Clinical Observation and Mechanism Study on Treatment of Senile Dementia with Naohuandan (脑还丹) *

MENG Rong-sen (蒙荣森), LI Qing-ming (李庆明), WEI Chang-xiu (魏昌秀)
CHEN Bo (陈 波), LIAO Hong-ying (廖洪映) and ZHOU Yu-tian (周雨田),

ABSTRACT Objective: To observe the therapeutic effect and mechanism of Naohuandan (脑还丹, NHD) in treating senile dementia (SD). Methods: Clinical study: Fifty-eight patients with SD, whose diagnosis conforms to the Diagnostic Standard of DSM-IV issued by American Association of Psychiatry, were enrolled and randomly assigned into two groups. The 30 patients in the treated group were treated with NHD, 4 capsules each time, 3 times daily. The 28 patients in the control group were treated with Piracetam, 1.6 g each time, 3 times daily. The therapeutic course for both groups was 3 months. The therapeutic efficacy was estimated and compared by comprehensive scores of memory and cognition, scores of Mini-mental State Examination (MMSE) and Activities of Daily Living (ADL). Experimental study: Rats were divided into the control group, the model group and the high-dosage and low-dosage NHD treated groups. The protective effect of NHD on the per-oxidative damage of hippocampal neurons in β-amyloid protein induced SD model was observed and the related criteria were determined. Results: Clinical study showed that both NHD and Piracetam could improve the clinical symptoms of patients, the two medicines showing insignificant difference in total effective rate. But NHD was better in elevating MMSE score and lowering ADL score in patients than Piracetam (P<0.05 and P<0.01). Experimental study showed that (1) 24 and 72 hrs after modeling, the activity of SOD and GSH were lower and the level of MDA higher in the model group than those in the control group (P<0.05 or P<0.01). Compared with the model group at the corresponding time points, in the high-dosage NHD group, SOD and GSH were higher, MDA was lower (P<0.05 or P<0.01); but in the low-dosage NHD group, SOD at the 72th hr was higher (P<0.05) and MDA at 24th and 72th hrs was lower (P<0.01). And most of the criteria in the high-dosage NHD group was improved better than that in the low-dosage NHD group. (2) The survival rates of neurons in various groups were not different significantly (P>0.05) 24 hrs after modeling, but that in the high-dosage NHD group was significantly higher than that in the model group (P<0.01) and in the low-dosage NHD group 72 hrs after modeling (P<0.05). Conclusion: NHD is an effective Chinese herbal preparation for treatment of SD, and its mechanism is related with its inhibition on peroxidative injury and protection on neurons.

KEY WORDS senile dementia, Naohuandan, amyloid protein, peroxidative injury

Senile dementia (SD), namely, Alzheimer's disease (AD) is a kind of degeneration in the nerve system that often occurs in mid-old aged persons, being one of the commonest disease that induces dementia, and mainly characterized by integral functional disorder of cognition, especially the memory disorder, changes in behavior and personality, as well as affectation of daily living capacity. Along with the development of the aging population in the world, an increasing trend was shown in the occurrence of AD. Because of its unclear pathogenesis, the Western medical approaches aimed at AD is mainly symptomatic, using mainly such effective remedies as choline esterase inhibitor, estrogen, anti-inflammatory agents, anti-peroxidant. However, these remedies mostly could only alleviate the symptoms but not delay or stop the course of disease, and also show adverse reaction to certain extent. Modern researches on Chinese drugs showed that many ingredients of them have effects of anti-inflammation, anti-aging and benefiting intelligence. As TCM therapy puts stress on integral regulation

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Department of TCM, The Second Hospital Affiliated to Sun Yet-sen University, Guangzhou (510120)
Correspondence to: Dr. Meng Rong-sen
Tel: 020-88518130; Fax: 020-81332419
E-mail: rongsenmeng@21cn.com
and balance in the body and possesses the superiority of having less adverse reaction and low medical expenses, to explore the clinical efficacy and action mechanism of Chinese drug therapy in treating SD is of important significance. Viewing from this, the authors conducted clinical observation and experimental study concerning the treatment of SD by Naohuanandan (NHD, 脳还丹), a Chinese herbal compound preparation. The results are reported as follows.

**CLINICAL STUDY**

**Materials and Methods**

1. **Diagnosis**

   Patients of SD were diagnosed and graded according to the AD related contents in the book “Manual for Diagnosis and Statistics for Mental Disorder (DSM2-IV)” issued by American Psychiatric Association(5). Their TCM diagnosis was made according to the “Standard for Diagnosis, Syndrome Typing and Therapeutic Effect Evaluation in Senile Dementia” set down by Branch of Senile Diseases, Chinese Association of Traditional Chinese Medicine, May 1990(6). Patients with vascular dementia, severe nerve system diseases, endocrinal diseases, metabolic diseases, diseases in liver, kidney, heart and lung, serious dementia as well as those who could not cooperate in clinical managing were excluded.

2. **Clinical materials**

   All the patients were in-patients from the integrative medicinal ward and the convalescent ward of the Second Hospital Affiliated to Sun Yet-sen University, hospitalized between Sep. 1997 and Dec. 2002. Altogether 58 of them were randomly assigned into two groups according to the randomization number table. The 30 patients in the treated group were 20 males and 10 females, aged 61–86 years, 70.2±7.1 years on average, their course of disease ranging from 6 months to 2.5 years, 1.2±0.6 years on average, 9 of them of mild degree and 21 moderate degree of dementia. The 28 patients in the control group were 17 males and 11 females, aged 58–87 years, 68.4±10.3 years on average, course of disease 4 months to 2 years and 4 months, 1.3±0.4 years on average, 10 of mild degree and 18 of moderate degree. The differences between the two groups in age, sex, average course of disease, literacy and condition of illness were statistically insignificant (P>0.05), and so, they were comparable.

3. **Treatment**

   The treated group was treated with NHD (consisting of drynaria rhizome, prepared rehmannia root, sweetflag rhizome, ginseng and earthworm, etc. produced by Guizhou Pharmaceutical Factory, Guangzhou, under supervision of the 2nd Hospital Affiliated to Sun Yet-sen University, each capsule containing 5.2 g of crude drugs), 4 capsules each time, 3 times per day. The control group was treated with Piracetam tablet (product North-East General Pharmaceutical Factory of Dongyao Group, batch number 200006066, each tablet containing 0.4 g piracetam), 4 tablets each time, 3 times per day. The therapeutic course for both groups was 3 months. Appropriate symptomatic treatment might be given also in the observation period, such as hypotensive agents to patients with extraordinary high blood pressure (excepting calcium channel blocking agent) and anti-infectious agent to those suffering from infection, but remedies for benefiting intelligence was prohibited.

4. **Criteria and methods of observation**

   The comprehensive scores of memory and cognition was monitored by the scoring form formulated according to the Standard of Therapeutic Effect Evaluation on Senile Dementia(6). The scores of memory and cognition function was accounted before and after treatment by appointed physician.

   Test on intelligence and daily life self-care capacity was conducted according to the questionnaires of Mini-mental State Examination (MMSE) and Activities of Daily Living (ADL, 20 items) respectively by special physician to record the data on a special form.

   For observation of adverse reactions, the three main routine tests (blood, urine and stool), changes of liver and kidney function, as well as the subjective complaints by patients such as nausea, vomiting, abdominal pain and hallucination, were watched.

5. **Statistical method**

   t-test was used for measuring data. χ² test was used for enumeration data, and statistical analysis was carried out by SPSS 11.0 software.

**Results**

1. **Standard of therapeutic efficacy evaluation**

   It was done according to the standard of