

## Changes in psychological states of caregivers of patients with moderate or severe Alzheimer's disease following Memantine therapy

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**Abstract: Objective:** To assess the psychological states of caregivers of patients with moderate or severe Alzheimer's disease and to explore the effects of memantine therapy for patients. **Methods:** 40 patients with moderate or severe Alzheimer's disease and their caregivers were studied. Patients were treated for 6 months with open-label memantine. Caregivers were assessed at baseline and at the end of the sixth month (month-6). Their psychological states were assessed by: Symptom Checklist 90, Self-Rating Anxiety Scale (SAS), and Self-rating depression scale (SDS). The difference of their psychological states between different time points and the average normal psychological state of Chinese people (hereby referred to as "Chinese normal scale") were analyzed by T-test. **Results:** There were significant differences in depression, anxiety, hostility, paranoia, and total SCL-90 scale between baseline and month-6 (all  $p < 0.05$ ). When compared to normal SCL-90 scale, there were significant differences in all of emotional states except compulsion, phobia, and psychosis at baseline, where no significant differences in all of them between month-6 and Chinese normal scale. There are significant differences in SDS and SAS scale of caregivers between baseline, month-6, and Chinese normal scale. **Conclusions:** Caregivers of patients with moderate to severe Alzheimer's disease may have worse psychological states than average normal population and memantine therapy for AD patients may alleviate these problems.

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**Key Words:** Alzheimer's disease; caregiver; psychological states; memantine

### 1. Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive and functional impairment, and behavioral and psychological symptoms of dementia (BPSD). While BPSD are highly prevalent at all stages of dementia, they are particularly common in severe dementia, with 90% of individuals with severe disease exhibiting one behavior and 50% having at least four<sup>[1]</sup>. AD caregivers are often subject to enormous stressors and are at high risk for depression with nearly half of caregivers in some studies meeting formal diagnostic criteria for depression<sup>[2]</sup>. Caregivers also show increased utilization of health services and psychotropic medications, and one study reported that caregivers who reported distress were 63% more likely than non-caregivers to die within 4 years. Thus, adverse effects of care giving seem to be especially pronounced among dementia caregivers, even after controlling for intensity of care giving involvement<sup>[3]</sup>.

The current study examined the effectiveness of memantine on psychological problems of caregivers of patients with moderate or severe Alzheimer's disease. The objective is to confirm the effectiveness of memantine in the real world setting and to determine whether treatment with memantine would be associated with decreases in nursing burden, caregiver distress and

use of as required medications.

### 2. Methods

#### 2.1 Subjects

All AD patients come from consecutive AD patients of neurological outpatient clinics and ward from September 2010 to September 2011. Each subject underwent a comprehensive diagnostic screening assessment including physical and psychiatric examinations, as well as a review of his/her medical history. All patients were residing in Zhengzhou, met NINCDS-ADRDA criteria<sup>[4]</sup> for probable Alzheimer's disease, had moderate to severe AD as demonstrated by a score of 0–15 on the Mini-Mental State Examination (MMSE). Their caregivers who interested in and agreed to the study were recruited.

#### 2.2 Study design

Patients meeting entrance criteria were treated for 6 months with open-label memantine. The memantine (Ebixa) used in this study was provided by Lundbeck Denmark, Inc.. The memantine dose was administered beginning at 5mg once daily for 1 week and increased to 10 mg twice daily for the remaining weeks in the increment of 5mg/week increase. Caregivers were assessed two times: at baseline and month-6. Psychological states were assessed used: ① Symptom

Checklist 90 (SCL-90) [5], which assesses 10 behaviors occurring in caregivers: somatization, compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobia, paranoia, and psychosis; ②Self-Rating Anxiety Scale (SAS) [5]; ③Self-rating depression scale(SDS) [5].

### 2.3 Data analysis

All data were shown as mean  $\pm$  SD and difference between baseline, month6 and Chinese normal scale were analyzed by T-test with SPSS 14.0 software. The P value less than 0.05 was considered to be significantly different.

### 3. Results

Forty AD patients and their caregivers who met the including criteria were enrolled . table 1 summarized their socio-demographic characteristics. The mean age of patients is  $73.30 \pm 7.54$  and of caregivers is  $61.55 \pm 5.77$ . Percentage of male in

patients is 40.25% whereas in caregivers is 55.00%. For education level, most of patients are less-educated and most of caregivers are moderate-educated. With regard to relation with patients, 62.5% of caregivers is spouse of patients and 20% is children of patients.

Table 2 shows the difference in caregivers' SCL-90 scales between baseline and month 6 ,normal scale . There are significant difference in depression, anxiety, hostility, paranoia and total SCL-90 scale between baseline and month-6. When compared to Chinese normal scale, there are significant difference in all of items except compulsion, phobia and psychosis at baseline. There is no significant difference in all of items between month 6 and normal scale .

Table 3 shows the of SAS,SDS scale of caregivers between baseline, month 6 and Chinese normal scale . There are significant difference in depression, anxiety scale of caregivers between baseline, month 6 and Chinese normal scale.

