Clinical Practice with Antidementia Drugs in a Geriatric Clinic

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Background: Cholinesterase inhibitors and N-methyl-D-aspartate antagonist have been used increasingly for patients with dementia. However, these products are relatively costly and have been linked to many adverse events. Only a few surveys of prescribing patterns of drugs for dementia have been conducted in developing countries, while the proportion of dementia patients is expected to become higher in these regions. We aim to evaluate the utilization patterns, adverse events, and cost of antidementia drugs in a geriatric clinic at Siriraj hospital.

Material and Method: Data was obtained from the medical records of dementia patients who were newly diagnosed between January 2007 and December 2009 in the Geriatric clinic, Siriraj hospital, Bangkok. The diagnosis was based on DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-IV) criteria.

Results: Ninety-six elderly patients were diagnosed with dementia during the studied period. Eighty patients (83.3%) with the average age of 80.6 (SD = 7) years received antidementia drugs. Donepezil was the most frequently prescribed drug (70%), followed by rivastigmine (22.5%). Concomitant use of interacting drugs was noted in 41.3% of patients. The average prescribed daily dose of rivastigmine, galantamine and memantine were lower than their effective defined daily dose. The highest average cost per year was galantamine (60,020.5 baht/year) and the lowest one was memantine (45,857.7 baht/year). Among cholinesterase inhibitors receivers, 43.5% had at least one adverse event. Thirty-seven percent of these were gastrointestinal side effects. Only 12.5% of memantine-receivers developed adverse events. One-year drug discontinuation rates were 26.1% and 12.5% in cholinesterase inhibitor and memantine groups, respectively. From multivariate logistic regression analysis, the only factor associated with adverse drug events was the presence of behavioral and psychological symptoms.

Conclusion: The majority of dementia patients in our study were prescribed antidementia drugs. Half of them developed adverse events, but one-year drug discontinuation was relatively low. The average daily doses were lower than recommended doses. Future prospective studies should be performed to determine the cost-effectiveness and establish evidence-based practice guideline for management of dementia patients.

Keywords: Adverse drug event, Cholinesterase inhibitor, Dementia, Geriatric, Prescribing pattern

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The proportion of the older population afflicted with dementia is rapidly increasing worldwide, representing a vulnerable population with respect to medication issues. In 2006, a study in Thailand found that there were 229,000 people with dementia and, in the next 20 years, the number will increase to 450,000⁽¹⁾. The economic burden associated with dementia reflects the progressive nature of the disease and the cost of caring for patients increases substantially as they become less able to care for themselves.

At present, there are two classes of medications approved by the US Food and Drug Administration

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Muangpaisan W, Department of Preventive and Social Medicine, Siriraj Hospital, Bangkok 10700, Thailand. Phone: 0-2419-8388, Fax: 0-2411-5034 E-mail: siwmp@mahidol.ac.th (FDA) for the treatment of Alzheimer's disease (AD). The cholinesterase inhibitors (ChEIs) are indicated for the treatment of mild to moderate AD, which include donepezil (Aricept[®]), galantamine (Reminyl[®]), and rivastigmine (Exelon®). The N-methyl-D-aspartate antagonist memantine (Ebixa®) is the only treatment licensed for the treatment of moderate to severe dementia^(2,3). Previous studies demonstrated the dramatic increase in the dispense rate of these types of medications^(4,5). However, these products have been linked to adverse events in older adults with dementia and the cost of all medications remains relatively expensive for people in developing countries. Only a few surveys of prescribing patterns of drugs for dementia have been conducted in developing countries, while the proportion of dementia patients is expected to become higher in these regions^(6,7). Existing studies have to date been conducted in developed countries⁽⁸⁻¹²⁾. The aim of the present study was to determine the current utilization patterns, adverse events and the cost of antidementia drugs in a geriatric clinic of a governmental tertiary health care center patient population. In addition, the authors wanted to determine the factors associated with adverse drug reactions in patients treated with antidementia drugs. Hence, the present study could be beneficial to the physicians who might use the findings from the present study when caring for their patients.

Material and Method Design and data collection

A retrospective chart review was conducted. Data was obtained from medical records of 96 newly diagnosed dementia patients in the Geriatric Clinic, Siriraj Hospital, Bangkok, Thailand between January 2007 and December 2009. The diagnosis was based on DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-IV) criteria. All data was recorded by the Geriatricians in the clinic. The data contained information about the baseline characteristics of the patients, co-morbidity, concomitant drug use, drug interactions with ChEIs^(13,14), caregivers, type and severity of dementia (assessed by the Thai Mental State Examination (TMSE))⁽¹⁵⁾, Activities of Daily Living (ADLs), Behavioral and Psychological Symptoms of Dementia (BPSD), prescription data, and adverse drug events. Patients with less than one-year follow-up were excluded from the study, which was approved by Siriraj Institutional Review Board.

