



Impact of an Education Program for Caregivers of Patients with Alzheimer's Disease on Treatment Discontinuation and Compliance in Korea

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Background and Purpose Reportedly 30–50% of patients being treated for chronic illnesses do not adhere to their medication regimen. We assessed the impact of a nurse-led education program for caregivers of Korean de novo Alzheimer's disease patients who had newly been prescribed donepezil.

Methods This multicenter study analyzed 93 participants in a caregiver education group and 92 participants in a caregiver no-education group. At every visit up to the end of the study (1 year), caregivers in the education group were given educational brochures regarding Alzheimer's disease and the efficacy and adverse events of donepezil treatment. The primary endpoint was the discontinuation rate of donepezil treatment during the 1-year observation period. The secondary endpoints included the effect of education on compliance with donepezil treatment assessed at each visit using a clinician rating scale (CRS) and visual analog scale (VAS), and changes from baseline in cognitive assessment tests.

Results The donepezil discontinuation rates at 1 year were 5.38% (5/93) and 6.52% (6/92) in the caregiver education and no-education groups, respectively ($p=0.742$). No significant between-group differences in donepezil compliance rates on the CRS and VAS were observed, but significant changes were observed in some cognitive tests from baseline to the end of the study.

Conclusions Caregiver education had no significant effect on treatment discontinuation, but this may have been due to the low severity of cognitive impairment among the included population at baseline. In addition, the low discontinuation rates meant that no significant difference in treatment compliance was observed.

Key Words Alzheimer's disease, caregiver education, dementia, Korea, treatment compliance.

INTRODUCTION

Alzheimer's disease is one of the most significant neurological disorders affecting the elderly,¹ and represents a major psychosocial burden on both affected individuals and their families. The global prevalence of Alzheimer's disease among those aged ≥ 60 years is 5–7%, and varies by region, urban or rural domicile, country of origin, as well as other causative factors.^{2–4}

Donepezil hydrochloride (Aricept[®], Eisai, Tokyo, Japan) is an acetylcholinesterase inhibitor that selectively and reversibly blocks the activity of acetylcholinesterase, an enzyme that hydrolyzes the neurotransmitter acetylcholine.⁵ The resulting increase in acetylcholine concentration in neuronal synapses leads to improvements in the memory and cognitive capabilities of patients with Alzheimer's disease.⁶ Thus, donepezil has been widely used to im-

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prove cognitive function in patients with Alzheimer's disease and also in some patients with vascular dementia.^{7,8} A previous study found that 140 (53.1%) of 264 patients with advanced Alzheimer's disease discontinued donepezil treatment during a 2-year observation period.⁹ Such nonadherence may have negative effects on cognition and neuropsychiatric symptoms and may result in a higher mortality rate.¹⁰

It has been estimated that 30–50% of patients prescribed medications for chronic illnesses do not adhere to their prescribed medication regimen.¹¹ Lack of adherence has been demonstrated to diminish treatment effects, which can result in prolonged illness, use of additional clinical resources, and prescriptions that may otherwise have been unnecessary. Notably, deficits in cognitive processes caused by Alzheimer's disease predispose older adults to medication nonadherence by impairing their abilities to plan, organize, and execute medication management tasks.^{12,13} Multiple patient-related factors as well as environmental and systemic factors may also affect medication adherence.¹⁴ Disease features, referral processes, clinical settings, therapeutic regimens, patient demographics, and treatment-related factors (e.g., costs, dosing frequency, and adverse events) provide inconsistent explanations for nonadherence, and thus do not represent adequate predictive factors.¹⁵

We hypothesized that an education program for the caregivers of patients with newly diagnosed Alzheimer's disease can influence their treatment discontinuation and compliance. We therefore assessed the impact of a nurse-led education program for caregivers of Korean de novo Alzheimer's disease patients who had newly been prescribed donepezil on their donepezil treatment compliance and cognitive symptoms.

