9	10.2	2	2.3
Physical symptoms	19	21.6	38	43.2	23	26.1	8	9.1
Interference with work, usual activities, or relationships								
Work efficiency or productivity, home responsibility	41	46.6	36	40.9	11	12.5	0	0.0
Social life activities	72	81.8	11	12.5	5	5.7	0	0.0
Relationships with coworkers or family	58	65.9	24	27.3	5	5.7	1	1.1
Athletic performance in training or competition	40	45.5	38	43.2	9	10.2	1	1.1

Table 3 Severity of premenstrual symptoms and interference with work, usual activities, or relationships with or without athletic interference (N = 88)

	Not at all	Mild	Moderate	Severe	P (Mann–Whitney U-test)
	n	*n*	*n*	*n*	
Depressed mood	24	9	5	2	0.001
	10	22	13	3	
Anxiety or tension	17	15	7	1	<0.001
	5	21	17	5	
Tearfulness	24	5	9	2	0.002
	8	20	18	2	
Anger or irritability	21	12	6	1	<0.001
	4	21	16	7	
Decreased interest in work, home, or social	25	9	4	2	0.066
activities	19	19	9	1	
Difficulty concentrating	24	12	4	0	<0.001
	11	25	11	1	
Fatigue or lack of energy	20	15	3	2	<0.001
	4	18	22	4	
Overeating or food cravings	20	8	12	0	<0.001
	6	11	16	15	
Insomnia or hypersomnia	27	5	6	2	<0.001
	8	24	13	3	
Feeling overwhelmed	31	5	3	1	0.003
	20	21	6	1	
Physical symptoms	15	18	5	2	<0.001
	4	20	18	6	
Work efficiency or productivity, home	30	7	3	0	<0.001
responsibility	11	29	8	0	
Social life activities	36	2	2	0	0.085
	36	9	3	0	
Relationships with coworkers or family	34	5	1	0	<0.001
	24	19	4	1	

Upper line, not disturbed (n = 40); lower line, disturbed (n = 48).

eight items (Table 4). We selected 'Age,' 'Equol non-producers,' 'Severe menstrual pain,' and 'Stress fracture,' because these factors were reported to be associated with the severity of PMS symptoms.[9,22] We further selected 'Participation in national or international competition,' 'Attendance of the lecture,' and 'Regular players' because these factors could influence the degree of interference. We also added 'Restriction of bodyweight' because this factor changed nutrition and might induce altered intestinal flora. Equol non-producers (odds ratio [OR], 3.34; 95% confidence interval [CI], 1.03–12.20) and restriction of bodyweight (OR, 4.94; 95%CI, 1.47–20.00) were shown to be significant risk factors for poor athletic performance. Age (OR, 0.56; 95%CI, 0.30–1.00) was associated with a decreased risk of poor performance in athletes.

Discussion

Our data showed that the prevalence of equol producers was 29.5% in this group. Our previous data showed that the prevalence of equol producers in reproductive-aged women in the general population was 41.8%.[22] The prevalence of equol producers in this athlete group seemed to be lower than that of women in the general population. This might come from the difference in the ages of the participants. The mean age of this study was younger than that in the previous study (19.8 ± 0.91 vs 35.8 ± 6.6 years). In fact, as shown in the Results section, the prevalence of equol producers in young adult women in the general population was the same as that in our population. The prevalence of equol producers in younger men in Japan is reportedly lower than that in older men.[28] Our data were in accordance with this report.

Table 4 Multivariate analysis of risk factors for interference with athletic performance due to premenstrual symptoms

Risk factors	OR (95%CI)	*P*
Age	0.56 (0.30–1.00)	0.049
Equol non-producers	3.34 (1.03–12.20)	0.045
Severe menstrual pain	2.99 (0.57–19.42)	0.199
Participation in national or international competition	2.28 (0.53–10.74)	0.272
Regular players	2.75 (0.86–9.22)	0.087
Restriction of bodyweight	4.94 (1.47–20.00)	0.009
Stress fracture	6.52 (0.97–130.92)	0.054
Attended the lecture	0.73 (0.20–2.53)	0.623

CI, confidence interval; OR, odds ratio.

Diet may change the bacterial population and then affect equol production.[20] Asian soy-rich dietary habits are considered to work in favor of equol production. Equol producers also report that they have higher physical activity than non-producers.[29] Thus, we expected that the prevalence of equol producers in athletes would be much higher than that in young adult women in the general population. However, our results fell short of these expectations. In general, athletes are expected to have healthy lifestyles in comparison with non-athletes, but their dietary habits are not always healthy. They tend to prefer to eat a high-rate of animal protein and a high-fat diet in the belief that this will lead to better performance. Such a Western-style diet may lower the capacity of equol production.

Multivariate analysis revealed that equol non-producers were associated with an increased risk of poor athletic performance. Equol producers could help to alleviate PMS-induced disturbances in athletic performance by two mechanisms. First, equol may be beneficial for PMS. One previous report demonstrated that isoflavone supplementation had beneficial effects on the relief of PMS symptoms.[30] Second, equol may be beneficial for improving athletic performance. Soy–whey supplementation for the improvement of athletic performance has been reported in a rat exercise model.[31] Further studies are needed to confirm the precise mechanism.

Multivariate analysis also revealed that restriction of bodyweight was associated with an increased risk of poor athletic performance. Restrictive eating patterns induce biased nutrition and may lead to the deficiency of micronutrients, such as calcium and vitamin D. It has been reported that both factors are dysregulated in PMS/PMDD patients, and supplementation of these factors has beneficial effects for the relief of PMS symptoms.[32–34] Restriction of bodyweight will lead to energy insufficiency and trigger menstrual dysfunction.[35] Energy insufficiency could induce chronic malnutrition and result in poor athletic performance.[36]

It should be recognized that our study has several limitations. The main limitation was that the study was of a cross-sectional design. It was impossible to determine causality, that is, whether these risk factors were a cause or effect of poor athletic performance. A second limitation was that our data – besides equol production status – were based on self-reporting; therefore, the study was susceptible to recall bias. The third limitation was the small sample size. The soy

challenge test required soy food to be consumed twice a day, and then the collection of first morning urine samples. These procedures might be bothersome for collegiate athletes and this might lessen their participation rates. A larger multicenter study will be necessary to overcome this limitation.

Despite these limitations, the findings from our study have several strengths. We collected data from female athletes with regular menstruation. Furthermore, we defined the PMS symptoms precisely according to the criteria for PMDD in the DSM. There are reportedly more than 150 symptoms related to PMS, so it is very important to define PMS symptoms clearly. These will enable the evaluation of PMS status precisely.

Our data showed a relation between interference from premenstrual symptoms and equol production status in athletes. It might be useful to analyze whether equol has positive effects for the alleviation of PMS-induced interference in athletic performance. A natural S-equol supplement was reported to be effective for the treatment of menopausal symptoms without any serious side-effects.[37] Dietary interventions might be the safest treatment strategy for athletes, in which case there would be no problems in regards to doping tests. Further research, including a placebo-controlled study, is warranted to confirm the effect of equol.

To the best of our knowledge, this is the first study to refer to the equol production status in athletes. The prevalence of equol producers was 29.5% in collegiate female athletes, which is as low as the rate in young adult women in the general population. Equol nonproducers and restriction of bodyweight were associated with an increased risk of poor athletic performance. We should monitor nutritional factors for PMS-induced disturbances in athletic performance.

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Disclosure

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