Statistical analysis

Characteristics of subjects, prescribing patterns and adverse events were described using

 Table 1. Baseline characteristics of patients in the Geriatric clinic, Siriraj Hospital who were newly diagnosed with dementia between January 2007 and December 2009

Baseline characteristics	Not received antidementia drugs	Received antidementia drugs	Total 96 (100)	
Number of patients (%)	16 (16.7)	80 (83.3)		
Age (years: mean \pm SD)	81.3 ± 8	80.6 ± 7	80.7 ± 7	
Female (%)	10/16 (62.5)	58/80 (72.5)	68/96 (70.8)	
Medical expense				
Reimbursement from government (%)	6/14 (42.9)	65/79 (82.3)	71/93 (76.3)	
Self-paid	8/14 (57.1)	14/79 (17.7)	22/93 (23.7)	
Co-morbid diseases (%)	15/16 (93.8)	80/80 (100)	95/96 (99.0)	
Neurological disease	8/16 (50.0)	24/80 (30.0)	32/96 (33.3)	
Cardiovascular disease	10/16 (62.5)	51/80 (63.8)	61/96 (63.5)	
Gastrointestinal disease	2/16 (12.5)	10/80 (12.5)	12/96 (12.5)	
Hepatobiliary disease	1/16 (6.3)	2/80 (2.5)	3/96 (3.1)	
Diabetes mellitus	6/16 (37.5)	35/80 (43.8)	41/96 (42.7)	
Hypertension	10/16 (62.5)	57/80 (71.3)	67/96 (69.8)	
Dyslipidemia	11/16 (68.8)	49/80 (61.3)	60/96 (62.5)	
Psychiatric diseases	4/16 (25.0)	10/80 (12.5)	14/96 (14.6)	
Concomitant drugs use (%)				
Analgesics and muscle relaxant	3/16 (18.8)	9/80 (11.3)	12/96 (12.5)	
Antipsychotic drugs	4/16 (25.0)	26/80 (32.5)	30/96 (31.3)	
Antihypertensive drugs	9/16 (56.3)	48/80 (60.0)	57/96 (59.4)	
Anticholinergic drugs	1/16 (6.3)	8/80 (10.0)	9/96 (9.4)	
Benzodiazepines	0	8/80 (10.0)	8/96 (8.3)	
Drug interaction with antidementia drugs (%)	8/16 (50.0)	33/80 (41.3)	41/96 (42.7)	

descriptive statistics. Associations between the potential risk factors and the adverse events in subjects using antidementia drugs were first assessed with the univariate logistic regression model. Age and potential risk factors associated with the dependent variables in the univariate analysis with p < 0.05 (two-tailed) were introduced into a multivariate logistic model. A backward stepwise procedure was used to identify variables independently associated with the dependent variable and the final model was tested for interactions. The level of significance used for tests was p < 0.05 (two-tailed). All analyses were conducted using SPSS statistical software version 18.0.

Results

Baseline characteristics of patients

Between January 2007 and December 2009, 96 elderly patients were diagnosed with dementia and

80 patients (83.3%) received medications for dementia. Table 1 provides the baseline characteristics of patients and Table 2 shows the type and severity of patients. The average age of the patients was 80.7 ± 7 years and the percentage of women was 70.8%. The most frequent co-morbidity was hypertension (69.8%). Forty-one percent of patients received drugs that interacted with antidementia drugs and eighty-nine percent of patients had polypharmacy (defined as concomitant use of five or more drugs). AD was the most common cause of dementia (39.6%), followed by unspecified dementia (21.9%), and mixed dementia (19.8%). The majority of patients had mild to moderate dementia with the average TMSE score of 19 ± 6 points. The authors found that 42.7%of the patients had BPSD and hallucination was the most common manifestation (28.1%), followed by aggressive behavior (19.8%) and depression (10.4%).

 Table 2.
 Type and severity of patients in the Geriatric Clinic, Siriraj Hospital who were newly diagnosed with dementia between January 2007 and December 2009

	Not received antidementia drugs	Received antidementia drugs	Total	
Type of dementia (%)				
Unspecified dementia	4 (25.0)	17 (21.3)	21 (21.9)	
Dementia in Alzheimer's disease	3 (18.8)	35 (43.8)	38 (39.6)	
Vascular dementia	4 (25.0)	8 (10)	12 (12.5)	
Mixed dementia	1 (6.3)	18 (22.5)	19 (19.8)	
Dementia in Parkinson's disease	3 (18.8)	1 (1.3)	4 (4.2)	
Dementia in Pick's disease	1 (6.3)	1 (1.3)	2 (2.1)	
Severity of dementia (%)	(n = 12)	(n = 68)	(n = 80)	
Mild	5 (41.7)	31 (45.6)	36 (45.0)	
Moderate	6 (50.0)	31 (45.6)	37 (46.3)	
Severe	1 (8.3)	6 (8.8)	7 (8.7)	
Activities of daily living (%)	(n = 16)	(n = 80)	(n = 96)	
Full BADLs without support	7 (43.8)	48 (60.0)	55 (57.3)	
Totally or partial dependent	9 (56.3)	32 (40.0)	41 (42.7)	
TMSE score (mean \pm SD)	$18 \pm 5 (n = 12)$	$19 \pm 6 (n = 68)$	$19 \pm 6 (n = 80)$	
BPSD (%)	5/16 (31.3)	36/80 (45.0)	41/96 (42.7)	
Hallucination	3/16 (18.8)	24/80 (30.0)	27/96 (28.1)	
Aggressive behavior	0	19/80 (23.75)	19/96 (19.79)	
Depression	2/16 (12.5)	8/80 (10.0)	10/96 (10.4)	
Paranoid	0	5/80 (6.3)	5/96 (5.2)	
Delusion	1/16 (6.3)	3/80 (3.8)	4/96 (4.2)	
Apathy	0	1/80 (1.3)	1/96 (1.0)	

