STUDIES OF CLINICAL EFFECTS OF GINSENG: 1ST REPORT; A DOUBLE BLIND STUDY OF UNSETTLED COMPLAINT-IMPROVING EFFECT OF GINSENG

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Introduction

In Japan, ginseng has long been used as a precious medicine effective for improvment of nutrition and reinforcement of vigor. Its action mechanism is said to improve the systemic condition in a variety of consumptive diseases and improve unsettled complaints through activating the resistance with which the living organism is endowed. For the purpose of demonstrating such claimed effects of ginseng from the standpoint of clinical medicine, we made a double blind study of the improvement rating of unsettled complaints with the drug.

Materials and methods

The test drug was Korean red ginseng powder capsule manufactured by Office of Monopoly Republic of Korea (hereafter referred to as KGC, each capsule containing 0.3 g of red ginseng powder). A placebo in capsule containing corn starch which had been confirmed as unidentifiable from the test drug beforehand was used as the control drug. Both the test drug and the placebo were used at an oral dosage of 3 capsules, 3 times a day, postprandially.

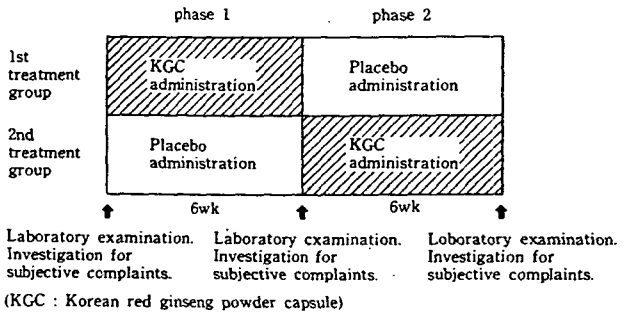
Table 1 shows the patients treated with the drug, classed by diagnosis, sex and age.

Table 1. Subjects

① Arteriosclerosis	9 cases
② Unsetteled Complaints	8 cases
③ Diabetes Mellitus	3 cases
④ Inactive Chronic Hepatits	3 cases
⑤ Collagen Disease	2 cases
⑥ Hypotension	2 cases
⑦ Livercirrhosis (conpensate stage)	1 case
⑧ Pulmonary Enphysema	1 case
⑨ Erythrodermia	1 case

sex / age	male	female	total
20～	0	3	3
30～	2	2	4
40～	4	1	5
50～	2	2	4
60～	3	4	7
70～	13	4	7
total	14	16	30
mean age	55.3 ± 15.0	53.1 ± 18.2	

The study schedule is presented on Fig. 1. The patients were allocated randomly to the lst and the 2nd treatment, and necessary investigations were made before, at specified stages of, and at the end of, the treatment.



(KGC: Korean red ginseng powder capsule)

Fig. 1. Schedule for the Trial

Table 2 shows the parameters investigated relating to symptoms. A total of 17 parameters, including general condition and symptoms in detail, were investigated.

Table 3 presents the questionnaire form handed to the patients. 7 levels (some in 5–6 levels) in questions which shown in Table 2. The patients were instructed to encircle the appropriate level of each question. After collection of the form filled in, the data were statistically analyzed.

The criteria for the evaluation of global effect of the drug and its effects on the evaluation parameters are shown on Table 4. The effects were evaluated in categories of marked effect, moderate effect, slight effect and no effect, with slight and better effects defined as indicating that the drug had been effective.

Table 2. Item of the question

①general condition	②fillings of fatigueness	③absent appetite
④sleeplessness	⑤coldness of the limb	⑥bowel movement
⑦palpitation	⑧short of brethness	⑨lumbago
⑩tinnitus	⑪vertigo and dizziness	⑫lightheadness
⑬stiffness in the the shoulder	⑭stiffness in muscles and joints	⑮headache
⑯pain in stomack	⑰abdominal dystension	

Table 3. Questionnaire(eliminated)

Results

Table 5 shows the global effects of the drug on symptoms.

Table 4.

The Criteria for the evaluation of global effects.

To evaluate KGC effect, plus, minus, or 0 points were given accordance with the change of symptom. (17 parameters, including general condition and symptoms in detail).

eg. As symptoms were improved 1 step in levels,..... + 1.
As symptoms were grow worth 1 step in levels,..... − 1.
As symptoms were unchanged..... 0.

Secondary, grand total of these points were calculated and the criteria were classified as follows.

marked effect .....degree of improvement were above 15 steps in levels.
moderate effect.....degree of improvement were above 10 steps in levels.
slight effect.....degree of improvement were above 5 steps in levels.
no effect.....degree of improvement were under 5 steps in levels and a case as no change or grow worth.

