

Experimental and Clinical Study of Korea Red Ginseng Treatment on Hypertension

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ABSTRACT

1. Experimental study

Preventive effect of Korea Red Ginseng (KPG) on hypertensive retinal arteriolosis in rabbits was studied. The results as follows:

Blood pressure: Hypertensive group (B) was obviously raised up in comparing with that in normal group(A) and in hypertension + KRG group(C).

Ocular fundus: Changes in B group including the retinal arteriospasm, crossing arterioveous, exudation and edema. But C group showed lightly.

Light microscope: HE stained vascular damage in retina including thickness hyalimisation, exudates and edema.

Electron microscope: The endothelial cells were arranged irregularly, different shape and showed cytoplasm loose and vacuole.

Immunohistochemistry: Ginseng can regulating endothelin-1, angiotension-II, endothelium grow factor expression and secretion in retinal blood circulation.

2. Clinical Study

66 of hypertensive patients(42 men, 23 women, 48-68 years old)and 20 normal person (7 men, 13 women, 47-68 years old) were administrated(P.O.) by KRG (3g per day for 6 weeks). The results showed that marked effective rate and total effective rate were 53% and 60.6% respectively and no severe side effects were found.

The above results suggest that Ginseng has a definite hypotensive effect and a role of preventing hypertensive arteriosclerosis.

Introduction

Hypertension and hyperlipidemia are known as established risk factor for coronary heart disease (CHD). Some antihypertensive agents may cause unwanted increase in TC., TG. of plasma or

decrease in HDL-c of plasma. In our previous study, we demonstrated that KRG could reduce TC, TG, and increase HDL-c of plasma in patients with hyperlipidemia. The goal of the present study was to investigate the effect of KRG on hypertensive patients and rabbits.

Materials and Methods

I. Experimental study

Animal and KRG: Japanese white rabbits, male, age of 4-6 months were purchased from Experimental Animal Center of Chinese Medical Science Academy, The powder of Korea Red Ginseng was provided by Korea Ginseng & Tobacco Res. Institute.

1. Hypertensive model

The bilateral-renal arteries of rabbits were narrowed with 0.8mm diameter silver clip which caused a part renal of stricture and 2 weeks later, blood pressure of the rabbits rose and maintained in a high level.

2. Groups and treatment of KRG

We divided 22 rabbits into three groups: A group (normal) had 6 rabbits, B group(hypertensive model) 10 rabbits, C group(B+KRG) 6 rabbits. The rabbits of C group were fed with rabbit's feed with KRG(2g/day) at 14 days after operation. They were killed separately 10th, 15th, and 20th. Weeks.

3. Blood pressure

We measured blood pressure on rabbit's ear artery with sphygomanometer once a day before operation and twice a week after operation

4. Examination of ocular fundus

We observed ocular fundus of rabbits with fundscope once a week and took photograph with lown Rc-Xv camera once a month.

5. Retinal pathology

The eye balls of the rabbits were fixed in 10% formalin or 2.5% glutaraldelyde. The balls were opened in a plane with the serrata and then vitrous was gently removed, retinal vascular area and underlying choroidal were excised. The specimens were dehydrated in ascending concentration of alcohol, embedded in paraffin wax, sectioned and stained with HE method.

6. Examination of electron microscope

Specimens of the eye balls were fixed in 1% asmic acid. A part of them were embedded by EPON 812 and observed under transmission electron microscope. Using critical point drying method, another parts were clad in material of LB-3 and observed under scanning electron, microscope (SEM).

7. Immunohistochemistry

With the Image-analyzer Carring on quantative analysis about endothelin-1(ET-1), angiotensin-II(ANGII) and endothelium growth factor(EGF).

II. Clinical study

1. Subject selection

66 patients (42 men and 23 women, 46-68 years old) and 20 normal persons(7 men and 13 women, 47-68 year old) were selected for KRG treatment. The differentiation of Traditional Chinese Medicine in patients was: Type I: Hyperactivity of Liver Fire. Type II: Hyperactivity of Yang due to deficiency of Ying. Type III: Dificiency of both Ying and Yang. Type IV: Damp-heat excess in interor.