METHODS

Study design

We conducted a randomized controlled study of an education program in Korean patients newly diagnosed with Alzheimer's disease and receiving donepezil monotherapy under routine clinical practice. The patients were observed for 1 year, and were enrolled from 14 of 15 included centers across Korea. The patients were randomly assigned to caregiver education and caregiver no-education groups at a 1:1 ratio. Randomization was performed by the designated personnel at each institution using block randomization according to a randomization table that was distributed in advance. For the randomization table, a sequence of random numbers was generated by SAS statistical software.

The study protocol, informed-consent form, and other documents related to this study were approved by the institutional review board of each participating institution. The study

was conducted in compliance with standard operating procedures and in accordance with the International Conference on Harmonization Good Clinical Practice guidelines and the ethical principles of the Declaration of Helsinki. The investigator fully explained the objectives and details of the study to caregivers and patients before they voluntarily signed the informed-consent form for participation in this study.

Patients

Inclusion criteria for patients were as follows: age ≥ 50 and < 90 years, diagnosis of Alzheimer's disease according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria,¹⁶ newly being prescribed donepezil monotherapy, written informed consent for study participation provided by both the patient and their caregiver, and joint attendance of both the patient and their caregiver at the scheduled study visits.

Patients who had previously been treated with memantine or acetylcholinesterase inhibitor at the time of enrollment were excluded from the study. During the study, patients who withdrew informed consent, were lost to follow-up, or were determined as no longer eligible for study participation by the investigator were withdrawn from the study. All patients were followed up until the end of the study (for up to 1 year), including those in whom the administration of donepezil was discontinued.

Study treatment and procedures

The method and duration of donepezil administration were determined at the discretion of the investigator in accordance with the donepezil package insert.¹⁷ If any other medications were added to the donepezil regimen for the treatment of Alzheimer's disease during the study, the patient was allowed to continue participating in the study once the modified regimen and the rationale for this change were accounted for. There were no prohibited drugs in this study.

Study participants were generally required to attend five study visits during the 1-year study period. Any additional visits were determined by the investigator based on the clinical course and disease progression of individual patients. Investigators educated and encouraged patients to maintain the established visit schedule and collected the required information by means of case report forms at each visit.

Data were collected at five visits during an approximate 1-year period: Visit 1, baseline (day 0); Visit 2, month 1; Visit 3, month 3; Visit 4, month 6; and Visit 5, end of study (year 1) (Supplementary Fig. 1 in the online-only Data Supplement). If a patient did not attend a scheduled visit, they were contacted via telephone, letter, or email, and the reason for the

schedule violation was recorded. In such cases, any required information was collected via telephone, letter, or email.

Nurse-led Alzheimer's disease education and knowledge translation program for patients and caregivers

All caregivers received routine disease education and drug administration instructions. Participants in the caregiver education group also received additional education on the disease and on the efficacy and adverse events of donepezil treatment. This information was provided to caregivers via information brochures at Visits 1 to 4. All education programs were led by nurses who were experts in Alzheimer's disease.

The contents of the educational program were as follows: At Visit 1, the brochure focused on general information about Alzheimer's disease and emphasized the importance of early and continuous treatment. Information from the donepezil package insert and about adverse events was also provided. At Visit 2, the brochure described the efficacy of donepezil in repairing cognitive function as well as the possible adverse events when increasing the dose. The brochure also provided information on the worsening of Alzheimer's disease symptoms and the importance of early and continuous treatment. At Visit 3, the brochure emphasized the importance of early and continuous treatment for Alzheimer's disease, and provided guidance on lifestyle modifications and exercise. At Visit 4, the brochure focused on the behavioral symptoms in Alzheimer's disease patients and re-emphasized the importance of early and continuous treatment for Alzheimer's disease.