Table 1. Socio-demographic characteristics of AD patients and caregivers

	AD patients (n=40)	AD caregivers(n=40)
Age (years)	$73.30 \pm 7.54$	$61.55 \pm 5.77$
Gender		
Male	17 (40.25%)	22 (55.00%)
Education (years)		
$\leq 6$	19 (47.50%)	13 (32.5%)
6~12	12 (30.00%)	21 (52.5%)
$> 12$	9 (22.50%)	6 (15.00%)
Relation to patient		
Spouse		25 (62.5%)
Sibling		3 (7.5%)
Children		8 (20.0%)
Others		4 (10%)

Table 2. Comparison of SCL-90 scale of caregivers between baseline, month-6, and Chinese normal scale

	AD caregivers (n=40)		Chinese normal (n=1388)	t1	t2
	baseline	month-6			
Somatization	$1.38 \pm 0.58$	$1.33 \pm 0.25$	$1.37 \pm 0.48$	-	$2.01^b$
Compulsion	$1.63 \pm 0.70$	$1.61 \pm 0.69$	$1.62 \pm 0.58$	-	-
Interpersonal Relation	$1.68 \pm 0.32$	$1.64 \pm 0.25$	$1.65 \pm 0.51$	-	$2.03^b$
Depression	$1.79 \pm 0.56$	$1.53 \pm 0.61$	$1.50 \pm 0.59$	$2.68^a$	$2.72^a$
Anxiety	$1.56 \pm 0.24$	$1.38 \pm 0.28$	$1.39 \pm 0.43$	$2.67^a$	$2.65^a$
Hostility	$1.55 \pm 0.39$	$1.49 \pm 0.57$	$1.48 \pm 0.56$	$2.65^a$	$2.05^b$
Phobia	$1.26 \pm 0.48$	$1.24 \pm 0.42$	$1.23 \pm 0.41$	-	-
Paranoia	$1.49 \pm 0.45$	$1.42 \pm 0.49$	$1.43 \pm 0.57$	$2.66^a$	$2.64^a$
Psychosis	$1.30 \pm 0.48$	$1.28 \pm 0.42$	$1.29 \pm 0.42$	-	-
Total	$138.02 \pm 34.12$	$130.11 \pm 30.46$	$129.96 \pm 38.76$	$2.70^a$	$2.69^a$

Note : t1—baseline vs. month 6; t2—baseline vs normal model. a— $p < 0.05$ , b— $p < 0.01$

Table3. Comparison of SAS, SDS scale of caregivers between baseline., month-6, and Chinese normal scale

	AD caregivers (n=40)		Chinese normal (n=1388)	t1	t2
	baseline	month-6			
SAS	$31.57 \pm 5.62$	$29.12 \pm 3.03$	$29.78 \pm 0.46$	$3.13^a$	$5.30^a$
SDS	$36.30 \pm 6.48$	$34.14 \pm 5.67$	$33.46 \pm 8.55$	$4.03^a$	$4.36^a$

Note : t1—baseline vs. month 6; t2—baseline vs. normal model. a— $p < 0.01$

#### 4. Discussion

The current study indicated that caregivers of patients with moderate or severe Alzheimer's disease had worse psychological states than normal population. These problems are: depression, anxiety, hostility, and paranoia. Psychiatric and behavioral symptoms occur in the majority of patients with AD over the course of the illness<sup>50–52</sup> especially in moderate or severe states, with symptoms of depression among 20%–50%; patients with AD; agitated or aggressive behaviors appearing in 70%; and delusions or hallucinations in as many as 30%–50%<sup>[6]</sup>.

In fact, depression and psychosis are included as descriptors in Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria for AD. One recent study have shown that the direct influence of patients' cognition on caregiver burden is limited and rather mediated by other disease indicators. Both ADL-abilities and behavioural disturbances are important predictors of perceived caregiver burden, where the latter has the strongest effect<sup>[7]</sup>. Another study<sup>[8]</sup> indicated that more severe psychiatric and behavioral problems, along with decreased quality of life were all significantly associated with higher levels of burden, and depression among caregivers.

The most frequently used pharmacological treatment for Psychiatric and behavioral symptoms is antipsychotics, particularly atypical antipsychotics. Although their use has been supported by evidence from randomized controlled trial (RCT) data, there remain concerns about potential side effects, such as cerebrovascular adverse events, extra pyramidal side effects and metabolic effects<sup>[9]</sup>.

The results of this study showed that memantine can alleviate the worse psychological states of caregivers of patients with moderate or severe AD. The best-studied treatment for moderate to severe AD is the non-competitive NMDA receptor antagonist memantine, which has been shown to be efficacious in RCTs. With regard to its effect on BPSD, a pooled analysis of the effect of memantine treatment in three large 6-month RCTs in moderate to severe AD patients with agitation and aggression or psychosis showed an advantage for memantine over placebo on the Neuropsychiatric Inventory (NPI) agitation/aggression subscale at week 12 and weeks 24/28<sup>[10]</sup>. The decreased agitated and aggressive behavior in institutionalized patients with moderate to severe AD following treatment with memantine was accompanied by improvements in nursing burden and decreased psychotropic use<sup>[11]</sup>.

In conclusion, this study indicate that caregivers of patients with moderate to severe Alzheimer's disease may have worse psychological states than normal population and memantine therapy for AD

patients maybe alleviate these problems.

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