



Pharmacist's role in pharmacotherapeutic management of Alzheimer's disease

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ABSTRACT

Alzheimer Disease (AD) characterized by the progressive cognitive and functional impairment, is the most common form of dementia affecting people worldwide. In this study, we aimed to investigate the profile of patients with AD, the perception of caregivers about the disease and the role of pharmacist in the pharmacotherapy of AD by implementing a questionnaire for the caregivers of 44 patients with AD. 70% of the evaluated patients with AD is female gender and in 52% of the cases, hypertension co-exists with AD. The combination of memantine/donepezil (34%) was found the most commonly used pharmacological treatment in the patients which was associated with various adverse effects such as headache, insomnia, fatigue, and hallucinations. An average of 70% of the caregivers benefit from the pharmacists in regard to the use of drugs (94%), information about disease and side effects (48%) and drug-drug interactions (42%). Additionally, the 77% of caregivers who benefit from pharmacists were well satisfied with this support. In conclusion, patients with AD and their caregivers need a professional assistance regarding the use of drugs and modalities how to fight with the disease. Pharmacists play a significant role in both following the pharmacotherapy of AD patients and the education of caregivers. Thus, pharmacist's role in the management of rational pharmacotherapy should be strengthened by providing a continued educational support.

Keywords: Alzheimer Disease, pharmacist, pharmacotherapy applications, caregivers, donepezil

INTRODUCTION

Alzheimer's Disease (AD) is the most common form of dementia characterized by progressive cognitive and functional impairment involving memory loss, language impairment and disorientation as well as deterioration in their ability to carry out activities of daily living (Mucke 2009). As the rate of the aging population increases throughout the world, the number of patients with AD is also increasing in Turkey that was comparable with the rates in western countries (Gurvit et al. 2008). In Turkey, the latest ratio of the population aged over 65 was 8.2% in 2015 and as the rate of the aging population increases, the proportion of elderly people who lost their lives from AD was 4% in 2014, which was 2.7% in 2010 (Turkish Ministry of Health, Statistics 2015). Patients with AD show pathological changes including increased deposits of amyloid β peptide in the cerebral cortex, which eventually form extracellular senile plaques and intraneuronal fibrillary tangles consisting of tau protein (Zheng et al. 2002; Mucke, 2009; Graham et al. 2017). There is a progressive loss of neurons, especially cholinergic neurons in the brain areas related to memory and learning (Cummings and Cole 2002). The loss of cholinergic neurons results in a marked decrease of neurotransmitter acetylcholine (ACh) in the brain and thus, selective acetylcholine esterase inhibitors that increase ACh concentrations in the synaptic cleft by inhibiting its break down, are commonly used in the first line treatment of AD (Graham et al. 2017).

Pharmacists have been accepted as the most accessible, trusted and respected healthcare professionals and they play a critical role in the pharmacotherapy of AD (Tett et al. 1993; Wiens 2003). Pharmacists can play an active role in counselling of the patients, caregivers and clinicians on the rational use of drugs as well as alternative products, monitoring or identifying drug-related problems such as adverse drug reactions, drug interactions, improper drug selection and inappropriate dosage form (Feinberg and Michocki 1998; Wiens 2003).

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AD is the major cause of nursing home admission because of the progressive cognitive and functional decline that directly affects families and caregivers. (Gaugler et al. 2007). Family caregivers play an essential role in optimal pharmacotherapy of these patients (Halley 1997). The present study was performed to determine the role of pharmacist in pharmacotherapy of patients with AD. Patients and their caregivers were surveyed to assess their socio-demographic characteristics, pharmacotherapy regimes of patients with AD, caregiver's attitudes to the patient and caregiver's perceptions about the the role of pharmacist in therapeutic management of AD.

MATERIALS AND METHODS

Subjects

This study was performed by administrating a questionnaire comprising 4 sections to a total number of 44 caregivers of patients with AD. Caregivers were selected through non-probability consecutive sampling among those who visited a community pharmacy to receive disease information and/or prescription drugs (n=20) and Turkish Alzheimer's Association Day Care Centre (n=24) in Istanbul (Turkey). The caregivers who live with the patients, were at least 18 years old, and those that were able to read and understand the questionnaire in Turkish and informed consent form were included in this study.

Procedure

The objectives of the study was explained on an individual basis and questionnaires were administrated to caregivers of patients with AD. The questionnaire consists of 4 sections regarding the socio-demographic characteristics of the patients and their caregivers (1), the pharmacotherapy (prescription drugs, adverse effects, alternative products, co-morbid diseases) (2), caregiver's approach to the patient (3) and perceptions about the the role of pharmacist in therapeutic management of AD (4).