Study endpoints

Endpoints in this study were analyzed according to the status of additional education received by the caregiver. The primary endpoint was the rate of discontinuation of donepezil treatment during the study period (i.e., up to 1 year) and intergroup differences in the discontinuation rate according to the status of additional education (i.e., caregiver education group versus caregiver no-education group). The secondary endpoints were compliance with donepezil treatment at each visit (Visits 2 to 5) as assessed using a clinician rating scale (CRS) and visual analog scale (VAS) according to the receipt of additional education. Changes from baseline to the end of the study period were assessed for the entire study population using several cognitive assessment tests [Mini-Mental State Examination (MMSE),¹⁸ Montreal Cognitive Assessment (MoCA), Trail-Making Test-Black and White (TMT-B&W), and the Clinical Dementia Rating (CDR)¹⁹], which were applied at Visits 1, 4, and 5 (Supplementary Material 1 in the online-only Data Supplement). Additional post-hoc analyses were also conducted to evaluate whether the education sta-

tus of the caregiver affected the cognitive function of their patient. Furthermore, we also compared donepezil discontinuation rates according to the baseline CDR score and caregiver education status.

Statistical analyses

Given the exploratory nature of this subgroup analysis, a required sample size was not calculated. The primary endpoint of the treatment discontinuation rate of donepezil during the 1-year study period and intergroup differences in the discontinuation rate according to the status of additional caregiver education was analyzed using Pearson's chi-square test. For the secondary endpoints, frequency and percentage values were presented for the CRS, and mean±standard-deviation, median, and range values were provided for the VAS. Intergroup differences according to the status of additional caregiver education were analyzed using Fisher's exact test for the CRS and Wilcoxon's rank-sum test for the VAS. Statistical significance was set at $p<0.05$. Cognitive tests were analyzed using Wilcoxon's signed-rank test. Fisher's exact test was used to compare donepezil discontinuation rates according to the baseline CDR score and caregiver education status. All statistical analyses were performed using SAS (version 9.3, SAS Institute, Cary, NC, USA).

RESULTS

Patient characteristics

The present exploratory analysis was applied to 259 Korean patients who were randomly assigned to the caregiver education and no-education groups (Fig. 1). Of these, 74 patients prematurely dropped out of the study for the following rea-

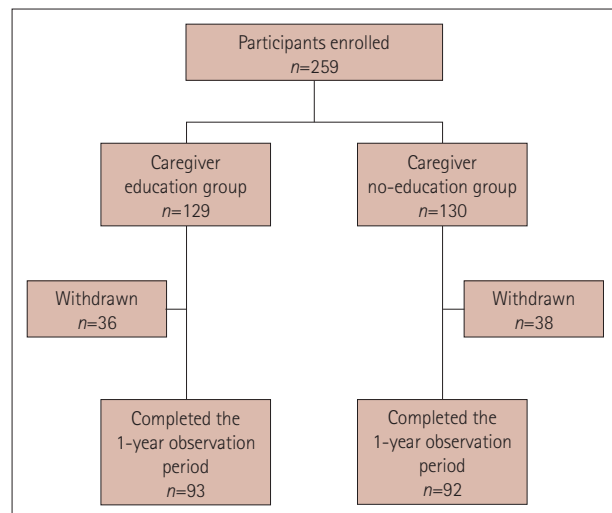


Fig. 1. Flowchart of patient enrollment after newly diagnosed with AD and receiving donepezil monotherapy (follow-up period: 1 year).

sons: consent withdrawal ($n=29$, 39.2%), loss to follow-up ($n=25$, 33.8%), investigator's decision ($n=6$, 8.1%), or another reason ($n=14$, 18.9%). Therefore, 185 patients were included during the 1-year observation period.

The baseline demographics and clinical characteristics did not differ significantly between the two study groups except for age (Table 1). The 185 analyzed patients comprised 54.05% ($n=100$) males and 45.95% ($n=85$) females, were aged 74.88 ± 6.95 years, and had an education period of 6.94 ± 4.83 years and a body mass index of 23.26 ± 3.01 kg/m². At baseline, their MMSE and MoCA scores were 20.61 ± 4.51 and 18.77 ± 4.09 , respectively. Based on the CDR global assessment, 44.05% of patients had very mild dementia (score of 0.5), 51.79% had mild dementia (score of 1), 4.17% had moderate dementia (score of 2), and no patient had severe dementia (score of 3).

