Chapter 14
The Clinical Analysis of Combined Effects of Huperzine A and Memantine for Alzheimer’s Disease

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ABSTRACT
The purpose of this study was to evaluate the clinical effects of a combination of Huperzine A and memantine for the treatment of Alzheimer’s disease (AD). Sixty patients (aged 69 ± 4.5), treated in both outpatient and hospital settings, were divided into two groups, the treated group and the control group. Over 24 weeks of clinical therapy, 30 patients received treatment with Huperzine A (0.2 mg/d), and the other 30 patients received a combination of Huperzine A (0.2 mg/d) and memantine (20 mg/d). Mini-mental State Examination (MMSE) was taken as the main value target. Activity of Daily Living Scale (ADL) and Neuropsychiatric Inventory (NPI) were secondary targets. Results: After 24 weeks, the scores from the MMSE, ADL, and NPI of the treatment group were more improved than those of the control group (P≤0.05). Combination treatment with Huperzine A and memantine will be more effective for treating AD than treatment with Huperzine A alone.

INTRODUCTION
Alzheimer’s disease (AD) is a neurodegenerative disorder affecting higher cognitive functions such as memory, orientation and attention, and is the most common cause of dementia. Cholinesterase inhibitors such as donepezil have shown the best efficacy and are approved for use in mild to moderate cases of AD. Another cholinesterase inhibitor, Huperzine A (from Huperziiaserrata) is
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The glutamate antagonist memantine is a low- to moderate-affinity, uncompetitive N-methyl-D-aspartate receptor antagonist. Controlled trials have demonstrated the safety and efficacy of memantine monotherapy for patients with moderate to severe AD. While memantine has been widely prescribed, often in the later stages of AD, there is little evidence to guide clinicians as to the treatment options to use as AD advances, particularly as the condition progresses from moderate to severe. Options include continuing treatment with cholinesterase inhibitors irrespective of decline, adding memantine to the cholinesterase inhibitors, or prescribing memantine instead of cholinesterase inhibitors. The aim of this trial is to establish the combinatorial value of Huperzine A and memantine for AD patients who are progressing from moderate to severe dementia.

EXPERIMENT

Subjects

Sixty AD patients (29 males, 31 females; age range 69 ± 4.5 years) treated in both outpatient and hospital settings were selected. All patients were required to have had stable physical health for the previous year and meet the National Institute of Neurological and Communicative Diseases and Stroke - Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) and the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria for probable Alzheimer’s disease (AD), have a Global Deterioration Scale (GDS) score of 4 to 5 at the time of enrollment, have no contraindication to taking Huperzine A, remained stable regarding other medications, and be able to give informed consent (or not object to participating).

Method

Patients were randomly assigned by lottery to the control (Huperzine A alone) or treatment group (Huperzine A and memantine) and given treatment for one year. Both groups received Huperzine A. The treatment group patients started taking memantine at the time of enrollment, beginning with a dose of 5 mg per day, which was increased to 20 mg per day by the end of the study. All follow-up assessments included baseline measurements. Patient assessment included the Mini-Mental State Examination (MMSE), Alzheimer’s Disease Cooperative Study – Activities of Daily Living (ADCS-ADL) and Neuropsychiatric Inventory (NPI). The MMSE, ADCS-ADL, and NPI results were evaluated, as well as cognition, the activities of daily living and behavioral and psychological symptoms. These outcomes were assessed at baseline and 24 weeks, and all participants will be subsequently followed for one year by telephone interview to record institutionalization.

RESULTS

The baseline characteristics of the patients are summarized in Table 1. Treatment and control group subjects did not differ significantly at enrollment with respect to MMSE, ADCS-ADL, NPI, gender or age. After 24 weeks, the scores of the MMSE, ADL and NPI tests for the control and treatment group subjects were statistically analyzed using SAS9.1.3 software. Data were expressed as Mean±SD. There were significant differences between the control and treatment groups.

DISCUSSION

Alzheimer’s disease (AD), the most common form of dementia, is a neurodegenerative disorder characterized by a gradual progression of cognitive, functional, and behavioral deficits. The effect of