

# *Panax ginseng* could Improve some Symptoms of Attention-deficit Hyperactivity Disorder

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## ABSTRACT

In this trial, *Panax ginseng* has been checked for its efficacy in treatment of attention deficit hyperactivity (ADHD) patients. Four 14-17-year old male psychiatric outpatients, diagnosed with ADHD were rated at baseline and while taking *Panax ginseng* or placebo respectively to determine its efficacy as a treatment for ADHD. Improvement was valuated using comparisons of Conners' parent ratings. Patients' mean scores improved for Conners' Hyperactivity, Inattention and Immaturity factors. Although the sample size is very small and therefore generalization is very difficult, this observation indicates that *P. ginseng* might also be a slightly effective treatment for ADHD.

**Keywords:** Conners' Hyperactivity, Inattention and Immaturity factors, monotherapy, phytotherapy

## INTRODUCTION

Psychostimulants (Greenhill *et al.* 1996; Swanson *et al.* 1998) are first choice pharmaceuticals for the treatment of attention deficit disorder (ADHD). Despite the impressive track record for the stimulants in the treatment of ADHD, they fail in 25% of patients due to lack of efficacy or the emergence of unwanted side effects (Crenshaw *et al.* 1999). The *de novo* onset of tics has also been documented in placebo-controlled, multiple-dose stimulant trials that excluded children with tic disorders (Barkley *et al.* 1992).

Atomoxetine is a selective norepinephrine reuptake inhibitor (SNRI), and is a unique ADHD medication, as it affects only norepinephrine, rather than dopamine. Norepinephrine and Dopamine are structurally very similar, differing only in the presence of a hydroxyl group. As a result, Atomoxetine has a lower abuse potential than psychostimulants (Wee *et al.* 2004).

With respect to alternative treatment options of ADHD, the Alpha<sub>2</sub>-receptor agonist clonidine has been used (Cohen *et al.* 1997). The findings from controlled studies, however, have been somewhat inconsistent, showing benefit (Connor *et al.* 2006) and negative results (Singer *et al.* 1995). The noradrenaline reuptake inhibitor Desipramine has also shown some benefit (Singer *et al.* 1995). The novel antidepressant bupropion was found to be superior to placebo (Conners *et al.* 1996).

Niederhofer could demonstrate that drugs also affecting the serotonin system may improve some symptoms associated with ADHD (Niederhofer 2004).

*Panax ginseng* is described to reduce stress and to improve concentration. We found only one study, investigating the efficacy of *P. ginseng* treating children suffering from ADHD, but in combination with *Ginkgo biloba* (Lyon *et al.* 2001). For that reason, this observation was conducted to examine the effects of *P. ginseng* as a monotherapy on a variety of target behaviors in a patient with ADHD.

## METHODS

After completing the screening procedures and a 7-day washout period, four 14-17-year old male patients diagnosed with ADHD disattention type after having excluded combined disorders like

hyperthyroidism, anxiety disorder, bipolar disorder, psychosis, EEG abnormalities and suicidality, who suffered from ADHD for at least 6 years, received *P. ginseng* (2 times/daily oral administration of tablets containing 250 mg) for 4 weeks and than placebo for 4 weeks and two patients received first placebo and then *P. ginseng*. We did not choose a larger sample size, because adverse side effects, especially cerebral bleedings, cannot be excluded. There are no data, if the risk is higher in adolescents, compared to adults. For that reason, we gave *P. ginseng* only to few adolescents for a short time. Prior to that medication two of them (one of the first placebo group and one of the first verum group) did not receive any ADHD-specific medication, the others received Methylphenidate 20 mg daily for approx. 6 years. They were recruited from our outpatient clinic. Before study entry, the patients were seen for a detailed clinical evaluation by an interdisciplinary team consisting of a psychiatrist, and a psychologist.

An interview was conducted to exclude anxiety disorder, depression, and psychosis. The DSM-IV diagnosis of ADHD was based on a review of the ADHD Rating Scale (DuPaul *et al.* 1998a).

The screening included routine laboratory tests, ECG, measurement of pulse and blood pressure, height and weight measurement, medical history, and a physical examination. An interview and Youth Self Report were conducted to exclude anxiety disorder, depression, and psychosis.

The patients (WISC-R IQ = 95-106) were free of all psychotropic medication for 1 week and free of any medical problem. They did not suffer from tic symptoms (Yale Global Tic Severity Scale (Leckman *et al.* 1998; total tic score >22) or obsessive-compulsive symptoms (Children's Yale-Brown Obsessive Compulsive Scale (Scahill *et al.* 1997) total score >15).

The diagnosis of ADHD was made on the basis of this clinical interview and ADHD Rating Scales (DuPaul *et al.* 1998a), to be completed by parents and teachers. These scales are 18-item measures of inattention and hyperactive/impulsive symptoms derived from DSM-IV. Each symptom was scored by the child, its parents and its teacher from 0 to 3 (0 = never [or rarely], 1 = sometimes, 2 = often, and 3 = very often). The scales yield three scores: an inattention score and a hyperactive/impulsive score (range = 0-27 for each score) and a total score (range = 0-54). The means of the three scores and of both forms were compared.

The Clinical Global Impression of improvement (CGI) score compares current symptom severity to baseline severity (Conners

*et al.* 1985). A score of 1 corresponds with very much improved and 2 with much improved, 3 denotes minimal change, and 4 represents no change. Scores of 5, 6, or 7 indicate deterioration (minimally worse, much worse, or very much worse, respectively).

Adverse effects were systematically assessed at each visit by the primary clinician using a modified version of the Systematic Assessment for Treatment of Emergent Events (SAFTEE) (Levine *et al.* 1986). The assessment for adverse effects also included questions about concomitant medications and concurrent illness.

## RESULTS

Regarding the ADHD rating scales, an improvement was observed for the inattention score (placebo 22, verum 18.5), the hyperactive/impulsive score (placebo 25.5, verum 21), and the total score (placebo 47.5, verum 39.5).

With respect to the CGI, there was an improvement of 2 in ADHD symptoms compared to 1 in the Placebo period, rated by a clinician, who did not have any information about the *P. ginseng* medication.

No serious side effects were observed. There were no alterations in laboratory test results, and the patients showed no clinically meaningful change in cardiac conduction. There were no changes in weight from baseline to endpoint. To evaluate cardiovascular effects, we compared blood pressure changes at each visit and could not detect any change.

## DISCUSSION

To our knowledge, this is the first study of *P. ginseng* in children with ADHD. The observed improvement is lower than the 50%–60% improvement reported in stimulant trials, studied in a sample of 76 children (Rapport *et al.* 1994), but is similar than the level of improvement observed in other nonstimulant studies such as that of Desipramine, studied in a group of 62 patients (Biederman *et al.* 1989). These finding also raises questions about the utility of combining *P. ginseng* with a stimulant. In patients with ADHD, this combination might permit lower doses of the stimulant. Questions about these effects can be answered only with further placebo-controlled, randomized studies with larger samples, that focuses on safety and efficacy in monotherapy with *P. ginseng* in this population.

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