Clinical Effectiveness of Korea Ginseng on Climacteric Disturbances and Its Possible Mechanism of Action

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Abstract The climacterium is that phase in the aging precess during which a woman passes from the reproductive to the non-reporductive stage. The signals, such as hot flashes, vaso-motoric disturbances, perspiration, stiff shoulders, emotinal symptoms, are referred to as climacteric disturbances. Treatment of climacteric symptoms centers around estrogen replacement and transquilizers, but ther are many problems to be solved to use these hormones/drugs as far as dossage, duration and complications are concerned. The care of women during the climacteric years should provide relief of distressing symptoms with as high a degree of safety as possible. From this view point, we used red ginseng powder to those patients with high menopausal index successfully. We studied its mechanism of action and proved that red ginseng improved the micro-circulation system via improvement of erythrocyte deformability which enhanced sex steroidgenesis consequently.

Introduction

The climacterium is that phase in the aging process during which a woman passes from the reproductive to the nonreproductive stage. The signals that this period of life has been reached are refered to as climacteric disturbance.

The climacteric disturbance is one of the most popular disease in the gynecological field. In fact, about 70% or more of the climacteric women suffer from the disease and 10 to 20% of them need to treat.

For the disease, there are such useful therapies as hormone therapy or drug therapies. Hormone therapy of estrogen replacement is more effective for the disease than anyother therapies either with tranquilizers or sedativas. But, there are many problems to be solved in the management with hormones. A more reasonable and yet clinically adequate therapy is required. From this view point, we studied effects of red ginseng powder on climacteric disturbance.

This study was supported by a grant provided by the Medical Society for Red Ginseng Research since 1986.

Materials and Methods

We studied of 83 women with climacteric disturbance on their climacteric or menopausal symptoms before and 8 weeks after administration of 6g red ginseng powder per day. The clinical effectiveness was expressed as % decrease of the menopausal index based on the questionnaire before and at 8 weeks after administration (Table 1). Gonadotropin of follicle stimulating hormone (FSH), prolactin (PRL) and ovarian sex steroids of esterone (E₁) and estradiol (E₂) were measured before and 4 or 8 weeks after administration of red ginseng powder.

Erythrocyte deformability was measured by a minor modification of the original method of Reid et al. Blood specimen obtained by venous puncture with a heparinized syringe was resuspended to the phosphate buffered saline of pH 7.4 as to make Ht 5%. Filterability was expressed as the volume (ml/min) of the specimen to pass through the polycarbonate sieve of nucleopore membrane with pore size $5\mu\phi$ under a negative pressure of $20 \, \mathrm{cm}$ of $\mathrm{H}_2\mathrm{O}$. ATP content in the erythrocyte was measured by a conventional method of ATP-Kit (Eiken, Japan).

Results and Discussion

After the menarch, gonadotropins, especially follicle stimulating hormone or FSH is secreted from the pituitary gland to the ovary. In the ovary, follicles grow up and secrete the major sex steroid of estradiol (E_2). FSH level closely related to or E_2 level, that is, a decrease of E_2 level in the blood causes a secretion of FSH from the pituitary. On the contrary, a increase of E_2 level causes a decreased secretion of FSH. There is a negative feedback system between pituitary and ovary.

During the reproductive stage, a slight increase of FSH level can give enough E_2 secretion from the ovary. However, with the menopause, FSH levels rise substantially due to the absence of the negative

feedback of ovarian steroids and possibly, inhibition of gonadotropin action. Thus, the hormone condition of the climacteric women is characterised by hyper-FSH and hypo-estrogenism, as shown in Fig. 1.

Alteration of menstrual function is usually the first clinical evidence of the climacterium. The average women goes through the menopause at 49 to 51 years of age. But there are a markedly wide individual variation ranging 37 to 57 years of age.

