Article

Enhancing Outcomes in Alzheimer's Disease: Exploring the Effects of a Diversified Rehabilitation Program Combined with Donepezil on Apathy, Cognitive Function, and Family Caregiver Burden

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Abstract

Background and objective: Alzheimer's disease is a progressive neurodegenerative disorder characterized by cognitive decline, behavioral changes, and functional impairments. Apathy, a common symptom in Alzheimer's disease, refers to a lack of motivation, interest, and emotional responsiveness. It can significantly impact patients' quality of life and increase caregiver burden. This study aimed to determine the effects of a diversified rehabilitation program combined with donepezil on apathy, cognitive function, and family caregiver burden of Alzheimer's disease patients.

Methods: A total of 105 Alzheimer's disease patients treated at our hospital between January 2020 and January 2023 were selected and analyzed retrospectively. They were assigned to the control group (n = 50) or the observation group (n = 55). The two groups did not differ in terms of general data such as age and sex. All patients were treated with donepezil orally. The control group was given routine nursing, whereas the observation group was given a diversified rehabilitation program intervention, including cognitive training and emotional support. The Hasegawa's dementia scale, mini-mental state examination, and Montreal cognitive assessment scale were adopted to evaluate the cognitive function of the two groups before and after treatment. A caregiver burden scale, the Zarit Burden Interview (ZBI) and the Apathy Evaluation Scale Informant version (AES-I) were used to evaluate the caregiver burden and apathy of the two groups.

Results: A significantly higher overall response rate to treatment was found in the observation group (94.55%) than in the control group (80.00%) ($p = 0.024$). After treatment, scores on the Hasegawa's dementia scale, mini-mental state examination, and Montreal cognitive assessment scale of the two groups increased to varying degrees, with greater increases in the observation group than in the control group ($p < 0.05$). The ZBI and AES-I scores of the two groups decreased to different degrees after treatment, with greater decreases in the observation group than in the control group ($p < 0.05$).

Conclusion: A diversified rehabilitation program combined with donepezil can substantially alleviate the apathy of Alzheimer's disease patients, improve their cognitive function, and reduce the burden on their families.

Keywords

Alzheimer's disease; senile dementia; rehabilitation program; donepezil; apathy; cognitive function; caregiver burden

Introduction

Alzheimer's disease is a common senile dementia, which is expected to afflict 130 million to 150 million peo-

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ple worldwide by 2050 [1]. Due to rapid population aging, China ranks first in the number of Alzheimer's disease cases worldwide. The disease has a course as long as 7–8 years, and patients need the care of others most of the time, so high-quality nursing care is crucial for their quality of life (QoL) and rehabilitation [2]. However, long-term care causes considerable mental stress for caregivers; such stress can trigger decreased immunity, worsen physical health, and cause negative emotions such as anxiety and depression, lowering their QoL [3]. Decreased QoL of caregivers may compromise the quality of care, compromising the rehabilitation of patients. In addition, patients with Alzheimer's disease are prone to apathy and cognitive impairment. Apathy often coexists with cognitive decline and can exacerbate the functional impairments associated with dementia [3]. Therefore, it is of great importance to understand the burden and anxiety of caregivers and to analyze the factors that influence caregiver support and patient care.

As of now, there is no clear and effective cure for senile dementia [4]. Drug therapy, the main treatment for Alzheimer's disease, can alleviate the clinical symptoms of patients and slow the progression of the disease. However, it is often impossible to achieve satisfactory results by relying only on conventional drug treatment [5]. Therefore, in addition to drug treatment, it is also necessary to adopt evidence-based nursing methods to improve the cognitive function of patients as much as possible and alleviate their symptoms comprehensively, so as to improve the overall treatment of Alzheimer's disease [6]. The combination of drug therapy and nursing is a crucial direction in the treatment of Alzheimer's disease. The diversified rehabilitation program is a scientific and effective nursing mode [7]. This study applied a diversified rehabilitation program to the nursing of elderly patients with vascular dementia and effectively improved their cognitive ability and QoL through psychological intervention, memory training, orientation training, and attention training. This nursing mode included individualized multi-intervention measures fully based on the characteristics of the course of dementia, which improved both the quality of nursing and the rehabilitation of patients.

