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Clinical Usefulness of Korean Red Ginseng in Postmenopausal Women with Severe Climacteric Disturbance

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Abstract : The aim of this study is to evaluate clinical usefulness of Korean red ginseng (RG) on various postmenopausal syndromes. Total plasminogen inhibitor-1 (tPAI-1) in peripheral blood from 9 postmenopausal women with climacteric syndromes (CS) was measured before and 3 months after treatment with daily oral administration of 6 g RG and that from 8 postmenopausal women without any CS was also measured as healthy controls. Blood samples were collected in the early morning on the bed-rest. Psychological conditions of postmenopausal women with CS were measured before and 3 months after treatment with RG using simplified menopausal index (SMI). In addition, OKETSU (blood stagnation) syndrome scores and KI deficiency (generalized energy stagnation) scores proposed by Terasawa *et al.*, were recorded before and 3 months after treatment with RG in postmenopausal women with CS and in healthy postmenopausal women. OKETSU syndrome scores and tPAI-1 levels in postmenopausal patients with CS were significantly ($P<0.001$ and $P<0.01$) higher than those in healthy postmenopausal women without CS. Similarly, SMI scores and KI deficiency scores in postmenopausal patients with CS were about three-fold higher than those without any CS. When RG was administered for 3 months, KI deficiency scores and OKETSU scores as well as SMI scores declined around the levels of healthy postmenopausal women. Although tPAI-1 levels significantly ($P<0.05$) decreased after treatment with RG, those did not reach the levels of healthy postmenopausal women. Clinical usefulness of administration of RG to postmenopausal women with CS was confirmed from evaluation not only by modern medicine but also by traditional KAMPO medicine.

Key words : Climacteric syndromes, Korean red ginseng, simplified menopausal index, OKETSU syndromes, total plasminogen inhitbitor-1, KI deficiency.

INTRODUCTION

Many menopausal symptoms have been considered to be resulted from estrogen deficiency during the climacteric. However, menopause accompanies not only estrogen deficiency but also a decrease of somatomedine by somatopause and a decrease of corticosteroid by adrenopause. Accordingly, there seems to be no psychological symptoms specific to the menopause.[1] Many women who have menopausal symptoms seek alternative or complementary remedies in stead of using estrogen alone.[2] Alternatives to estrogen have been consistently used by women, often supported by health care providers and promoted by the lay press. However, limited acceptable alternatives to hormone replacement therapy exist for use by postmenopausal women. The use of complementary therapies is receiving increasing alternative medicine within the United States.[3] A 12% use of herbal medicine in a survey of postmenopausal women has been reported.[4] In vitro studies have demonstrated estrogen-like actions of herbs, and case reports have reported uterine bleeding with herbal therapies.[5] A number of investigators are currently conducting clinical trials to assess the efficacy of herbal therapies for menopausal symptoms.

Korean red ginseng (RG) used in the present study has been reported to have multi-potential activity, including estrogenic action,[6] anti-stress action,[7,8] and immunostimulative action.[9] We have reported improved effects of RG on psychological functions in postmenopausal women.[10] In the present study, we attempted to determine effects of RG on climacteric syndromes using not only Western medical parameters such as simplified menopausal index (SMI) scores and total plasminogen inhibitor-1 (tPAI-1) but also traditional KAMPO medical

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Table 1. Patients' characteristics.

