

# Clinical Efficacy of Korean Red Ginseng for Erectile Dysfunction -Multi-national Approach

Hyung Ki Choi, Young Deuk Choi and Woong Hee Lee

*Department of Urology, Yonsei University College of Medicine, Seoul, Korea*

## ABSTRACT

Ginseng has been used in maintaining physical vitality all over the East Asian countries and recently its metabolism and actions on neurologic, cardiovascular and endocrinologic systems are being elucidated. Korean red ginseng (KRG) has been used in various ailments, and to prove its efficacy for erectile dysfunction an international study on Asians other than Korean was performed.

Patients with borderline organic and psychogenic erectile dysfunction were included. KRG were given daily, and placebo were given as controls. Treatment lasted a total of 3 months. Surveys including libido, erectile potency, the sexual satisfaction were given. Serum testosterone and erectile function study were taken. Among the 23 patients with KRG, 18 patients were followed. Four had diabetes, 2 hypertension, 3 hypercholesterolemia, 1 low testosterone, 4 psychogenic, and 4 idiopathic. In 10 patients with placebo, 7 were followed for more than three months.

The clinical efficacy of KRG was 66.7% on objective questionnaire and 72.2% on subjective analysis. When KRG were given, all parameters surveyed have shown improvements compared to the controls. Serum testosterone levels were normalized in 2 patients with KRG, whose serum testosterone levels were reduced from pre-study. When the erectile functions after audiovisual stimuli evaluated using Rigiscan in 6 patients with KRG, 4 showed rigidity more than 70%. One patient reported constipation, and 2 gastric upsets in the KRG group. In conclusion, KRG has beneficiary action on male erectile capabilities with minimal side effects. Thus KRG has been proven effective in Koreans, and results on other Asians is pending. The exact action mechanism and the active ingredients in KRG need to be studied.

**Key words:** Korean red ginseng, erectile dysfunction, efficacy

## Introduction

Sexual dysfunction encompasses a broad spectrum of conditions ranging from erectile dysfunction, ejaculatory dysfunction to sensory abnormality. Among them, the erectile dysfunction in the most common problem facing patients and physicians. Recently, rapid industrialization, prolongation of life expectancy, increased prevalence of degenerative diseases, and above all more open atmos-

phere concerning sexual performances all contribute to the steep rise of number of patients visiting erectile dysfunction clinics.

Recently great strides were made in the research of erectile dysfunction, in etiology, diagnosis, and treatment. Some of currently available treatments for erectile dysfunction are eradication of underlying diseases, systemic pharmaceutical therapy, endocrine therapy, psychotherapy, intracavernosal vasodilator injection, vacuum devices and penile prosthesis. These methods are limited by its suboptimal efficacy or invasiveness. Most erectile dysfunction patients are more willing to undergo noninvasive medical treatment such as psychotherapy rather than invasive therapies. Yohimbin, an adrenergic agonist, apomorphine, a dopamine receptor agonist, and trazodone which acts on the serotonin receptors are the commonly used drugs today, but these drugs often exhibit unwanted side effects, and most of all its effectiveness is only about 50%. An ideal drug should be orally absorbed, highly effective, and without any detrimental effect. If any successful research discovering or producing such drug which will maintain homeostasis with minimal complication will be monumental on the long, colorful history of the quest for aphrodisiacs.

Ginseng is a time-proven herb medication for general stimulation of health and sexual powers. Today, many researches found out the mysteries behind the active ingredients and pharmacological action mechanisms of the honored herb. Korean red ginseng is a widely used herb remedy for various diseases. Recently it is under extensive investigations to elucidate the exact analysis of its active ingredients, and tried in clinical studies for other diseases. However, there have been few attempts in the field of erectile dysfunction to utilize ginseng as a valid therapy. Traditional oriental herb treatment and centuries of clinical observations have led to the widespread belief that the Korean red ginseng can be a valuable alternative to the currently available therapeutic modalities.

We have previously found that KRG had profound relaxation effect in *in vitro* experiments with rabbit and rat corpus cavernosum. Thus to elucidate the efficacy of Korean red ginseng in treating erectile dysfunction, and to develop a natural drug without complications, the results of ginseng treatments are compared to placebo. These therapeutic trials were carried out not only for Koreans, but also for other Asians in a multinational experimental effort.