The current study was designed to determine the effects of a diversified rehabilitation program combined with donepezil medication guidance on apathy, cognitive function, and family caregiver burden of Alzheimer's disease patients.

Methods and Data

Clinical Data

A total of 105 Alzheimer's disease patients treated at the Second Affiliated Hospital of Hainan Medical University between January 2020 and January 2023 were selected and analyzed retrospectively. Among them, 50 patients given routine nursing were assigned to the control group and 55 patients given a diversified rehabilitation program intervention in addition to routine nursing were assigned to the observation group. This study was performed with approval from the Medical Ethics Committee of the Second Affiliated Hospital of Hainan Medical University (ethical approval number: LW2022260) and in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Inclusion criteria: Patients who were diagnosed with Alzheimer's disease according to clear diagnostic tests such as electroencephalogram (EEG) and brain computed tomography (CT) and met the diagnostic criteria of Alzheimer's disease [8]; patients >60 years old; patients with detailed clinical data.

Exclusion criteria: Patients comorbid with other critical illness; patients who required emergency interventional therapy; patients comorbid with serious heart, liver, or renal dysfunction.

Treatment and Nursing Scheme

All patients were administrated donepezil orally (Eisai China Inc., Shanghai, China, State Food and Drug Administration approval number: H20050978; 5 mg), 5 mg/time, once a day, and the dosage was changed to 10 mg/time after one month of administration.

The control group: Routine nursing methods were adopted, including providing medication guidance, nutritional care, life intervention, etc., and providing appropriate exercise guidance for patients under the premise of ensuring their safety. In this nursing approach, the focus was placed on the treatment of complications of patients and on providing various types of nursing guidance.

The observation group [9]: For caregivers of patients with Alzheimer's disease, a comprehensive training and support program was developed, aiming at ensuring that caregivers can master the required clinical knowledge and nursing skills. The program was divided into five modules,

each of which had been carefully designed to ensure that caregivers received many aspects of support.

Basic theoretical knowledge training: The nursing staff systematically explained the etiology, pathogenesis, clinical manifestations, and diagnostic criteria of Alzheimer's disease, as well as differences from other dementias. The training was conducted to correct misunderstandings of caregivers about Alzheimer's disease and to enhance their confidence in care. Nursing skills training: Through scenario simulation, role-playing, and on-site observation, caregivers were taught about the measures for ensuring the physical safety of patients with Alzheimer's disease, cultivating their living habits, and maintaining their daily hygiene. Psychological intervention: Cognitive behavioral therapy was provided. The nursing staff instructed the caregivers regarding strategies to manage stress, helped them deal with anxiety and depression, and provided them with necessary social support. Communication skills training: Communication skills training was conducted to help caregivers better understand and cope with behavioral and psychological symptoms of dementia (BPSD) of patients, improve the communication with patients, and thus improve the QoL of patients. BPSD coping strategies: The caregivers were taught about techniques for calming patients' negative emotions, dealing with their impulsive behavior, and seeking professional help in an emergency. In addition, supportive psychological intervention was provided. A series of psychotherapy methods were adopted according to the specific situation of caregivers, such as listening, praise, explanation, and encouragement, to help caregivers eliminate doubts, lift their emotions, and enhance their capacity for self-care. The whole training and support program lasted for 6 months. It was conducted once a week, half a day each time. A combination of group training and individual guidance was adopted to ensure that every caregiver could receive adequate attention and support. Prognostic follow-up: According to the psychological status of patients with Alzheimer's disease, a regular follow-up system was formulated. During the follow-up, the nursing staff was required to patiently listen to the patients and their families and correctly guide and comfort them by encouraging the patients to maintain a good state of mind and fully comforting the caregivers, so that the caregivers could patiently and effectively provide care in the patients' daily life and improve their psychological well-being.

Functional Score

The positive and negative symptom scale [10]: This scale is used to evaluate the positive and negative symptoms of patients. According to the scoring results, the treatment effect is classified into four grades: Cured: The score is reduced by more than 75% after treatment; markedly effective: The score is reduced by 50%–75% after treatment; effective: The score is reduced by 25%–50% after treatment. Ineffective: The score is reduced by less than 25% after treatment. The overall response rate = the ratio of the total number of cases with cured outcome, cases with markedly effective outcome, and cases with effective outcome to the total number of cases.