Statistical analysis

Data were expressed as percentages. The diagnosis age of the patients with AD were expressed as means and standard deviations (SD) and assessed by the Student-t test. The statistical analysis was performed using Graph Pad (Prism 7) software. $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Sociodemographic characteristics of the patients with AD and their caregivers

This study was surveyed in 44 patients and their caregivers. The socio-demographic characteristics of the patients and their caregivers are shown on Table 1. The patient profile was 77 year-old whom diagnosed at age 69.6 ± 2 for women and 73.7 ± 2 for men ($p > 0.05$) with a primary education. The caregiver profile was consistent with the 52-year-old first-degree relative (mostly daughters) with a retired working status (Table 1).

Pharmacotherapy of patients with AD

Among 44 patients, 15 (34%) were on memantine and donepezil combination therapy and they reported to have some side effects such as insomnia, hallucinations, urinary incontinence and fatigue (Table 2). Other therapies were memantine+rivastigmine combination therapy (n=8; 8%), memantine (n=7; 16%), donepezil (n=7; 16%), memantine+donepezil+ rivastigmine (n=4; 9%),

Table 1. Socio-demographic variables of patients with AD and their caregivers

Patients (n=44)		Caregivers (n=44)	
Variable	n (%)	Variable	n (%)
Sex		Sex	
Male	13 (30)	Male	10 (23)
Female	31 (70)	Female	34 (77)
Mean age (SD)	77 (7.6)	Mean age (SD)	52 (13.2)
Range (years)	58-94	Range (years)	24-83
Mean Age (SD)		Relationship	
(at the time of Diagnosis)		Daughter	19 (43)
Male	69.6 (2)	Wife	7 (16)
Female	73.7 (2)	Husband	4 (9)
		Son	5 (11)
		Grandchild	3 (7)
		Daughter-in law	3 (7)
		Son-in law	1 (2)
		Niece	1 (2)
		Nurse	1 (2)
Education level		Working status	
Primary	30 (68)	Working-full time	3 (7)
High School	7 (16)	Working-part time	4 (9)
Bachelor's Degree	6 (14)	Not-working	18 (41)
Master's Degree	1(2)	Retired	19 (43)

rivastigmine only (n=2,5%) and donepezil+rivastigmine (n=1, 2%) and their reported side-effects were presented on Table 2. Only three of these 44 patients were using alternative products. These products were melatonin, fish oil and ginkgo biloba extract. Co-morbid diseases in patients with AD were hypertension (53%), depression (43%), diabetes (30%), heart disease (18%), hyperlipidemia (18%), osteoporosis (16%), vertigo (11%), epilepsy (9%) peptic ulcer (5%), Parkinson disease (5%) and prostate (2%).

Caregiver's attitudes to the patient

Caregiver's attitudes to the patient were reported as "always positive" for 52% (n=23) of caregivers and "sometimes nervous" for 48% (n=21) of caregivers. Only, 13 out of 44 (30%) caregivers reported to get psychological support for their own health, taking into account the challenges they are experiencing (Table 2). Twenty-three of remaining caregivers who did not receive (31) psychological support indicated that they would accept such support from a practitioner, while 8 refused to receive such support. Data related to the caregiver's approach is shown on Table 3.

Caregiver's perceptions about the the role of pharmacist in therapeutic management of AD

Among 44 caregivers 31 (70%) reported to get support from community pharmacy. 24 out of 31 patients who received support from pharmacists stated that support was sufficient, while 7 was stated as inadequate. Caregivers asked the pharmacist for information about drug usage (94%), the disease (48%), side-effects (48%), drug-drug interactions (42%) and psychological support (%32). While a large majority (70%) of

Table 2. Drug therapy and reported side effects in patients with AD

Side-effects	Drug therapy						
	Memantin+ Donepezil (34%)	Donepezil (16%)	Memantin (16%)	Memantin+ Donepezil+ Rivastigmin (9%)	Memantin+ Rivastigmin (8%)	Rivastigmin (5%)	Donepezil+ Rivastigmin (2%)
Headache	6		1	3	2		
Dizziness	3	3		2	2	1	
Fatigue	6	2	2	3	2		
Insomnia	9	3	3	1	5	1	1
Loss of consciousness	2	1	3	1	2		
Excitement	4		1	3	2		
Extreme fear	5	1	2	2	4		
Halusination	8	3	1	3	5		
Urinary incontinence	5	4	3	3	4		
Nausea	4		1	2	2	1	
Vomitting	3			1	1		
Diarrhea	1	2			1		
Loss of appetite	3	1		1	3		
Sweating	2		2	1			

Table 3. Caregivers approach to the patient with AD

Questions	Yes, n (%)	No, n (%)
Do you agree to receive training from an expert on Alzheimer's care?	37 (92)	7 (8)
Do you get psychological support for your own health, taking into account the challenges you are experiencing?	13 (30)	31(70)
If not, do you accept such pyhschological support from a practitioner?	23 (74)	8 (26)
Are you lean towards nursing home admission of the patient with AD?	12 (27)	32 (73)
Would you accept a new drug which being developed for the treatment the patient with AD?	24 (55)	20 (45)

caregivers reported that they received support from pharmacies, there were also those (%30) who did not receive any support as they feel more confident in their experience or believe in an insufficient knowledge of pharmacists about this disease.