During the climacterium, they complain such symptoms as autonomic nerve disorder, vasomotoric symptoms, psycologic and emotional symptoms. For example, hot flashes, perspiration, stiff shoulders, palpitation, headache and so on, as listed in the quationaire (Table 1). With this questionnaire,

Table 1. QUESTIONNAIRE for subjective complaint

	Name:	, Age:		, W	eight:	K,	g, Hei	ght:	cm						
WI	Wks. after adominist.			-2-0			4				8				
Syn	mptoms/Seve	erity	8	2	1	0	8	2	1	0	8	2	1	0	Remarks

Hot flash

Hypersweat

Cold extremities

Irritable bladder

Abnormal sensation

Sleeplenssenss

Nervousness

Melancholy

Weariness

Stiff shoulder

Lumbago

Headache

Dizziness

Emesis

Palpitation

Stomach ache

Constipation

Diarrhea

Amenorrhea

Irregular cycle

Menorrhagia

Hypomenorrhea

Hypermenorrhea

Premenst, tension

Sexual disturbance

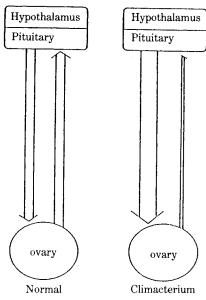


Fig. 1. Pathogenesis of climacterium

Table 2. Effect of Red Ginseng powder on climacteric complaints

Patients: 83 cases with climacteric disturbances Dosage: 6.0g/day for 8 weeks

Improvement of climacteric index

- %	80 ≦	~60	~30	~ 0	0>	Total	
No.	15	24	31	11	2	83	
(%)	(18.1)	(28.9)	(37.4)	(13.2)	(2.4)	(100)	

we studied effects of red ginseng power on menopausal symptoms of 83 women with climacteric disturbance.

As a result, ginseng was effective for 70 out of 83 patients (84.3%), whose menopausal symptoms decreased 30% or more as compared before and 8 weeks after (Table 2). Such marked effects of ginseng powder on menopausal women strongly suggested that it might relate to their ovarian function. We, hence, examined the various sex hormones before and after administration.

There was no change in prolactine (PRL) level and esterone (E_1) level. However, although there were no significant difference, we observed that FSH was tend to decrease and that E_2 was tend to increase²⁾ (Fig. 2).

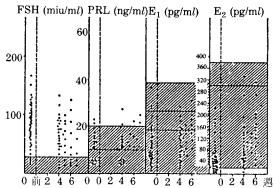


Fig. 2. Effect of Red Ginseng of endocrine system

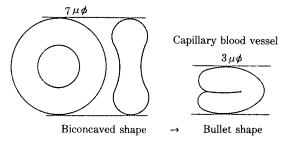


Fig. 3. Deformability of erythrocyte

This reason is not clear but ginseng might affect directly the pituitary gland to decrease FSH. However, it is more logical to consider that ginseng stimulated sex steroidgenesis in the ovary and accerelated the secretion of E_2 repressing the secretion of FSH. It may be due to a vasodilative action of ginseng, since many patients feel disappearing coldness in their extremities during administration of ginseng. The long acting of warmness is somewhat different from other vasodilators. Therefore, we studied its effects on a point view of erythrocyte deformability.

To maintain the microcirculation, red blood cell with a diameter of 7μ have to pass through the capillary vessel with a diameter of $3\mu\phi$. Red blood cell, therefore, is forced to deform its bi-concave shape to a bullet shape when it passes through peripheral tissues (Fig. 3).

In our earier study on a pathogenesis of hemolytic disease of the newborn, we proved that neonatal jaudice was caused not only by immaturity of liver function but also by immaturity of spleen function to allow aged or less deformable red cells

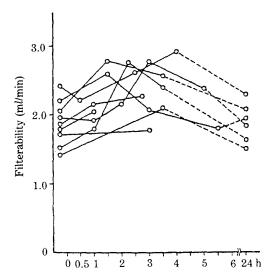


Fig. 4. Erythrocyte filterability after administration of Red Ginseng powder (4.5g)

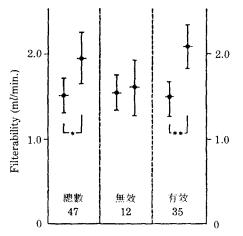


Fig. 5. Filterability after administration of Red Ginseng for one month.

to pass through narrow sieves in the spleen. 3-5)

Simulating the splenic structure, deformability or filterability was measured by using $5\mu\phi$ sized nucleopore membrane under a negative pressure of 20 cm H₂O. The fasting patients was given 4.5g ginseng powder and their erythrocyte filterability was measured pediodically.