The Hasegawa's dementia scale (HDS) [11]: The scale is used to evaluate the dementia degree of patients. Normal intelligence: the score is higher than 30 points; mild mental retardation: the score is between 20 and 29 points; severe mental retardation: the score is less than 10 points. An individual with a total score less than 15 points can be diagnosed with dementia.

The Blessed dementia scale (BDS) [12]: This scale is used for QoL evaluation of patients. It has a total score of 0–18 points in six scoring items, each with a score of 0 to 3 points, and a lower score indicates higher QoL.

The Mini-Mental State Examination (MMSE) [13]: This scale is used to evaluate the mental function of patients. Scores >24 points indicate normal mental function; scores ≤23 points indicate loss of mental function.

The Montreal cognitive assessment (MoCA) [14]: The scale is used to evaluate patients' cognitive function, including attention, executive function, memory, language, visual structure skills, abstract thinking, calculation, and orientation. A higher score in each dimension indicates better function.

The Zarit Burden Interview (ZBI) [15]: This scale is used to evaluate the burden of caregivers. It has a total score of 0–88 points, and a higher score indicates heavier burden.

The Apathy Evaluation Scale Informant version (AES-I) [16]: This scale is used to evaluate the apathy of patients based on responses provided by family members. The AES-I covers four dimensions, namely, interest, cognition, emotion, and behavior, with a total of 18 items. The opinions of "not at all" to "very consistent" are given 1–4 points. It has a total score of 18–72 points, and a total score of ≥33 points indicates apathy. A higher score indicates a higher degree of apathy.

The above-mentioned rating scales were used for scoring by corresponding trained and certified healthcare professionals with relevant expertise and experience.

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Table 1. Baseline data.

Factors	Control group (n = 50)	Observation group (n = 55)	χ^2 value	p value
Age				
$\geq$60 years old	28	34	0.367	0.545
<60 years old	22	21		
Sex				
Male	27	33	0.3850	0.535
Female	23	22		
BMI				
$\geq$25 kg/m^2	13	15	0.0217	0.883
<25 kg/m^2	37	40		
Course of disease				
$\geq$12 months	24	22	0.680	0.409
<12 months	26	33		
History of hypertension				
Yes	10	14	0.441	0.506
No	40	41		
History of diabetes mellitus				
Yes	10	8	0.548	0.458
No	40	47		
History of smoking				
Yes	25	25	0.216	0.641
No	25	30		
History of alcoholism				
Yes	4	6	0.257	0.612
No	46	49		

Note: BMI, body mass index.

Outcome Measures

Primary outcome measures: The clinical efficacy of the two groups was compared. The dementia level, QoL, and intelligence level of the two groups were compared. The changes of intelligence and cognitive function between the two groups were compared.

Secondary outcome measures: The clinical data of the two groups were compared. The burden of caregivers before intervention and after 6 months of intervention was analyzed.

Statistical Analyses

SPSS 26.0 software (SPSS Co., Ltd., Chicago, IL, USA) was used for data analysis. For continuous data, normality was assessed using K-S test, and normally distributed variables are presented as mean $\pm$ standard deviation ($\bar{x} \pm s$). For continuous variables, independent sample t-tests were used to assess differences between two groups, and paired t-tests were used for within-group comparisons. Associations between categorical variables were assessed using the χ^2 test. p values < 0.05 were considered statistically significant.

Results

Clinical Data

Comparison of clinical data revealed that the control and observation groups did not differ significantly in age, sex, body mass index (BMI), course of disease, history of hypertension, history of diabetes mellitus, history of smoking, or history of alcoholism (p > 0.05, Table 1).

Evaluation of Treatment Efficacy

Comparison of treatment efficacy between the two groups revealed a significantly higher overall response rate in the observation group than in the control group (p = 0.024, Table 2).

Table 2. Efficacy evaluation.

Group	Clinical efficacy [case (%)]				Overall response
	Cured	Markedly effective	Effective	Ineffective	
Control group (n = 50)	10	21	9	10	40 (80.00%)
Observation group (n = 55)	15	25	12	3	52 (94.55%)
χ^2 value					5.108
p value					0.024

Table 3. Dementia level and quality of life changes.