Discontinuation rate of donepezil treatment

For the primary endpoint, the percentage of patients who discontinued donepezil treatment during the 1-year study period was 5.38% (5/93) in the caregiver education group and

6.52% (6/92) in the caregiver no-education group ($p=0.742$) (Table 2).

The rates of treatment discontinuation and reasons for discontinuation according to the physician, patient, and caregiver are presented in Table 2. Five cases of discontinuation were attributed to physicians: three cases because of an adverse event (two and one in the caregiver education and no-education groups, respectively) and two cases because of administration inconvenience (both in the caregiver no-education group). Five cases of discontinuation were attributed to patients, which were all because of adverse events (two and three in the caregiver education and no-education groups, respectively). One case of discontinuation was attributed to caregivers, which was due to concern about adverse events (in the caregiver education group).

Compliance during the 1-year observation period

Patients were assessed for compliance as a secondary endpoint (Supplementary Tables 1 and 2 in the online-only Data Supplement). The donepezil compliance rate according to the

Table 1. Baseline demographic and clinical characteristics

	Total ($n=185$)	Caregiver education group ($n=93$)	Caregiver no-education group ($n=92$)	<i>p</i>
Sex, male	100 (54.05)	51 (54.84)	49 (53.26)	0.830*
Age, years	74.88 ± 6.95	75.90 ± 6.60	73.85 ± 7.19	0.044 [†]
Education period, years	6.94 ± 4.83	6.69 ± 4.71	7.20 ± 4.96	0.486 [†]
BMI, kg/m ²	$n=170$ 23.26 ± 3.01	$n=85$ 23.50 ± 2.95	$n=85$ 23.03 ± 3.06	0.309 [†]
MMSE score	$n=167$ 20.61 ± 4.51	$n=84$ 20.99 ± 4.52	$n=83$ 20.23 ± 4.51	0.375 [†]
MoCA score	$n=39$ 18.77 ± 4.09	$n=20$ 19.90 ± 3.06	$n=19$ 17.58 ± 4.74	0.165 [†]
CDR sum-of-boxes score	$n=168$ 4.48 ± 2.15	$n=84$ 4.45 ± 2.28	$n=84$ 4.51 ± 2.01	0.376 [†]
CDR global score	$n=168$	$n=84$	$n=84$	0.494 [§]
0	0 (0.00)	0 (0.00)	0 (0.00)	
0.5	74 (44.05)	38 (45.24)	36 (45.05)	
1	87 (51.79)	41 (48.81)	46 (52.75)	
2	7 (4.17)	5 (5.95)	2 (2.38)	
3	0 (0.00)	0 (0.00)	0 (0.00)	
TMT-B&W (Part A: time to completion), seconds	$n=157$ 170.82 ± 79.96	$n=79$ 169.22 ± 78.26	$n=78$ 172.44 ± 82.13	0.732 [†]
TMT-B&W (Part A: no. of errors)	1.52 ± 3.20	1.54 ± 3.63	1.49 ± 2.72	0.970 [†]
TMT-B&W (Part B: time to completion), seconds	$n=153$ 270.98 ± 56.65	$n=77$ 268.39 ± 62.07	$n=76$ 273.60 ± 50.86	0.457 [†]
TMT-B&W (Part B: no. of errors)	2.37 ± 3.55	2.04 ± 3.06	2.71 ± 3.97	0.160 [†]

Data are *n* (%) or mean \pm standard-deviation values, except where indicated otherwise.

*Pearson's chi-square test, [†]Two-sample *t*-test, [‡]Wilcoxon's rank-sum test, [§]Fisher's exact test.

BMI: body mass index, CDR: Clinical Dementia Rating, MMSE: Mini-Mental State Examination, MoCA: Montreal Cognitive Assessment, TMT-B&W: Trail-Making Test-Black and White.