Degree of improvement were also evaluated for each symptoms. (except general condition).

marked effect.....degree of improvement were above 3 steps in levels.
moderate effect.....degree of improvement were above 3 steps in levels.
slight effect.....degree of improvement were above 2 steps in levels.
no effect.....degree of improvement is under 1 step and a case as no change or grow worth.

Table 5. Clinical Effects of KGC (Global Effects)

Treatments	Level of effect	marked effect	moderate effect	slight effect	no effect	total	P value	authorization methods
1 st treatment group (KGC → P)	Placebo	3	2	1	9	15	0.03	
			6 (40.0%)		(60.0%)	(100%)	<P<	
	KGC	5	3	4	3	15	0.05	Fischer's
			12 (80.0%)		(20.0%)	(100%)		method
2nd treatment group (P → KGC)	Placebo	1	1	0	13	15	0.001	
			2 (13.3%)		(86.7%)	(100%)	<P<	Fischer's
	KGC	2	3	4	6	15	0.002	method
			9 (60.0%)		(40.0%)	(100%)		
general evaluation	Placebo	4	3	1	22	30	0.001	
			8 (26.7%)		(73.3%)	(100%)	<P<	chy-square
	KGC	7	6	8	9	30	0.005	test
			21 (70.0%)		(30.0%)	(100%)		

KGC is prefer than placebo through 1st and 2nd treatment

KGC was evaluated as effective in 12 of the 15 patients of the lst treatment group (with an effective rate of 80%), whereas the placebo was evaluated as effective only in 6 of the 15 patients of the same group (with an effective rate of 40%). KGC proved preferable to the placebo at a less than 5% level of significance.

In the 2nd treatment group, KGC gave an effective rate of 60% (9/15 patients), while the placebo gave an effective rate of 13.3% (2/15 patients). KGC again proved preferable to the placebo at a less than 0.2% level of significance.

The global effects, combining the effects attained in both the 1st and the 2nd treatment group together, were that KGC gave an effective rate of 73.3% (21/30 patients) and the placebo, 26.7% (8/30 patients).

KGC thus proved preferable at a less than 0.5% level of significance.

Table 6 compares the preference for the 1st treatment with KGC administered first and the 2nd treatment with the placebo administered first.

An effective rate of 40% (6/15 patients) was attained during the placebo medication in the 1st treatment and 13.3% (2/15) in the 2nd treatment. The apparent effect of the placebo in the 1st treatment was greater. The effective rate during the KGC medication was 80% (12/15) in the 1st treatment, and 60% (9/15) in the 2nd treatment: the apparent effectiveness of KGC was thus greater in the 1st treatment. The hypothetical difference between the 2 treatments was, however, great than 10%: therefore, it was discouraged.

Table 6. Comparison of Preferbility between 1st and 2nd Treatment

Classifications	Treatment	No. of case	No. of improved case	rate of improved case	P value	authorization by Fischer's method
Placebo phase	1st treatment group	15	6	40.0%	$0.1 < P < 0.2$	NS
	2nd treatment group	15	2	13.3%		
KGC phase	1st treatment group	15	12	80.0%	$0.1 < P < 0.2$	NS
	2nd treatment group	15	9	60.0%		

No significant preferbility were find out between 1st and 2nd treatment.

Table 7. Classified improvement rates of symptoms (No. 1) 1st + 2nd treatment, KGC phase

Item of symptom	No. of the patient which had the symptom	marked effect	moderate effect	slight effect	total	no effect	improvement rate
fillings of fatigueness	28	3	2	11	16	12	57.1%
absent of appetite	26	4	0	6	10	16	38.5
sleeplessness	22	4	3	3	10	12	45.5
coldness of the limb	27	1	2	11	14	13	51.9
bowel movement	29	0	4	4	8	21	27.5
palpitation	22	3	2	5	10	12	45.5
short of brethness	21	4	1	7	12	9	57.1
lumbago	19	3	3	6	12	7	63.2
tinnitus	9	0	0	2	2	7	22.2
vertigo and dizziness	20	1	4	6	11	9	55.0
lightheadness	17	4	2	4	10	7	58.8
stiffness in the shoulder	26	1	6	11	18	8	69.2
stiffness in muscles and joints	20	1	2	9	12	8	60.0
headache	21	5	2	9	16	5	76.2
pain in the stomack	17	2	4	2	8	9	47.1
abdominal dystension	20	1	1	5	13	7	65.0

Therefore, a conclusion was drawn that the preference for KGC did not change with the treatment schedule, i.e., whether KGC or the placebo preceded the other.