Group	HDS score		BDS score	
	Before treatment	After treatment	Before treatment	After treatment
Control group (n = 50)	18.22 ± 3.77	$20.34 \pm 2.77^*$	17.65 ± 2.74	$22.34 \pm 2.99^*$
Observation group (n = 55)	18.36 ± 3.25	$24.38 \pm 3.58^{*,\#}$	17.94 ± 2.05	$25.87 \pm 3.08^{*,\#}$

Notes: $*p < 0.05$ *vs.* Before treatment, $\# p < 0.05$ *vs.* the control group; HDS, Hasegawa's dementia scale; BDS, Blessed dementia scale.

Dementia Level and QoL Changes

Before treatment, no significant differences were observed in HDS or BDS scores between the two groups ($p > 0.05$), whereas after treatment, the scores of HDS and BDS increased significantly in both groups ($p < 0.05$). Further comparison revealed significantly higher HDS and BDS scores in the observation group than in the control group after treatment ($p < 0.05$, Table 3).

Changes in Intelligence and Cognitive Function Scores

Before treatment, there were no significant differences in MMSE or MoCA scores between the two groups ($p > 0.05$), whereas after treatment, the MMSE and MoCA scores increased significantly in both groups ($p < 0.05$), with significantly higher MMSE and MoCA scores in the observation group than in the control group ($p < 0.05$, Table 4).

Comparison of Caregiver Burden and Patients' Apathy

Before treatment, the two groups did not differ significantly in ZBI or AES-I scores ($p > 0.05$), whereas after treatment, the ZBI and AES-I scores decreased significantly in both groups ($p < 0.05$) with significantly lower ZBI and AES-I scores in the observation group than in the control group ($p < 0.05$, Table 5).

Discussion

Clinically, Alzheimer's disease generally occurs among people over 60 years old, and its incidence displays an upward trend with age [17]. Alzheimer's disease patients typically have symptoms including cognitive decline, loss of language function, and cognitive dysfunction, which compromises the overall QoL and brings a great burden to their families and society [18]. At present, China is still in the exploratory stage in terms of identifying the optimal nursing treatment for Alzheimer's disease. The main nursing modes include home nursing, old-age nursing, apartment nursing for the elderly, and hospital-community-family nursing [19]. Since different nursing modes have their own advantages and disadvantages, it is necessary to make a specific analysis according to the specific situation. As a manifestation of high-quality nursing, the diversified rehabilitation program adopted in this study is a comprehensive nursing guidance in the hospital stage of "hospital-community-family nursing". Its purpose is to provide guidance and training through rehabilitation nursing in a hospital setting, so as to improve the self-care ability and cognitive function of patients with Alzheimer's disease [20]. With the ability to activate neurotransmitters and delay brain tissue atrophy, donepezil is suitable for patients with mild-to-moderate Alzheimer's disease; the drug has potent and long-lasting effects and is not affected by food intake or medication time [21]. In this study, after nursing, the observation group showed a significantly higher response rate to treatment than the control group. After nursing, the observation group showed greater improvements in HDS, BDS, and MMSE scores than the control group, and presented better cognitive function than the control group. The results reveal that the diversified rehabilitation program com-

Table 4. Changes in intelligence and cognitive function scores.

Group	MMSE score		MoCA score	
	Before treatment	After treatment	Before treatment	After treatment
Control group (n = 50)	19.44 ± 2.84	22.74 ± 3.25*	10.74 ± 2.87	16.77 ± 4.54*
Observation group (n = 55)	18.74 ± 3.14	25.77 ± 2.64*,#	11.02 ± 2.48	20.41 ± 4.02*,#

Note: *$p < 0.05$ *vs.* Before treatment, # $p < 0.05$ *vs.* the control group; MMSE, Mini-Mental State Examination; MoCA, Montreal cognitive assessment.

Table 5. Comparison of caregiver burden and patients' apathy.