CRS at each study visit did not differ significantly between the two groups. The proportion of patients assessed as compliant with donepezil treatment (CRS score ≥ 5) ranged from 94.25% to 100% at all visits. Similarly, compliance with donepezil treatment according to the VAS at each study visit did not differ significantly between the two study groups, with mean values ranging from 88.35% to 94.37%.

Changes in cognitive function from baseline to the end of the 1-year observation period

Table 3 summarizes the changes in cognitive tests and in dementia severity (CDR score) from baseline to the end of the study for the entire study population. Donepezil was effective in improving cognitive function, as shown by the numerical changes from baseline to the end of the study for all cognitive assessments, with the changes assessed using the MoCA score (increase of 0.46 ± 1.25) and TMT-B&W (Part A: time to completion) (decrease of 7.06 ± 58.47 seconds) being statistically significant ($p=0.034$ and 0.005 , respectively). The increase

from baseline to the end of the study in the CDR global score was also statistically significant (0.10 ± 0.35 , $p < 0.001$).

Rate of discontinuation according to baseline factors

Caregivers were most commonly female (65.73%), and the most common relationships with the patient were as a wife (33.70%) or daughter (21.74%) (Supplementary Table 3 in the online-only Data Supplement). The effect of the relationship between the caregiver and patient on treatment discontinuation rates was assessed (Table 4). The rate of discontinuation differed significantly depending on caregiver relationship with the patient ($p=0.004$). Furthermore, there was a significant difference between spouse and child ($p=0.003$) (Pearson's chi-square tests).

The relationship between disease severity at baseline and treatment discontinuation rates was assessed (Supplementary Table 4 in the online-only Data Supplement), and the discontinuation rates were compared between high- and low-drop-out-rate institutions (defined as the seven institutes with the

Table 2. Discontinuation rate and reasons for discontinuation of donepezil

	Caregiver education group (n=93)	Caregiver no-education group (n=92)	p
Discontinuation of donepezil	5 (5.38)	6 (6.52)	0.742*
Reasons for discontinuation			
Physician			
Adverse event occurred	2	1	
Inconvenience of administration	0	2	
Patient			
Adverse event occurred	2	3	
Caregiver			
Concern about adverse events	1	0	

Data are n or n (%) values.

*Pearson's chi-square test.

Table 4. Effect of caregiver relationship with the patient on treatment discontinuation

Relationship with the patient	n	Treatment discontinuation		p
		Yes	No	
Relationship with the patient				0.004*
Husband	30	1 (3.33)	29 (96.67)	
Wife	64	4 (6.25)	60 (93.75)	
Husband+wife	94	5 (5.32)	89 (94.68)	
Daughter-in-law	15	0 (0.00)	15 (100.00)	
Son	34	6 (17.65)	28 (82.35)	
Daughter	46	10 (21.74)	36 (78.26)	
Son+daughter	80	16 (20.00)	64 (80.00)	
Son-in-law	1	1 (100.00)	0 (0.00)	
Others	7	2 (28.57)	5 (71.43)	

Data are n (%) values.

*Fisher's exact test.

Table 3. Changes in cognitive function tests, TMT-B&W parameters, and CDR scores

Test	Baseline	1 Year	Change	p*
MMSE score (n=167)	20.61 \pm 4.51	20.58 \pm 5.19	-0.03 \pm 3.38	0.947
MoCA score (n=39)	18.77 \pm 4.09	19.23 \pm 3.51	0.46 \pm 1.25	0.034
TMT-B&W, seconds				
Part A: time to completion (n=157)	170.82 \pm 79.96	163.76 \pm 86.54	-7.06 \pm 58.47	0.005
Part B: time to completion (n=153)	270.98 \pm 56.65	275.23 \pm 44.92	4.25 \pm 55.23	0.986
CDR (global) score (n=168)	0.82 \pm 0.35	0.93 \pm 0.42	0.10 \pm 0.35	<0.001
CDR (sum of boxes) score (n=168)	4.48 \pm 2.15	5.05 \pm 2.51	0.57 \pm 2.01	<0.001

Data are mean \pm standard-deviation values.