All patients were refrained from taking any medicine at least 1 month before the study. All patients were free from liver, renal and other major organ disease. The woman who were pregnant or lactating were exluded.

2. Administration of KRG

Patients was administered with KRG(9g per day) by P.O. for 6 weeks. Routine examinations, including lipoprotein, CPK, blood sugar, electrocardiogram, echocardiam, Ultrosonography found-scope *et al.*, were performed to each patient before and after adminstration. Ocular fundus of some patients was observed with fundscope and took photograph with lown Rc-Xv camera once a month.

3. Standard of evaluation

The standard of evaluation made by the Ministry of Health of China is

1) Remarkable effect

A: Diastolic blood pressure(DBP) decreased more than 10 mmHg (1.3KPa) and riached normal range.

B: DBP not reached normal range but decreased more than 20 mmHg(2.7KPa)

2) Moderate effect

A:DBP decreased less than 10 mmHg(1.3 KPa) but reached normal range.

B:DBP decreased 10-19 mmHg(1.3-2.5 KPa) but not reached normal range.

C:SBP decreased more than 30 mmHg(4KPa)

Patient reaching one of the parameter is considered positive

3) Non effect: Not reached above parameter

4. Statistical methods

All data are expressed as mean+SD. The statistical analysis was performed by using T test. Differences were considered to be significant when $P < 0.05$.

Results

I. Results of experimental study

1. Blood pressure(BP)

As Fig.1 shown that BP of the rabbits in A group were maintained at a range of 4.6-5.8 KPa.; in B group, BP rose obviously in 2 weeks after operation, 2-3 KPa higher than that of A group. BP of the rabbits in C group was lower than that of B group in six weeks after operation. The peak value of BP in C group was 8.5 Kpa, while in B group that was 11 KPa.

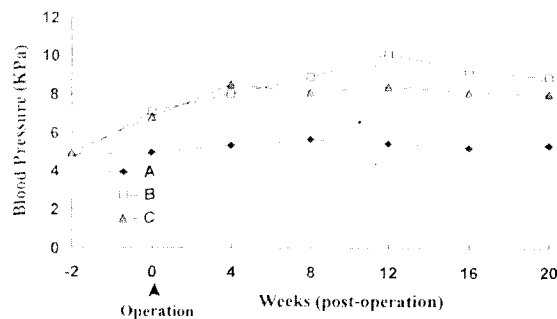
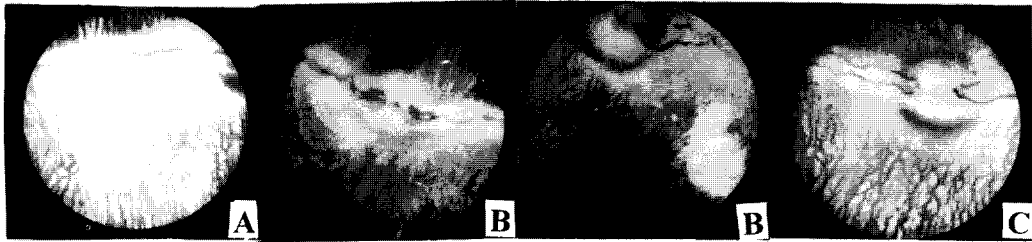


Fig.1, Effect of Ginseng on Blood Pressure of Renal Hypertensive Arteriosclerosis of Rabbits

2. The result of examining ocular fundus

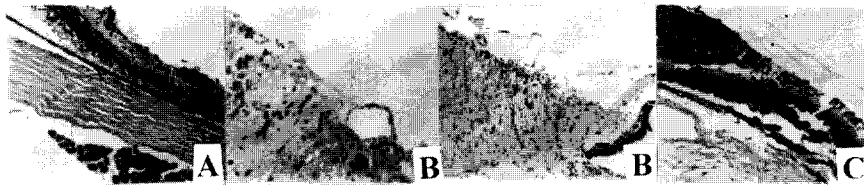
As photograph 1 shown that on 4 weeks post-operation, the rabbits in B group appeared the retinal arteriospasm and local choroidal anemia changes. On 8 weeks post-operation, they showed obviously crossing arteriovenous(A-V), exudation and edema around arteriola. After 12 weeks post-operation, their arteriolas showed white wire, the whole post-retinal exudate, a few piece of hemorrhage and choroidal newborn capillary formed compensatively and irregularly. but in C group, there were only changes of arteriospasm and crossing A-V. This result indicated that Ginseng could reduce the ocular fundus changes induced by hypertension.