Patients	No.	Age	BW	BMI	Years after menopuse
Patients without CS	8	51.3±2.3[a]	49.0±2.6	21.3±1.0	2.1±1.5
Patients with CS[b]	9	51.2±2.4	49.0±3.9	20.2±1.4	2.3±1.2

[a]Mean±SD, BW:body weight (kg), BMI:body mass index
[b]Patients with severe climacteric syndrome (CS) were treated with daily oral administration of Korean red ginseng (6 g/day) for 3 months.

parameters such as KI deficiency scores and OKETSU syndrome scores proposed by Terasawa *et al.*[11]

MATERIALS AND METHODS

Patients' characteristics enrolled in the present study are summarized in Table 1. Age of women without climacteric syndrome (CS) and with CS was 51.3±2.3 (mean±S.D.) and 51.2±2.4, respectively. Body mass index (BMI) and years after menopause were 21.3±1.0, 2.1±1.5 and 20.2±1.4, 2.3±1.2, respectively. These values did not show statistically significant difference between both groups. Patients with CS were treated with daily oral administration of 6 g Korean red ginseng (RG) for 3 months with signed informed consents, while women without CS were not treated.

Blood samples were drawn in the early morning on the bed-rest and fasting state. Plasma was separated immediately and frozen at -80°C for future analysis. Total plasminogen activator inhibitor-1 (tPAI-1) in peripheral blood was measured using latex photometric immuno assay (LPIA) system (Diayatron Co. Ltd., Tokyo, Japan)[12] to assess state of blood stagnation in patients with CS.

Patients with CS and women without CS were assessed with the use of the simplified menopausal index (SMI), modified Kupperman's indices,[13] KI deficiency scores and OKETSU syndrome scores proposed by Terasawa *et al.*[11]

In order to determine the effect of RG in patients with CS, plasma tPAI-1 levels, SMI, KI deficiency scores and OKETSU syndrome scores after treatment with RG were compared to those before treatment and those of women without CS. Statistical analysis was performed using unpaired or paired Student's t-test.

RESULTS

Scores of OKETSU syndromes which have been considered in KAMPO medicine to be associated with blood stagnation were significantly ($P<0.001$) higher in postmenopausal patients with CS (58.3±7.3) than in healthy postmenopausal women without CS (42.0±4.1). After treatment

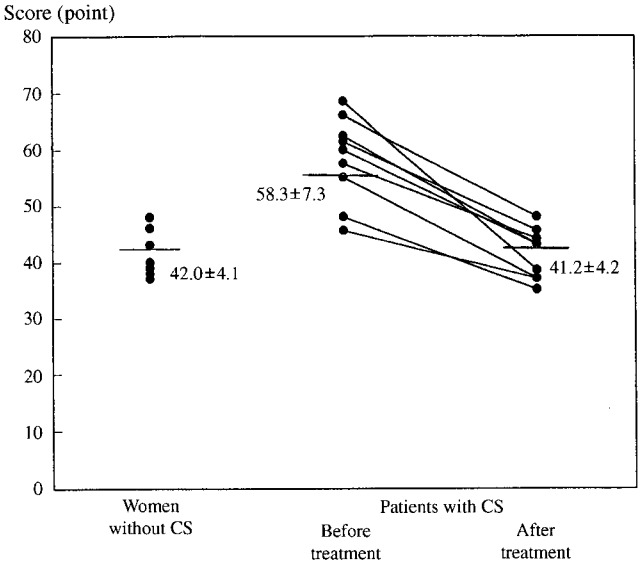

Fig. 1. OKETSU score in postmenopausal women without CS and the effect of RG on OKETSU score in postmenopausal patients with CS. Horizontal bar shows the mean average.