*Wilcoxon's signed-rank test.

CDR: Clinical Dementia Rating, MMSE: Mini-Mental State Examination, MoCA: Montreal Cognitive Assessment, TMT-B&W: Trail-Making Test-Black and White.

highest and lowest dropout rates, respectively) (Supplementary Table 5 in the online-only Data Supplement). The discontinuation rate was significantly higher among patients with a CDR score of 0.5 than among those with a CDR score of 1 at baseline (17.02% and 7.29%, respectively; $p=0.040$). Age, sex, education period, MMSE score, and TMT-B&W (Part B) parameters were identified as characteristics that differed significantly between high- and low-dropout-rate institutions.

Further analysis was conducted to compare baseline characteristics in the discontinuation and continuation groups according to sex (Supplementary Table 6 in the online-only Data Supplement). The results showed that when comparing between all female and male patients, female patients were significantly older, had a shorter education period, lower MMSE and MoCA scores, and higher scores for TMT-B&W (Part A: time to completion), TMT-B&W (Part A: no. of errors), TMT-B&W (Part B: time to completion), and TMT-B&W (Part B: no. of errors) compared with male patients. When comparing baseline characteristics between the discontinuation and continuation groups according to sex, there was no difference between these two groups among female patients. However, among male patients, the discontinuation group showed lower MMSE scores and higher CDR scores, and there was a significant difference in the caregiver's relationship with the patient (the discontinuation rate was lower when the caregiver was the spouse). The baseline characteristics did not differ significantly between male and female patients in the discontinuation groups. When comparing the discontinuation rates according to the caregiver's sex, the discontinuation rate was 9.68% for caregivers who were male and 13.24% for caregivers who were female ($p=0.480$, Fisher's exact test).

Additional analyses

While the changes in CDR scores for orientation, memory, personal care, and home and hobbies did not differ significantly between the groups, the scores for other CDR subcategories (memory, judgement and problem-solving, and community affairs) were better in patients with caregivers who received additional education (data not shown). Furthermore, patients with caregivers who did not receive additional education exhibited significantly worse CDR scores for the subcategory of judgement and problem-solving and that of community affairs.

The rate of donepezil discontinuation differed with the baseline CDR score but not with the education status of the caregiver (Supplementary Table 7 in the online-only Data Supplement).

DISCUSSION

This study investigated the impact of caregiver education on continuation of treatment with donepezil in patients from Korea who were newly diagnosed with Alzheimer's disease and had newly been prescribed donepezil. The rate of discontinuation of treatment with donepezil after 1 year, which was the primary endpoint of this analysis, was 5.38% in the group of caregivers who received education regarding the disease and the efficacy and adverse events of donepezil. This discontinuation rate did not differ significantly from that observed in the group of caregivers who did not receive such education (6.52%, $p=0.742$).

The severity of Alzheimer's disease at baseline was mild in most of the patients in the present population. In baseline cognitive assessments, patients had a mean MMSE score of 21, indicating mild to moderate cognitive impairment. Similarly, the mean MoCA score was less than 26, indicating the presence of at least mild cognitive impairment. In addition, most patients had either very mild or mild dementia based on a CDR score of 0.5 or 1, respectively. Therefore, it is possible that no significant differences were observed in treatment discontinuation rates between caregivers who received or did not receive education because the overall cognitive impairment in this population at baseline was not sufficiently severe to allow the effect of the education to be measured. Additionally, the present findings suggest that providing an education program to caregivers does not affect treatment compliance among their patients. However, the discontinuation rates might have been too low to reveal a significant difference.

A common reason for poor treatment adherence is experiencing adverse events.²⁰ Consistent with previous studies, the occurrence of adverse events was a major reason for discontinuation in our study (8 of 11 patients) and was cited as the most common reason for treatment discontinuation by both physicians and patients.