Phot.1, Effect of Ginseng on retinal arteriole changes
 (The result of fundusoscopic observation)

3. The result of pathology

As photograph 2 shown that the changes of retinal vascular, included arterioli thickness, hyalini-sation, edema and infiltration of white blood cells red blood cells moved around vessel wall, were found in the rabbits in B group. In C group, the retinal vascular changes were very light, similar to that in A group.



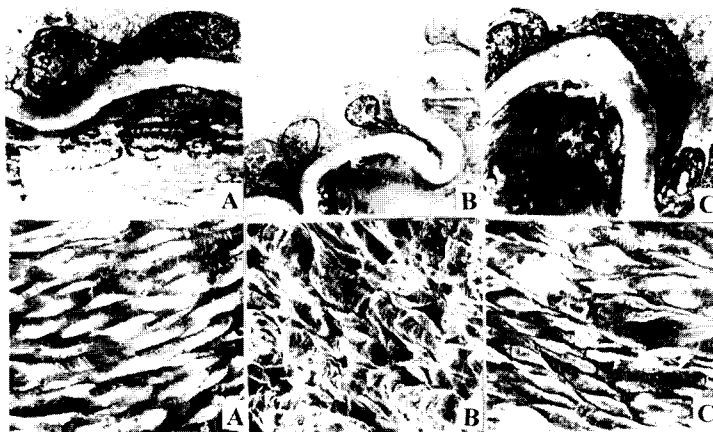
Phot.2, Effect of Ginseng on the retinal vascular changes
 (The result of pathology)

4. The result of electron microscope

The result of transmission electron microscope appeared that epithelial cells in retinal vascular or B group changed from shuttle to round, protruding into the vessel, and the vacuole denaturation was found in the cytoplasm. The shape and construction of epithelial cells in C group were normal, as similar as that in A Group(photograph 3).

The result of scanning electron microscope showed that in B group, shape of endothelial cells changed, larger or smaller than in A group. Their arrangement was irregular and the gap junction were disappeared. There were some white blood cells, platelets adhered on the surface of vessel;s wall. In C group, most of endotuelial cells arranged shuttle and regular. There were gap junction between cells. Only a few of cells were different in scope and shape(photograph 4)

These results suggest that Ginseng could prevent hypertensive arteriosclerosis of rabbits.



Phot.3 & 4, Effect of Ginseng on the retinopathy
(The result of electron microscope)

5. The result of immunohistochemistry

As shown in Table 1, Ginseng regulating ET-1, ANG-II and EGF expressing and secretion in retinal blood circulation. This may be the mechanism of Ginseng lowering the blood pressure.

II. Results of clinical study

1. Efficacy analyses

According to the evaluative standard made by the Ministry of Health of China, remarkable effective rate and total effective rate were 53% and 60.6% respectively (Table 2). There was a significant difference in BP of the patients between before and after administrating KRG but not in that of normal person (Table 3). Comparing effective rate with differentiation (stage) by Western Medicine, we found that the total effective rates in the patients with type III and IV or stage I were more than that in the patients with type I and II or stage II and III, especially in elder patient (table 4, 5). Observing ocular fundus of some patients with funduscope, we found that 52% of patients with changes of ocular fundus improved (table 6). After treatment with KRG, the symptoms of hypertensive patients improved (table 7).

2. Side effect possibly related with KRG

The results of laboratory examination and symptoms of the hypertensive patients administrated by KRG showed that there were no significant changes in laboratory parameters and no severe side effects (table 8, 9).