## **Materials and Methods**

### *A. Subjects*

Patients visiting urologic clinic at Yongdong Severance Hospital, Yonsei University College of Medicine (Seoul, Korea) due to erectile dysfunction underwent basic medical history and physical examinations, complete blood profile, SMA-12, testosterone, and prolactin. Those who were highly suspected of having organic dysfunction on audiovisual stimulatory (AVS) radioisotope penogram, duplex ultrasonography, and nocturnal penile tumescence studies were excluded.

## *B. Experimental designs*

### 1. Experimental model

Patients who were with informed consents about the study, were randomly assigned into two groups. Group A received daily dose of six tablets (one tablet contains 300 mg of Korean red ginseng extracts) and group B received placebo equivalent. All patients received drugs for three months if there were no drug-related complications.

### 2. Parameters

#### 1) Effects on sexual functions

All patients were surveyed on their self-reported status of sexual desire, quality of erection, ejaculation, sexual performance, and satisfaction rate of intercourse. The same questionnaire were filled out after the treatment of KRG.

#### 2) Changes in serum testosterone levels

In the patients after three months of treatment, the level of testosterone was measured again.

#### 3) Changes in erectile function

In the patients after three months of treatment, the AVS penogram was taken again and rigidity and duration of erection was compared.

#### 4) Complications

Complications were evaluated at the monthly visits to the clinic. At the end of the treatments, SMA-12 were repeated for changes in biochemical profiles. Any complications the patients have experienced were carefully recorded and evaluated.

### 3. *Determination of clinical efficacy of KRG*

Clinical efficacy of KRG was determined by the monthly visits to the clinic, which included the baseline survey similar to the one performed at the start. Each category had points from 1 to 5, 5 being the most satisfactory state. If post-treatment score was improved from the initial survey, it was determined as effective. Final determination of efficacy was based on the summation of each category.

### 4. *Statistics*

Using Stat Works and SPSS program on a personal computer, the therapeutic results were compared with Chi-square test, and categories on surveys were compared using Student' s t-test. When p value was smaller than 0.05, it was regarded as significant.

## Results

In the Korean arm of the study, the 23 patients were enrolled to the study and 18 were followed. Four had diabetes, 2 hypertension, 3 hypercholesterolemia, 1 low testosterone, 4 psychogenic, and 4 idiopathic. In 10 patients with placebo, 7 were followed for more than three months. Patients characteristic and their respective etiologies for erectile dysfunctions are as shown (Tables 1 and 2). The mean ages of the patients of the group A, B were  $43.4 \pm 6.7$  years (ranges: 26-56),  $45.2 \pm 8.7$  years (26-59), respectively. The duration of inflication was  $4.2 \pm 2.4$  years (ranges: 1-30),  $4.5 \pm 2.3$  years (1-30), respectively.

**Table 1.** Patient characteristics

	Ginseng	Placebo
No. Patient starting study	23	10
No. Patient follow up >3month	18	7
Mean Age* (years)	$43.4 \pm 6.7$	$45.2 \pm 8.7$
Duration of onset*	$4.2 \pm 2.4$	$4.5 \pm 2.3$
No. Marriage	18	7
Smoking	15	7

**Table 2.** Etiologies of erectile dysfunction

	Ginseng (n=18)	Placebo (n=7)
DM	4	1
HiBP	2	1
Psychogenic	4	2
Low testosterone	1	
Idiopathic	4	3

\* Values are expressed as mean  $\pm$  SED

No statistically significant differences between each group ( $p > 0.05$ )

### 1. Therapeutic efficacy of KRG on survey

In patients with KRG, changes by questionnaires in libido, erection, ejaculation, sexual activity, satisfaction were 50.0%, 66.7%, 55.6%, 55.6%, 61.1%, respectively, which were significantly higher than that of placebo groups ( $p < 0.05$ ). In patients with KRG, result reported by the patients in libido, erection, ejaculation, sexual activity, satisfaction were 83.3%, 72.2%, 61.1%, 61.1%, 40.0%, respec-

tively, which were significantly higher than that of placebo groups ( $p<0.05$ ). The improvement after KRG administration was 66.7% on objective questionnaire and 72.2% on subjective analysis. When KRG were given, all parameters surveyed have shown improvements compared to the controls (Table 3).