As a result, filterability increased with a peak after 2-3 hours, and then returned to the initial value gradually (Fig. 4).

Besides, the filterability after administration of

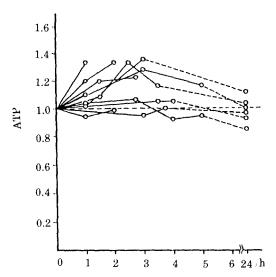


Fig. 6. ATP content in RBC after administration of Red Ginseng powder (4.5g)

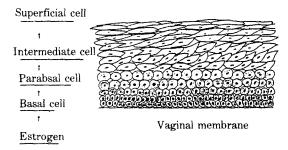


Fig. 7. Estrongen effect on the vaginal smear

ginseng for one month increased significantly. The most interesting and suggestive findings were that no significant difference was observed in the non-effective cases, while a significant increase was observed in the effective cases (Fig. 5).

In our earier studies³⁻⁵⁾, we observed that the deformability depended on pH, glucose level, temperature and ATP contents in the red blood cell. We, therefore, measured ATP contents before and after administration of ginseng powder pediodically. ATP levels was increased just after administration of ginseng and decreased gradually which coinsided with the pattern of deformability (Fig. 6).

Based on the effects of ginseng on the erythrocyte deformability, there was a possibility that the microcirculation in the ovary was improved and stimulated the steroidgenesis in the ovary, although

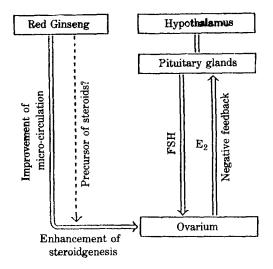


Fig. 8. Possible mechanism of action of Red Ginseng on climacteric disturbances

conventional hormone assays were failed to demonstrate significant changes 8 weeks after administration of ginseng powder. So, we studied it by a more sensitive biological method by means of the vaginal smear.

Genital organs, especially the vaginal membrane has receptors to estrogens. Estrogen proliferates basal membrane cells to superfitial cells (Fig. 7). We can easily differentiate it by staining, that is, the estrogen affected cell stains red by red ink, while the deeper cell stains blue by blue ink.

We could observed successfully the estrogen effects in the atrophic vaginal smear of the post-menopausal women by appearing intermediate and superficial cell which stained faint red.

The result obtained indicates that administration of red ginseng powder caused an increase of estro-

gen, although available hormone assays failed to detect. Hence, a possible mechanism action of red ginseng powder on the climacteric symptoms could be safely explained as shown in Fig. 8.

We believe that red ginseng is an ideal medicine to overcome the climacteric disturbance, since it may ensure endogeneous sex steroids in those climacteric women who came short of sex steroids by the ovary due to aging.

Acknowledgement

I appreciate Prof Young Dong Cho, President of the Society for Korean Ginseng, Prof. Woo Ik Hwang, Prof. Sung Dong Lee, Prof. Chong Hwa Lee, Prof. Soon Hee Lee, Prof. Sang Chul Shim, Prof. Kwang Tae Choi, Prof. Jae Seon Cho and Prof. Yong Nam Han for inviting me as a speaker in this esteemed International Symposium on Korean Ginseng. I am grateful to Korea Ginseng and Tabacco Research Institute and Japan-Korea Ginseng Co. Ltd. for supplying the authorized red ginseng powder.

Literature Cited

- 1. Reid, H.R. et al.: J. Clin. Pathol., 29, 855 (1976).
- Ogita, S.: Yakuyo Ninjin '89-Advances in foudamental and clinical studies-p.173, ed. Y. Yamamura and A. Kumagai, Kyouritu Shuppan, Tokyo (1989).
- 3. Ogita, S. et al.: Europ. J. Pediatr., 127, 67 (1978).
- 4. Ogita, S.: Sanfujinka Ketueki, 3, 69 (1979).
- Ogita, S.: Aged erythrocytes and neonatal jundice of the newborn. Shougai Sanfujinkagaku, ed. H. Murooka, Kanehara Shuppan, Tokyo (1984).