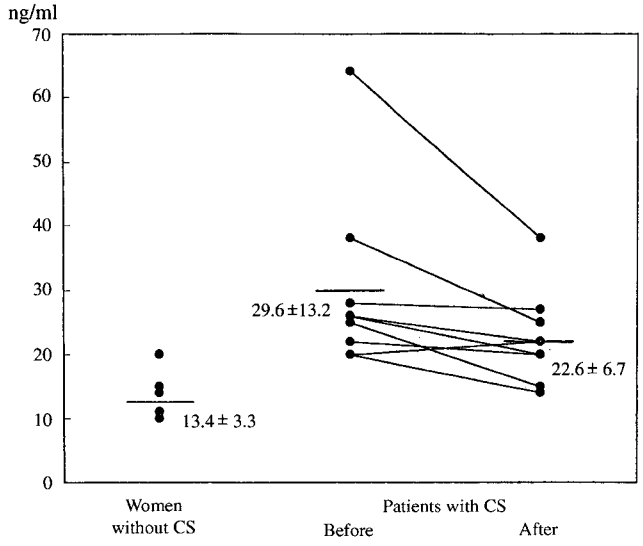

Fig. 2. Plasma total PAI-1 levels in postmenopausal women without CS and the effect of RG on plasma total PAI-1 levels in postmenopausal patients with CS. Horizontal bar shows the mean average.

with RG the scores significantly (P<0.001) decreased to levels (41.2±4.2) comparable to healthy postmenopausal women (Fig. 1). When used plasma tPAI-1 levels as a parameter of OKETSU syndromes, the plasma tPAI-1 levels (29.6±13.2) before treatment with RG were significantly (P<0.001) higher than those (13.4±3.3) of postmenopausal women without CS. After treatment with RG, the plasma tPAI-1 levels (22.6±6.7) significantly (P<0.01) decreased but did not reach healthy control levels (Fig. 2). SMI scores (66.6±6.0) in postmenopausal patients with CS were also significantly (P<0.001) about 3-fold higher than those (21.8±2.9) in postmenopausal women without CS. After treatment with RG, those (28.4±2.5) significantly (P<0.001) declined around the healthy control levels (Fig. 3). Similarly, although KI deficiency (generalized energy stagnation) scores (60.9±7.0) in postmenopausal patients with CS were significantly (P<0.001) about 3-fold higher than those (22.3±3.9) in postmenopausal women without CS, those after treatment with RG significantly (P<0.001) decreased and showed around healthy control levels (Fig. 4). These data are summarized in Table 2.

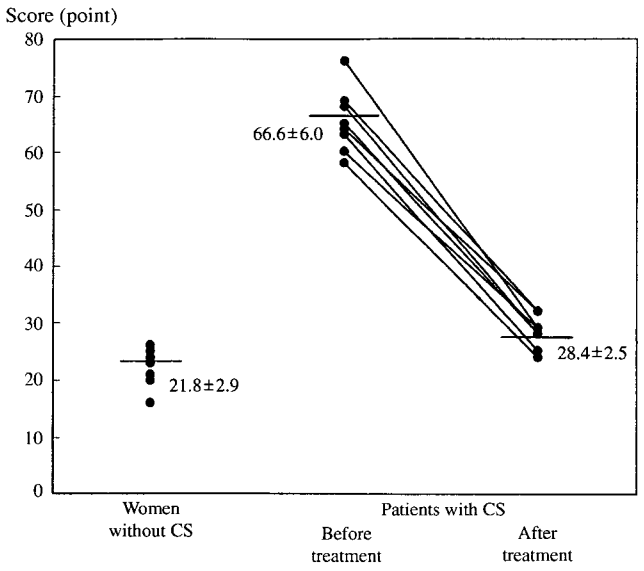

Fig. 3. SMI score in postmenopausal women without CS and the effect of RG on SMI score in postmenopausal patients with CS. Horizontal bar shows the mean average.