**Table 3.** Comparison of improved patients by each symptoms in questionnaires.

Symptom	% of improved patient in questionnaires	
	Ginseng (n=18)	Control (n=7)
<b>Libido*</b>	50.0	14.3
Result by patient	83.3	14.3
<b>Erection*</b>	66.7	28.6
Result by patient	72.2	14.3
<b>Ejaculation*</b>	55.6	14.3
Result by patient	61.1	14.3
<b>Sexual activity*</b>	55.6	28.6
Result by patient	61.1	42.8
<b>Satisfaction*</b>	61.1	28.6
Result by patient	40.0	14.3
<b>Total</b>	66.7	25.0
<b>End result by patient</b>	72.2	37.5

\* : Sum of each presenting portion

Result by patient means patient rate of his effect after medication and improve state is more than “4” in questionnaires.

Statistically significantly difference are noted in all categories between ginseng group and placebo group ( $p<0.05$ ).

## 2. Effect on serum testosterone

In two patients the serum testosterone levels were below normal range before treatments. It was normalized after treatment. In other patients the testosterone levels increased, but without statistical significance ( $p>0.05$ ). There was no significant change in the level of serum testosterone in control group.

## 3. Effect on penile erection

Among the ten patients receiving KRG 6 underwent evaluation of the erectile functions using Rigiscan. Four showed rigidity greater than 70%. Five exhibited increased rigidity with longer erection duration after treatment. The remaining one patients did not show significant change.

#### 4. Complications

Among the ten patients receiving KRG, one constipation, and 2 gastric upsets were reported. Among the 9 with placebo, 3 reported gastric upsets.

### Discussion

Korean red ginseng (KRG) is reported to be having various pharmacological effects on protein, fat and nucleic acid metabolism, endocrine, neurologic, cardiovascular and gastrointestinal systems. Ginseng also as beneficiary effect on diabetes, hypertension, hypercholesterolemia, and aging and all theses entities are well known to adversely affect male erection. KRG improves peripheral circulation, which also can aid penile erection.

KRG is a time-honored aphrodisiac in the Orient and recent studies have proven such effects on serum testosterone and sexual performances. Some proposed that decrease in sexual intercourses due to chronic stress can be prevented by the administration of KRG. We have previously reported the therapeutic efficacy of KRG on patients with erectile dysfunction. We also have previously found that KRG had profound relaxation effect in *in vitro* experiments with rabbit and rat corpus cavernosum.

In peripheral microvasculature, the role of nitric oxide (NO) is receiving more attention. NO increases the free calcium concentration in endothelial cell, which activated guanylate cyclase increasing cyclic GMP. This is a key mechanism in vascular smooth muscle relaxation. *In vitro* experiments have shown that KRG affects this relaxation mechanism. When KRG was administered for a considerable period, the activity of NO and vascular relaxation increases. The single most important step in penile erection is the relaxation of cavernosal smooth muscles. Thus it is obvious that ginseng plays a vital role in erection. In this experiment, among the ten patients receiving KRG 6 underwent evaluation of the erectile functions using Rigiscan. Four showed rigidity greater than 70%. Five exhibited increased rigidity with longer erection duration after treatment. This is a solid objective clinical evidence proving the effect of ginseng.

The administration of Korean red ginseng showed significant increase in early detumescence, rigidity, general erectile profiles, and patient and partner satisfactions. 60% of studied patients reported improvement in their erectile ailments. A previous study with ginseng on rats has failed to show improved sexual functions, but supporting result of another study which has showed that 55% effectiveness compared to 40% of control group is also available. The mechanism of ginseng in erec-

tion can be summarized as the combination of vasodilation, anti-depression, anxiolytic (anti-stress), microvascular flow improvement action. If further researches are made on the effects of saponin and other constituents of ginseng and clearer picture of erectile mechanisms are available, more effective methods of treating erectile dysfunctions could be found.

## Conclusions

In conclusion, KRG has beneficiary action on male erectile capabilities with minimal side effects. Thus KRG has been proven effective in Koreans, and results on other Asians is pending. The exact action mechanism and the active ingredients in KRG need to be studied.

