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> FILE: • Korean White Ginseng (*Panax ginseng*) • Alzheimer's Disease • Cognitive Performance

> > HC 100381-364

Date: November 14, 2008

RE: Korean White Ginseng Improves Cognitive Performance in Patients With Alzheimer's Disease

Lee S-T, Chu K, Sim J-Y, Heo J-H, Kim M. *Panax ginseng* enhances cognitive performance in Alzheimer disease. *Alzheimer Dis Assoc Disord*. July-September 2008;22(3):222-226.

The modern pharmacologic effects of ginseng and its components, ginsenosides, have been demonstrated in the cardiovascular, endocrine, and immune systems.¹ Also, ginseng has been reported to increase the cognitive performance of healthy persons.²⁻⁵ For Alzheimer's disease, investigators have examined the neuroprotective and tropic effects of ginseng in experimental models. These authors report on their investigation of Korean white ginseng's (*Panax ginseng*) effect in enhancing the cognitive function in patients with Alzheimer's disease.

They conducted a prospective, open-label study at the Seoul National University Hospital in South Korea from June 2004 until October 2005. Ninety-seven patients who met NINDS-ADRDA (National Institute of Neurological Disorders and Strokes, and Alzheimer's Disease and Related Disorders Association) criteria for probable Alzheimer's disease were included (aged 47 to 83 years).

The authors excluded patients who had evidence of other neurodegenerative disorders or cognitive impairments resulting from acute cerebral trauma, dysthmia, hypoxic cerebral damage, vitamin deficiency, infection, cerebral neoplasia, metabolic disease, mental retardation, oligophrenia, or a coexisting medical condition that could prevent them from completing the study.

The patients were randomly assigned to the ginseng group (n=58; 20 men and 38 women) or to the control group (n=39; 15 men and 24 women). The ginseng group was treated with Korean white ginseng powder (4.5 g/d of 6-year-old *Panax ginseng* roots from Hongcheon and Heongsung provinces in South Korea, powdered and encapsulated by Nonghyup Co., South Korea) for 12 weeks. According to the authors, the ginseng contained total 8.19% of ginsenosides, plus essential oils, diacetylenic compounds, acidic polysaccharides, phenolic compounds, peptidoglycans, amino acids, vitamins, and carbohydrates.

To evaluate possible dose-response effect, an additional 9 patients were administered a higher dose of ginseng (9 g/d).

After the 12-week period of ginseng treatment, the patients were monitored for another 12 weeks.

To evaluate cognitive functions, the authors used scores on the mini-mental state examination (MMSE) and Alzheimer's disease assessment scale (ADAS), including the ADAS cognitive subscale (ADAS-cog) and noncognitive subscale (ADAS-noncog). Efficacy variables included changes of MMSE and ADAS from baseline scores at 4, 12, and 24 weeks after the start of treatment.

The authors report that efficacy analyses were primarily preformed on an intention-to-treat (ITT) basis; a per-protocol analysis was also done. Intergroup comparisons for changes from baseline in ADAS and MMSE scores were performed using the Student's *t* test. They used repeated measures analysis of variance to compare the raw MMSE and ADAS scores in addition to the comparison of the changes from baseline. The frequencies of side effects and withdrawn patients were compared by using chi-square test. All P values are two-tailed; statistical significance was accepted for P values <0.05.

At 4 weeks, 91 patients (54 in the ginseng group, 37 in the control group) were reevaluated and included in the efficacy analysis. Eighty-two patients (50 in the ginseng group, 32 in the control group) completed 12 weeks of treatment, and 58 patients (ginseng group, 36; control group, 22) were reevaluated at 24 weeks after the treatment began.

Baseline characteristics including age, sex, ADAS cog, ADAS-noncog, MMSE and clinical dementia rating scale scores were similar between the 2 groups.

The authors report improved MMSE scores in the ginseng group on the efficacy analysis. At 4 weeks, the ginseng group showed an improvement in MMSE score by 1.0 ± 2.4 points from the baseline, whereas the control group changed by -0.58 ± 2.4 points (P = 0.033 between the 2 groups). At 12 weeks, the ginseng group improved by 1.8 ± 2.8 points, whereas the control group changed by only -0.03 ± 3.1 (P = 0.009 between the 2 groups). However, after the 12-week period of ginseng discontinuation, no difference was observed between the 2 groups (control = 0.88 ± 2.5 , ginseng = 0.56 ± 3.6 , P = 0.673).

ADAS-cog scores were also improved in the ginseng group at 4 weeks and at 12 weeks after the ginseng treatment compared with the control group on ITT basis. And, again, after the ginseng had been discontinued for 12 weeks, the differences between the ginseng and control groups disappeared.

In contrast, say the authors, the ADAS-noncog scores, which represent neuropsychiatric symptoms, showed no significant difference between the ginseng and control groups on ITT basis at 4 weeks, 12 weeks, or at 24 weeks.

According to the authors, the repeated measures analysis of variance revealed that at 4 weeks, the ginseng group showed an improvement in ADAS-cog score compared with the control group after

adjusting the baseline values. At 12 weeks, the ginseng group showed improvements in both ADAScog and MMSE scores after adjusting the baseline values.

The ADAS-cog and ADAS-noncog and MMSE changes for the 9 patients treated with 9 g/d of the ginseng powder for 12 weeks were not different compared with those treated with 4.5 g/d of ginseng.

Adverse events (reported by 7 of the 58 patients in the ginseng group and 6 of the 39 patients in the control group) were mild and transient.

Among the limitations of this study are the small number of patients involved, the short duration, and the fact that because this was an open-label study, the effect of the ginseng was not relative to a placebo.

According to the authors, these results suggest that Korean white ginseng is clinically effective in the cognitive performance of patients with Alzheimer's disease and that longer-term, placebo-controlled, double-blinded studies are warranted.

-Shari Henson

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Editor's Note: It is rather curious that this Korean research group has published a parallel study with Korean red ginseng (see HC 090381.362), but neither that publication nor the one here reviewed cite the other. The two manuscripts were received by the respective journals on September 11 and November 14, 2007. Unexpectedly, there seems to have been no significant difference in effectiveness between white and red ginseng, whereas the latter would have been expected to be superior. The efficiency of conversion from white to red bears investigation.

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