Table 6. Effect of ginseng on eyeground of hypertension

	Before trial cases(%)	6 weeks non-change cases(%)	6 weeks improvel cases(%)
Thinness of artery	18(72)	9(36)	9(36)
Bleeding and exudation	4(16)	2(8)	2(8)
Edema of optic papilla	3(12)	1(4)	2(8)
Total	25(100)	12(48)	13(52)

Table 7. Effect of ginseng on symptoms of hypertensive patients

symptoms	Total cases	Improvement	Rate(%)
Tinnitus	35	18	51
Dysphoria	33	23	70
Hyperhidrosis	21	18	86
Lumbocrural Pain	52	35	67
Palpitation	32	27	84
Short breath	33	26	79
Oppressed Feeling in Chest	30	21	70
Intolerance of Cold	20	17	85
Flushing	22	12	55
Diarrhea	13	10	77
Nocturia	31	11	35
Headache	43	31	72
Dizziness	59	47	80
Insomnia	43	24	56
Amnesia	48	12	25
Dreaminess	34	12	35
Xerocheilia	35	22	63

Discussion

We studied the preventive effects of KRG on the experimental hypertension of rabbits by oral administration of KRG. The blood pressure of hypertension+KRG group was lower than that of hypertension group. The results of optical microscope and electroscope suggested that KRG has a role of preventive hypertensive effect. This results were our basic for clinical study.

In recent years, pharmacologic effects of KRG in cardiovascular system have been studied deeply and widely. In present paper, we investigated the effect of KRG on hypertensive arteriosclerosis by means of experimental and clinical study. The results of clinical study showed that KRG could decrease BP of the hypertensive patients. The remarkable effective rate and total effective rate were

Table 8. Changes of laboratory parameters before and after treatment of ginseng

	Before trial (mean + SD)	3 Weeks (mean + SD)	6 Weeks (mean + SD)
U. protein	0.16 + 0.50	0.06 + 0.19	0.03 + 0.10
U. Glu.	0.09 + 0.51	0	0
BUN(mmol/L)	17.39 + 5.39	17.18 + 4.11	16.19 + 3.46
Crea(mmol/L)	1.10 + 0.39	1.03 + 0.16	0.98 + 0.19
UA(mmol/L)	5.73 + 1.47	5.07 + 1.47	5.34 + 1.31
CHO(mmol/L)	189.85 + 32.28	187.58 + 46.88	175.44 + 32.16
TG(mmol/L)	160.08 + 71.39	169.16 + 82.15	152.64 + 78.88
LDL-c(mmol/L)	112.40 + 30.93	103.32 + 28.99	108.57 + 26.60
HDL-c(mmol/L)	44.63 + 12.98	45.32 + 16.63	45.63 + 11.29
Glu.(mmol/L)	99.88 + 44.34	96.48 + 20.74	92.82 + 13.40
K(mmol/L)	4.21 + 0.44	4.08 + 0.35	4.17 + 0.32

Table 9. Side effect possibly related with ginseng in 86 cases

symptoms	Cases with effect	Rate(%)
Increased BP	5	5.8
Nose bleeding	1	1.2
Dizziness	1	1.2
Insomnia	3	3.5
Dry mouth with bitter taste	2	2.3
Hyperhidrosis	3	3.5
Tinnitus	2	2.3
Fatigue	1	1.2
Palpitation	1	1.2

53% and 60.6% respectively

Comparing effective rate with differentiation (types) by Traditional Chinese Medicine (TCM) and with differentiation (stage) by Western Medicine, we found that the total effective rates in the patients with type III and IV or stage I were more than that in the patients with type I and II or stage II and III, especially in elder patient. 52% of hypertensive patients with changes of ocular fundus improved and the symptoms of hypertensive patients improved after treatment with KRG. The results of laboratory examination and symptoms of the hypertensive patients showed that there were no significant changes in laboratory parameters and no severe side effects.

In our previous study, we demonstrated that KRG could increase HDL-c and decrease TC. TG. of plasma in the patients with hyperlipidemia. Combining with the result of this study, we consider that KRG therapy is effective in improving the lipid profile and blood pressure without appreciable adverse effects.

Conclusions

In this study KRG had a certain effect in preventing retinopathy of hypertensive arteriosclerosis. KRG was well tolerated and effective on lowering blood pressure during treatment with hypertension.

Acknowledgement

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