Cognitive improvement by ginseng in Alzheimer’s disease

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(Received November 11, 2006; Accepted March 5, 2007)

Abstract: Ginseng shows protective and trophic effects in neurodegenerative diseases in experimental models, and showed cognitive improvement in normal population. To investigate the efficacy of ginseng in patients with Alzheimer’s disease, patients, who met NINDS-ADRDA criteria for AD were studied. Subjects were randomly assigned to ginseng group and control group, and ginseng group was treated with Korean white ginseng powder (4.5 g/day) for 12 weeks. Efficacy variables included changes in mini-mental status exam (MMSE) and cognitive subscales of Alzheimer’s disease assessment scale (ADAS-cog) at 4 weeks and 12 weeks. Baseline MMSE and ADAS scores showed no difference between the two groups. Results showed that ginseng improved ADAS-cog compared to the control group at 12 weeks (p<0.05). MMSE was also increased by ginseng treatment compared to the control at 12 weeks (p<0.01). This study suggests the symptomatic efficacy of ginseng in patients with Alzheimer’s disease.

Key words: Ginseng, Alzheimer’s disease, mini-mental status exam (MMSE), Alzheimer’s disease assessment scale (ADAS)

INTRODUCTION

Alzheimer’s disease (AD) is the most common cause of dementia. AD shows a progressive decline of memory and intellectual abilities, which eventually becomes severe enough to interfere with functioning in daily living, the overall quality of life, and ultimately leads to death. Although pharmacologic treatments are currently approved for treating mild- to moderate AD using acetylcholinesterase inhibitors (ACEI) and one NMDA antagonist, memantine, for advanced AD, the therapeutic efficacies need to be further improved.

Ginseng has been used to treat a wide variety of medical conditions, including age-related memory impairment for a long time. Pharmacologic effects of ginseng and its component have been demonstrated in the CNS and in cardiovascular, endocrine and immune system.1) Recent experimental evidences suggest protective and tropic effects of ginseng in AD and ginseng was suggested to be beneficial in relation to symptomatic treatment and neuroprotection in age-associated cognitive disorders.2)

Thus, we investigated whether ginseng treatment can improve the cognitive function of AD patients.

METHODS

Subjects and methods.

Study was designed as randomized, prospective, and open-label study. Ninety seven consecutive patients (aged 47 to 83 years, mean=66.1±9.1), who met NINDS-ADRDA criteria for AD were included. After subjects were randomly assigned to ginseng group and control group, ginseng group were additionally treated with Korean white ginseng powder (Panax ginseng; n=58). Both Ginseng group and control group continued the conventional therapy (control group, n=39) for 12 weeks. At 4 weeks, 91 patients (ginseng group=54, control group=37) were re-evaluated and included in the efficacy analysis. Efficacy variables included changes from baseline scores of mini-mental status exam (MMSE) and Alzheimer’s disease assessment scale - cognitive subscale (ADAS-cog scored

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0-70) at 4 weeks and 12 weeks.

All eligible patients (or a legal representative) and the
caregiver provided written informed consent to participate
in the study, which was approved by institutional review
boards of Seoul National University Hospital.

**Statistical analysis.**

Efficacy analyses were done on an intention-to-treat (ITT)
basis. Changes from baseline scores of ADAS and
MMSE showed normal distribution. Inter-group compar-
sions for changes of ADAS and MMSE were performed
using the Student-t test. P values are two-tailed and statis-
tical significance was accepted for p values<0.05.

**RESULTS**

A total of 82 patients (50 ginseng, 32 control) com-
pleted all 12 weeks of treatment. Baseline characteristics
including sex and mean age, as well as the baseline
ADAS-cog and MMSE score were not different between
ginseng and control groups (Baseline ADAS-cog: 20.8±
8.5 in the control group, 21.9±9.3 in the ginseng group;
Baseline MMSE: 22.0±3.9 in the control group, 21.5±3.8
in the ginseng group). The proportion of patients with-
drawn did not differ significantly for control group
(17.9%) versus ginseng group (13.9%) (p=0.581, Chi-
square test). No treatment emergent condition and no
treatment-related death were reported.

Efficacy analysis showed that ginseng group improved
ADAS-cog score compared to control group at 4 weeks
(Changes from baseline, Control = +1.1±3.9, Ginseng
group = -4.2±4.1, p = 0.012), and at 12 weeks (control =
-0.45±6.0, Ginseng group= -3.3±5.3, p = 0.029).

MMSE also showed improvement in ginseng group.
Baseline MMSE of were 22.0±3.9 in control group, and
21.5±3.7 in ginseng group (p=0.435). At 4 weeks, ginseng
group showed an improvement of MMSE by 1.0±2.4
points from baseline, while control group changed by
-0.58±2.4 (p=0.033). At 12 weeks, ginseng group improved
by 1.8±2.8 points, while control group changed by
-0.03±3.1 (p=0.009).

**DISCUSSIONS**

In this study, we investigated the effect of ginseng treat-
ment on the cognitive function of AD, and found that
administration of ginseng to AD patients can further
improve the cognitive function scales including ADAS-
cog and MMSE.

The major active constituents of the *Panax* genus are
also thought to be saponins, in this case species-specific
triterpenoid glycosides known as ginsenosides, of which
over 30 individual examples have been identified. Among the variable ginsenosides, Rb1 is often used to
represent the panaxadiol ginsenosides, whereas Rg1 re-
presents the panaxatriol ginsenosides. The different spe-
cies of ginseng have been shown to have different relative
amounts of panaxadiols and panaxatriols. American
ginseng has the smaller ratio of Rg1/Rb1, and Asian gins-
eng has the larger ratio of Rg1/Rb1. We used Asian
ginseng, because Rg1 is reported to be a neuronal stimulant and Some evidence shows that ginsenosides can stimulate the cognitive function. Ginsenosides have the ability to intercalate into the plasma membrane due to their amphipilic in nature, can alter membrane function.
and secondarily alter membrane receptor function.\(^1,^5\) Ginseng has high agonistic affinity for the nicotinic receptor.\(^3\)

In addition, neuroprotective and neuro-regenerative property of ginsenosides are also well investigated. Ginseng showed efficacy in reduction of A\(_\beta\) level\(^7,^8\), and the associated memory loss.\(^9,^{10,11}\) Ginsenosides have antioxidant properties and the ability to scavenge free radicals.\(^12,^{13,5}\) Ginsenosides can increase proliferation and differentiation of neural progenitor cells in dentate gyrus of hippocampus of normal adult mice.\(^14\) Increase of expression of brain derived neurotrophic factor, Bel-2 and antioxidant enzyme, enhanced new synapse formation, inhibition of apoptosis and calcium overload are also important neuron protective factors induced by ginsenosides.\(^14,^{15}\)

The present study, however, presents little about the mechanistic aspect. In addition, further studies are warranted because of the following reasons. First, dose-response effect should be analyzed. Second, more long-term efficacy of ginseng or the symptom change with ginseng withdrawn should be verified. In addition, given the systemic effect of ginseng, appropriate blood test will increase the safety profile of ginseng.

In summary, ginseng treatment was safe and effective in AD patients. Although it needs further placebo-controlled trials to conclude the efficacy, ginseng may be the additional option for AD treatment.

REFERENCES