Discussion

All postmenopausal women accompany not only

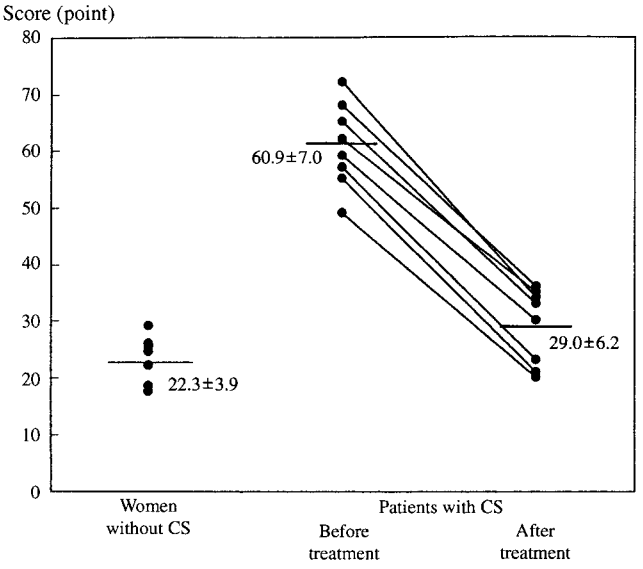

Fig. 4. KI deficiency score in postmenopausal women without CS and the effect of RG on KI deficiency score in postmenopausal patients with CS. Horizontal bar shows the mean average.

Table 2. Comparison of OKETSU score, t-PAI-1 level, SMI score and KI deficiency score in postmenopausal women without and with climacteric syndrome (CS) and those changes before and after treatment with Korean red ginseng (RG)

Parameters	Healthy women[a](8)	Before treatment[b]	After treatment
OKETSU score	42.0±4.1[c]	58.3±7.3[d,e]	41.2±4.2
t-PAI-1 level	13.4±3.3	29.6±13.2[f,g]	22.6±6.7[h]
SMI score	21.8±2.9	66.6±6.0[d,e]	28.4±2.5
KI deficiency score	22.3±3.9	60.9±7.0[d,e]	29.0±6.2

[a]Postmenopausal women without CS.
[b]Postmenopausal patients with CS were daily treated with oral aministration of 6 g RG for 3 months and each value was measured before and after treatment with RG.
[c]Mean±SD.
[d]P<0.001, compared to women without CS.
[e]P<0.001, compared to after treatment.
[f]P<0.01, compared to women without CS.
[g]P<0.05, compared to after treatment.
[h]P<0.05, compared to women without CS.

menopause but also somatopause and adrenopause. Accordingly, complaints of postmenopausal patients with CS are so complex, including not only hot flush and sweat which may be resulted from menopause but also psychologic dysfunctions which may be resulted from somatopause and adrenopause. In oriental KAMPO medicine, symptoms such as hot flushes, cool limbs and palpitation are defined as OKETSU syndromes. The OKETSU score in postmenopausal patients with CS was significantly ($P<0.001$) higher than that in healthy postmenopausal women without CS. If these patients were daily treated with 6 g RG for 3 months, the OKETSU score returned to that of healthy controls (Table 2 and Fig. 1).

Plasminogen activator inhibitor 1 (PAI-1) is the most important regulator of fibrinolysis.[14] Clinical studies have suggested a relationship between PAI-1 in plasma and thromboembolic disease.[15] Increased levels of PAI-1 have been demonstrated in atherosclerotic vessels.[16] It is hypothesized that PAI-1 has not only systemic but also local effects on the development of arterial thrombosis.[17] These conditions with hypercoagulation close resemble to the OKETSU syndromes. In fact, plasma PAI-1 levels changed with parallel to the OKETSU scores before and after treatment with RG (Fig. 1 and 2). Such improved effects of RG on blood stagnation (blood coagulation) may link to recovery of generalized energy stagnation so called KI deficiency. SMI (modified Kupperman's score) and KI deficiency scores in postmenopausal patients with CS were significantly about 3-fold higher than those in healthy postmenopausal women without CS (Table 2). When treated daily with 6 g RG for 3 months, these both scores returned to those in healthy controls (Fig. 3 and 4). Namely, changes of SMI (modified Kupperman's score) used in Western medicine close resembled to those of the KI deficiency scores in oriental KAMPO medicine. We have reported that effects of RG on stress-related hormones improve insomnia, frustration, depression and fatigue.[10]

Thus, we conclude that RG affects not only blood stagnation but also stress-related hormones and subsequently can improve various climacteric syndromes such as hot flush, sweat, palpitation, insomnia, frustration, depression, cool limb and fatigue.

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