Few studies have assessed factors associated with drug adherence in the Korean population. Nursing intervention programs aimed at improving medication adherence²¹ and medication counseling by pharmacists²² were reported to be effective in improving treatment compliance in patients receiving hemodialysis within Korean primary medical care and at secondary medical care centers. Meanwhile, a study of drug compliance found that patients reported having high confidence in the treatment provided in university hospitals, and most patients believed they would benefit from taking their prescribed drugs, resulting in high drug compliance.²³ All of the centers included in our study were tertiary hospitals, which may have diminished the impact of caregiver education on drug persistence, resulting in low discontinuation rates (around

6% in the total study population).

Our study also assessed how discontinuation rates were associated with the change in disease severity as measured by the CDR global score, and with the sex of the caregiver and their relationship with the patient. The discontinuation rate was significantly higher among patients with very mild disease than among those with mild disease at baseline (17.02% and 7.29% in those with CDR scores of 0.5 and 1, respectively). This finding suggests that a lower CDR score (milder disease) is associated with a higher discontinuation rate. We speculate that the patients with lower CDR scores in our study had higher discontinuation rates because they refused to believe that they had dementia. Therefore, patients with a lower CDR score in our study may have considered that they did not require medication, and thus tended to discontinue treatment more than those with disease that was more severe. Caregivers were more commonly females (68.69%), and accordingly the most common relationships with the patient were as a wife or daughter. Discontinuation rates varied significantly according to the relationship of the caregiver to the patient ($p=0.004$; spouse vs. child, $p=0.003$). However, the small numbers in each subgroup, particularly for son-in-law ($n=1$), restrict the ability to interpret these data.

The present study found that age, sex, education period, MMSE score, and TMT-B&W (Part B) parameters differed significantly between high- and low-dropout-rate institutions. Similarly, female patients were found to be more likely to discontinue treatment in a Finnish study.²⁴ Our findings are also consistent with a previous study of geriatric patients finding that the level of compliance was associated with their education level,²⁵ and another study finding that treatment adherence was higher among male patients and those with a higher education level.²⁶

In both the present discontinuation and continuation groups, the baseline characteristics were less favorable (e.g., older age, shorter education period, and worse cognitive state) in female patients than in male patients. The education level is known to be associated with variations in discontinuation rates in patients with other diseases.²⁷⁻²⁹ There were no significant differences in baseline characteristics between male and female patients in the discontinuation groups, which suggests that sex is not associated with discontinuation, whereas the severity of cognitive impairment and functional decline are associated with discontinuation. Our findings support a previous report of sex not being a significant factor associated with medication adherence level among elderly subjects.²⁷ Furthermore, a recent systematic review found inconsistent results for whether sex is associated with treatment adherence.³⁰ In the present study, when the caregiver was female, the discontinuation rate was higher for female patients than for male

patients; in other words, the effect of the caregiver's sex on the discontinuation rate differs with the sex of the patient. However, the discontinuation rate of all patients did not differ significantly between whether the caregiver was male or female.

This study had some limitations. In Korea, the choice of treatment for Alzheimer's disease is mainly decided by the physician rather than by the patient or their caregiver. In addition, all patients were enrolled at tertiary hospitals that already had well established education programs, and so the knowledge level of the patients and caregivers about the disease was likely to already have been high. This situation might make it difficult to observe the impact of caregiver education on continuation of treatment in this setting. Finally, although this was not an interventional study, the dropout rate was high; there were only small numbers of male caregivers and male patients, and seven of the included patients had a CDR score of 2, which may have affected the results.

In conclusion, this study did not identify any significant differences in the rate of discontinuation of donepezil treatment between patients in the caregiver education group and those in the no-education group. However, significant effects of the education program on treatment compliance were identified.

Supplementary Materials

The online-only Data Supplement is available with this article at <https://doi.org/10.3988/jcn.2021.17.3.368>.

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Conflicts of Interest

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