In the present study, we surveyed the caregivers of the patients with AD to assess their socio-demographic characteristics, pharmacotherapy regimes of the patients with AD, caregiver's attitudes to the patient and perceptions about the the role of pharmacist in therapeutic management of AD.

The caregiver profile was consistent with the 52-year-old first-degree relative (mostly daughters) with a retired working status. The characteristics of caregivers were very similar to those found in other studies (Verez Coteló et al. 2015; Yikilkan et al. 2014) despite the small sample size of our group who lives in a spesific region (İstanbul).

N-methyl-D-aspartic acid antagonists (memantine) and cholinesterase inhibitors (ChEIs) are the only two approved classes of drugs to treat AD addressing respectively, the cholinergic and glutamatergic dysregulation which underlies the pathophysiology of AD (Mucke, 2009). The main ChEIs in use are donepezil, galantamine and rivastigmine. Among them donepezil was favored by caregivers in one study over other ChEIs particularly due to its ease of use (Sevilla et al. 2009). The combination

therapy with memantine and donepezil in patients with moderate to severe AD have positive effects on both behaviour and cognition (Atri et al. 2008; Tariot et al. 2004). The outcomes of this survey also suggest the common use of memantine and donepezil combination therapy in patients with AD despite its anticholinergic side effects (Table 2). Diseases such as hypertension, diabetes, depression often co-exist since AD more commonly occurs in older age groups (Schubert et al. 2006).

Caring for patients with AD can lead physical, psychological, emotional, social and financial burdens (Novais et al. 2017). In Turkey, the caregivers (with the majority of women, often being daughter) had high prevalence of depressive and anxiety symptoms (Yikilkan et al. 2014). The high percentage of caregivers who report their attitudes to the patient as "sometimes nervous" and accept a psychological support from a practitioner indicates a psychological burnout among these individuals. As supporting our findings, high percentage of Alzheimer's patient caregivers exhibited depressive symptoms (Papastavrou et al. 2007) and treated with anxiolytics and antidepressants (Verez Coteló et al. 2015).

The survey revealed that 70% of caregivers benefit from pharmacists regarding the use of drugs (94%), the disease (48%), side effects (48%), drug-drug interactions (42%) and psychological support (32%). This finding is providing the pharma-

cist's role in both pharmacotherapy of patients with AD and the management of caregiver burden.

Pharmacist's roles in management of AD are described as: assessment of medications and prescriptions, counselling of patients and caregivers and surveillance or monitoring of medications (Wiens 2003). Donepezil consultation provided by hospital pharmacist for patients with AD and their caregivers lead better adherence to pharmacotherapy (Watanabe et al. 2012). Patients with AD particularly susceptible to risk of anticholinergic side effects with certain medications (Wiens 2003) and should be assisted by a pharmacist in selecting safe formulation such as over-the-counter (OTC) products. Pharmacists can also counsel patients and their caregivers on the safe use of herbal (alternative) products that high majority of caregivers had requested relaxing plants and vitamins from the pharmacy for anxiety and insomnia (Verez Cotelto et al. 2015). As being one of the most accessible and regularly visited healthcare professionals in primary care (Patwardhan et al. 2012), pharmacists can also play a vital role in recognising the early symptoms of AD and may encourage patients to seek an early diagnosis (Ricklees et al. 2014). While a large majority of caregivers benefit from pharmacists who make significant contribution to the management of AD, there were also those who did not receive any support as they feel more confident in their experience or believe in an insufficient knowledge of pharmacists about this disease. Supporting this, inadequate knowledge on risk factors, disease and its progression, caregiving issues and pharmacological management of AD has been recently reported in community pharmacists (Zerafa and Scerri 2016) and highlighted the need of training and educational support about AD (Skelton 2008).

Present results suggest that pharmacists play an active role in the pharmacotherapeutic management of AD and their involvement could improve clinical outcomes and caregiver's quality of life. In Turkey, with the expected increase in the number of patients diagnosed with AD in future, the pharmacist's involvement in AD management should be expanded by providing occupational training and continued educational support.

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