Group	ZBI score		AES-I score	
	Before treatment	After treatment	Before treatment	After treatment
Control group (n = 50)	33.55 ± 4.84	19.45 ± 4.58*	40.25 ± 4.32	33.74 ± 3.58*
Observation group (n = 55)	32.74 ± 5.33	12.77 ± 3.81*,#	39.55 ± 3.77	30.45 ± 2.75*,#

Note: *$p < 0.05$ *vs.* Before treatment, # $p < 0.05$ *vs.* the control group; ZBI, Zarit Burden Interview; AES-I, Apathy Evaluation Scale Informant version.

bined with donepezil medication guidance can strongly alleviate the apathy of patients with Alzheimer's disease and improve their cognitive function. We believe the diversified rehabilitation program can play a vital part in the care of Alzheimer's disease patients. Based on the people-oriented principle, this program ensures that all nursing measures are formulated based on the actual situation and needs of patients, during which special attention is paid to the rehabilitation of patients' cognitive function, and all nursing and rehabilitation activities are based on the actual point of view of patients to ensure that every step is designed to meet the actual needs of patients. In addition, with donepezil, we can effectively control the disease and ensure that patients are in a stable health state. Finally, this comprehensive nursing method not only improved the QoL of patients, but also created an active and healthy rehabilitation environment for them.

In the complex symptom spectrum of Alzheimer's disease, apathy is a symptom that is often ignored but of great significance [22]. Apathy, as a lack of emotion and behavior, is manifested in patients' reduced interest and motivation in daily activities, social interaction, and personal concern. It may be a consequence of the degeneration of the areas associated with emotion and reward system in the brain [23]. For medical professionals and caregivers, apathy is a sign of disease progress, and also a key factor in the decline of patients' QoL. Therefore, understanding and mitigation of apathy is crucial in the comprehensive treatment of Alzheimer's disease [24]. In this study, the observation group displayed significantly lower ZBI and AES-I scores than the control group, which indicated that the diversified rehabilitation program combined with donepezil medication guidance could reduce patients' apathy and the burden of caregivers. The reasons are as follows: The di-

versified rehabilitation program provides a comprehensive intervention for the individual needs of patients, emphasizing the rehabilitation of cognitive, emotional, and social functions [9]. The comprehensive treatment can more effectively activate the brain function of patients, delay the progression of the disease, and thus alleviate the symptoms of apathy. In addition, donepezil, as a drug that has been verified to improve the emotional and behavioral symptoms of Alzheimer's disease patients, can further enhanced rehabilitation during the treatment. Moreover, because of the improved symptoms of patients, the challenges and pressures faced by caregivers in daily care are correspondingly reduced, which reduces their psychological and physical burdens. Therefore, the comprehensive treatment provided by the diversified rehabilitation program combined with donepezil brought substantial benefits to Alzheimer's disease patients and their caregivers. This study has achieved some positive results, but it still has some limitations. First, the sample size may not be sufficient to represent the population of all Alzheimer's disease patients, so the results may be biased. Second, this study mainly relies on qualitative evaluation tools, such as ZBI and AES-I, which may be influenced by subjective factors. In addition, the implementation of diversified rehabilitation programs may vary in different research centers with different medical staff, which may lower the consistency of treatment effects. Finally, this study did not include other possible confounding factors, such as patients' baseline health status, complications, and other concurrent diseases, which may also affect the research results.

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Conclusion

To sum up, the comprehensive treatment represented by the diversified rehabilitation program combined with donepezil provided clear benefits for Alzheimer's disease patients and their caregivers, especially in alleviating the apathy and caregivers' burden. Although this method has demonstrated a positive effect in the current study, a larger and more rigorous randomized controlled trial is still required to further verify the long-term effect and safety. We hope future research can overcome the existing limitations to provide more effective and individualized treatment programs for Alzheimer's disease patients.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

XJ designed the research study. XJ and LL performed the research. XJ and LL analyzed the data. Both authors contributed to the drafting or important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was performed with approval from the Medical Ethics Committee of the Second Affiliated Hospital of Hainan Medical University (ethical approval number: LW2022260) and in accordance with the Declaration of Helsinki. It is a retrospective study, obtaining informed consent in advance is not necessary as the research uses anonymized or deidentified data that does not directly disclose personal identifying information.

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Conflict of Interest

The authors declare no conflict of interest.

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