## References

- Brindley GS. Pilot experiments on the actions of drugs injected into the human corpus cavernosum penis. *Br J Pharm* 1986; 87 (3) : 495.
- Bush JP. Disorders of ejaculation. In Bennett AH Eds.: *Impotence: Diagnosis and management of erectile dysfunction*. Philadelphia. Saunders Co., 1994. p186.
- Choi HK, Seong DH, Rha KH. Clinical efficacy of Korean red ginseng for erectile dysfunction. *Int J Impotence Res*. 1995 (7) ; 181-186.
- Choi KJ. Effect of ginseng in blood flow and circulation. *Ginseng Research* 1989; 2: 34.
- Choi YD, Xin ZC, Choi HK. Effect of Korean red ginseng on the rabbit corpus cavernosal smooth muscle. *Int J Impotence Res*, 10 (1), 37-43, 1998
- Fovaeus M, Andersson KE, Hedlund H. Effects of some calcium channel blockers on isolated human penile erectile tissue. *J Urol* 1987; 138: 1267.
- Gerber GS, Levine LA. Pharmacological erection program using prostaglandin E1. *J Urol* 1991; 146: 786.
- Goldstein I, Krane RJ. Diagnosis and therapy of erectile dysfunction. In: Patrick C. Walsh, Alan B. Retik, Thomas A. Stamey and E. Darracott Vaughan, Jr., editors. *Campbell' s Urology*. 6th ed. Philadelphia, Saunders, pp.3033, 1992.
- Goldstein I, Payton T, Padma-Nathan H. Therapeutic roles of intracavernous papaverine. *Cardiovasc Interven Radiol* 1988; 11: 237
- Hah JS, Kang BS, Kang DH. Effect of *Panax ginseng* alcohol extract on cardiovascular system. *Yonsei Medical Journal* 1978; 19: 11.
- Holmquist F, Andersson K-E, Fovaeus M, Hedlund H. K<sup>+</sup>-channel openers for relaxation of isolated penile erectile tissue from rabbit. *J Urol* 1990; 144: 146.
- Kim N, Azadzo KM, Goldstein I, Tejada IS. A nitric oxide-like factor mediate nonadrenergic-non-

- cholinergic neurogenic relaxation of penile corpus cavernosum smooth muscle. *J Clin Invest* 1991; 88: 112.
- Lee LM, Stevenson RWD. Prostaglandin E1 versus phentolamin/papaverine for the treatment of erectile impotence: A double blind comparison. *J Urol* 1989; 141: 549.
- Lue TF, Tanagho EA. Physiology of erection and pharmacological management of impotence. *J Urol* 1987; 137: 829.
- Lue TF. Physiology of erection and pathophysiology of impotence. In: Walsh, PC, Retik, AB, Stamey TA and Vaughan, Jr. ED, editors. *Campbell's Urology*. 6th ed. Philadelphia, Saunders, pp.709, 1992.
- Montorsi F, Guazzoni G, Bergamaschi F, Dodesini A, Rigatti P, Pizzini G, Miani A. Effectiveness and safety of multidrug intracavernous therapy for vasculogenic impotence. *Urology* 1993; 42 (5) : 554.
- Morales A, Condra MS, Owen JE, Fenemore J, SurrIDGE DH. Oral and transcutaneous pharmacological agents in the treatment of impotence. *Urol Clin North Am*, 1988; 15: 87.
- Morales A, Heaton PW: The medical treatment of impotence: An update. *World J Urol*, 1990; 8:80,.
- Padma-Nathan H, Goldstein I, Payton T, Krane RJ. Intracavernous pharmacotherapy: The pharmacological erection program. *World J Urol* 1987; 5: 160.
- Rajfer J, Aronson WJ, Bush PA, Dorey FJ, Ignarro LJ. Nitric oxide as a mediator of relaxation of the corpus cavernosum in response to nonadrenergic, noncholinergic neurotransmission. *New Engl J Med* 1992; 326 (2) : 90.
- Sarosdy MF, Hudnall CH, Erickson DR, Hardin TC, Novicky DE. A prospective double blind trial of intracorporeal papaverine versus prostaglandin E1 in the treatment of impotence. *J Urol* 1989; 141: 551.
- Tejada IS, Blanco R, Goldstein I, Azadzi K, Morenas A, Krane RJ, *et al*. Cholinergic neurotransmission in human corpus cavernosum. I. Responses of isolated tissue. *Am J Physiol* 1988; 254: H459.
- Tejada IS, Kim N, Lagan I, Krane R, Goldstein I. Regulation of adrenergic activity in penile corpus cavernosum. *J Urol* 1989; 142: 1117.
- Tong YC, Broderick G, Hypolite J, Levin RM. Correlations of purinergic, cholinergic and adrenergic functions in rabbit corporal cavernosal tissue. *Pharmacology* 1992; 45 (5) : 241.
- Virag R, Shoukry K, Floresco J, Nollet F, Greco E. Intracavernous self-injection of vasoactive drugs in the treatment of impotence: 8-year experience with 615 cases. *J Urol* 1991;145:287.