

## 6. Nervous System Diseases (including Alzheimer's Disease)

**Reference**

Higashi K, Rakugi H, Yu H, et al. Effect of kihito extract granules on cognitive function in patients with Alzheimer's-type dementia. *Geriatrics & Gerontology International* 2007; 7: 245-51. Ichushi Web ID: 2008113647

**1. Objectives**

To evaluate the efficacy and safety of kihito (帰脾湯) for Alzheimer-type dementia.

**2. Design**

Randomized controlled trial (RCT).

**3. Setting**

Hanwa Daini Senboku Hospital, Japan.

**4. Participants**

Seventy-five elderly patients diagnosed with Alzheimer's disease according to DSM-IV criteria, with Hachinski ischemic score of  $\leq 4$  points and Mini-Mental State Examination (MMSE) score of 10–26 points. Patients with marked hypertension, diabetes, hypercholesterolemia, heart disease, renal failure, or depression, or MRI findings of marked cerebral infarction were excluded.

**5. Intervention**

Arm 1: no treatment, n=20.

Arm 2: oral administration of 2.5 g of TSUMURA Goshajinkigan (牛車腎気丸) Extract Granules t.i.d. after meals for 3 months, n=24.

Arm 3: Oral administration of 2.5 g of TSUMURA Kihito (帰脾湯) Extract Granules t.i.d. after meals for 3 months, n=20.

**6. Main outcome measures**

MMSE score, activities of daily living (ADL) evaluated in all patients at baseline and 3 months. Brain blood flow measured by single photon emission computed tomography (SPECT) in 6 patients in arm 2 and 4 patients in arm 3 at baseline and 3 months (selection criteria for performing SPECT not indicated).

**7. Main results**

Of 75 participants, 64 were included in the analysis population. MMSE score in arm 3 was significantly improved from baseline at 3 months and was also significantly improved compared with arm 1 and arm 2. In particular, disorientation and attentiveness were markedly improved. There were no among-arm differences in ADL and between baseline and 3 months. SPECT revealed no obvious changes in brain blood flow.

**8. Conclusions**

Kihito is an effective treatment for Alzheimer-type dementia.

**9. From Kampo medicine perspective**

None.

**10. Safety assessment in the article**

One patient in arm 2 experienced diarrhea and 1 patient in arm 3 increased blood pressure, leading to discontinuation of treatment.

**11. Abstractor's comments**

This excellent clinical study investigated and demonstrated the efficacy of kihito for Alzheimer's dementia using a non-Kampo-treatment and goshajinkigan as controls. The authors selected goshajinkigan as a control because of its *onji*-free composition and the lack of reports showing an effect on cognitive function. However, since the efficacy of hachimijiogan, containing goshajinkigan ingredients other than gohitsu and shazenshi, for elderly dementia has already been reported (Iwasaki K, Kanbayashi S, Chimura Y, et al. A randomized, double-blind, placebo-controlled clinical trial of the Chinese herbal medicine "Ba wei di huang wan" in the treatment of dementia. *Journal of the American Geriatrics Society* 2004; 52: 1518-21.), goshajinkigan was considered inappropriate for a control, although the results showed significantly improved MMSE score only with kihito. Furthermore, although they attribute, in the discussion, the absence of a difference in brain blood flow to the small sample size, information on selection criteria for performing SPECT would be necessary. The number of dropouts in arm 1 should be indicated. Although these details were omitted, this clinical research demonstrated the efficacy of kihito for treatment of dementia, and investigation of the mechanism of action and long-term effect using a larger sample size is expected.

**12. Abstractor and date**

Goto H, 28 November 2008, 1 June 2010.