Table 7 shows the classified improvement rates of symptoms as a result of KGC treatment.

KGC gave rise to a 50% more effective rate in almost all symptoms, especially high improvement rates in headache (and dull headache) (76.2%) and stiff shoulder (69.2%).

On Table 8, the classified improvement rates of symptoms with the placebo medication are shown. The placebo gave rise to a 50% or more effective rate only against stiffness in muscles and joints.

Table 9 presents the principal laboratory findings before and after the treatment with KGC and the placebo. No abnormalities for which KGC or the placebo seemed responsible were found, nor did any adverse effect of either medication manifest.

Discussion

In Occidental medicine effects of drugs have usually been discussed in terms of the effects on target organs, whereas in Oriental medicine diseases are not, in principle, understood to be abnormalities of individual organs only but an overall imbalance of the living organism. From such a viewpoint, we have been trying to make an approach to the specificity of individual diseases one after another, with the improvement rating of unsettled complaints as a clue, in discussing the clinical effects of red ginseng powder.

The present study provided objective evidence that red ginseng powder is a drug which improves a vast variety of symptoms and is safe. Because the targets for evaluation of effects were subjective symptoms, it was presumed that there would be some effect of medication sequence when KGC and the placebo were crossed over. However, KGC proved statistically preferable in either medication sequence.

When KGC was administered first as in the 1st treatment, its effects manifested rapidly, and remained even during the placebo medication period to a certain extent. On the other hand, when the placebo was administered first as in the

Table 8. Classified improvement rates of symptoms (No. 2) 1st + 2nd treatment, placebo phase

Item of symptoms	No. of the patient which had the symptom	marked effect	moderate effect	slight effect	total	no effect	improvement rate
fillings of fatigueness	28	0	4	6	10	18	35.7
absent of appetite	26	3	0	4	7	19	26.9
sleeplessness	22	1	3	3	7	15	31.8
coldness of the limb	27	1	3	4	8	19	29.6
bowel movement	29	1	2	3	6	23	20.7
palipitation	22	2	0	4	6	16	27.3
short of brethness	21	1	2	3	6	5	28.6
lumbago	19	0	1	2	3	16	15.8
tinnitus	9	0	0	1	1	8	11.1
vertigo and dizziness	20	0	4	4	8	12	40.0
lightheadness	17	2	0	3	5	12	29.4
stiffness in the shoulder.	26	1	3	8	12	14	46.2
stiffness in muscles and joints	20	0	3	10	13	7	65.0
headache	21	3	1	6	10	11	47.6
pain in the stomack	17	1	4	1	6	11	35.3
abdominal dystension	20	0	2	3	5	15	25.0

Table 9. Bloodchemical studies

		before administration	after administration of placebo	after administration of KGC
RBC × 10^4	(/mm^3)	432.3 ± 74.3	427.9 ± 70.9	435.8 ± 83.2
WBC	(/mm^3)	6122 ± 1274	6231 ± 1230	6315 ± 1746
T. P	(g/dl)	6.9 ± 0.7	7.1 ± 0.6	7.3 ± 1.4
Al-P	(KAU.)	7.9 ± 4.2	7.8 ± 3.9	8.2 ± 4.1
LDH	(u.)	363.8 ± 91.6	353.3 ± 71.4	355.3 ± 65.8
Cholesterol	(mg/dl)	182.1 ± 39.3	184.4 ± 36.9	177.8 ± 36.7
S-GOT	(u.)	23.2 ± 7.8	22.2 ± 7.2	23.8 ± 8.7
S-GPT	(u.)	19.1 ± 15.4	15.6 ± 13.0	21.0 ± 15.2
BUN	(mg/dl)	14.9 ± 2.8	15.5 ± 3.0	15.1 ± 4.3
FBS	(mg/dl)	131.2 ± 68.9	116.0 ± 43.0	107.6 ± 34.7

Mean ± SE, F test Ns.

2nd treatment, the placebo was hardly effective, and when the KGC medication was started, its effects manifested slowly. KGC thus exhibited clinically interesting characteristics that it was infallibly effective, and that its effects were relatively long-lasting.

Summary

From its effects on a variety of symptoms, red ginseng powder proved clinically usable as a therapeutic for many diseases.

Chairman: Now the time is open to discussion.

Questioner: It is not a question. In relation to Dr. Kaneko's presentation, I'd like to show a preliminary data on ginseng effect on brain circulation. The blood flow of the internal cardiartery and artery constantly increased by muscle administered with 4.5 gram of red ginseng per day for one week. It's just a preliminary report and the work is going on and another point Dr. kaneko's data on plasma lipid and lipoprotein is quite agree with our data.