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	Donepezil (Aricept [®])	Rivastigmine (Exelon [®])	Galantamine (Reminyl [®])	Memantine (Ebixa [®])	Total
Duration of follow-up (days)					
Mean (SD)	-	-	-	-	609 (332)
Median (min, max)	-	-	-	-	588 (15, 1,460)
First prescription drug (%)	56 (70.0)	18 (22.5)	3 (3.8)	3 (3.8)	80 (100)
Dose of drugs (mean \pm SD)					
Initial dose (mg)	3.6 ± 1	2.9 ± 1	8.0 ± 0	7.5 ± 3	-
Maximum dose (mg)	7.5 ± 3	7.5 ± 3	14.0 ± 4	14.1 ± 5	-
Safety dose (mg)	5.8 ± 3	6.4 ± 3	12.0 ± 8	12.8 ± 7	-
Mean dose (mg)	6.0 ± 2	5.5 ± 2	13.2 ± 3	12.6 ± 4	-
Cost of drugs (baht)					
Mean	57,806.1	53,850.0	60,020.5	45,857.7	-
Standard deviation	12,341.0	12,963.0	15,451.0	13,494.0	-
Median	55,115.0	58,765.0	59,892.0	36,500.0	-
Minimum	27,557.5	5,578.4	41,245.0	32,850.0	-
Maximum	84,566.9	63,145.0	79,052.9	69,654.2	-

 Table 3. Prescribing patterns of antidementia drugs in dementia patients in the Geriatric Clinic, Siriraj Hospital who were newly diagnosed with dementia between January 2007 and December 2009

 Table 4. One-year responses in functional performance (ADLs), behavioral and psychological symptoms in dementia (BPSD) and cognitive function in dementia patients in the Geriatric Clinic, Siriraj Hospital who were newly diagnosed with dementia between January 2007 and December 2009

Responses	Antidementia drugs				Total, n (%)
	Donepezil n (%)	Rivastigmine n (%)	Galantamine n (%)	Memantine n (%)	
Activities of daily living					
Improve	4/50 (8.0)	4/24 (16.7)	0	0	8/87 (9.2)
Stable	43/50 (86.0)	20/24 (83.3)	2/3 (66.7)	10/10 (100)	75/87 (86.2)
Worse	3/50 (6.0)	0	1/3 (33.3)	0	4/87 (4.6)
Behavioral and psychological symptoms					
Improve	5/50 (10.0)	5/24 (20.8)	0	2/10 (20.0)	12/87 (13.8)
Stable	41/50 (82.0)	17/24 (70.8)	3/3 (100)	8/10 (80.0)	69/87 (79.3)
Worse	4/50 (8.0)	2/2 4 (8.3)	0	0	6/87 (6.9)
Cognitive function					
Improve	6/50 (12.0)	7/24 (29.2)	0	1/10 (10.0)	14/87 (16.1)
Stable	37/50 (74.0)	16/24 (66.7)	1/3 (33.3)	8/10 (80.0)	62/87 (71.3)
Worse	7/50 (14.0)	1/24 (4.2)	2/3 (66.7)	1/10 (10.0)	11/87 (12.6)

Prescribing patterns and cost of medicine for dementia Donepezil was the most frequent initially prescribed drug (70%), followed by rivastigmine (22.5%), as indicated in Table 3. The average prescribed daily dose of donepezil was 6.0 mg, for rivastigmine, it was 5.5 mg, for galantamine, it was 13.2 mg, and for memantine, it was 12.6 mg. The highest average cost per year was galantamine (60,020.5 baht/year) and the lowest average cost per year was memantine (45,857.7 baht/year).

Responses

At the one-year follow-up, approximately 90% of the patients had stable and improved conditions in functional levels (ADLs), BPSD, and cognitive functions both in ChEIs and memantine groups (Table 4).

Drugs adverse events

Of the 80 patients receiving antidementia drugs, 22 patients were changed from the first to the second antidementia drug regimen and seven patients were changed the prescription to the third antidementia drug regimen. Ninety-two patients received ChEIs and 16 patients received memantine. The main reason for the change of the prescription was the adverse events (82%), followed by the deterioration of dementia symptoms (9%), and no improvement of dementia symptoms (5%). Forty (43.5%) out of 92 patients who received ChEIs had at least one adverse event. Thirty-four (37%) of these were gastrointestinal side effects, which included anorexia, nausea, vomiting, and weight loss. Only two (12.5%) of the patients who received memantine had adverse events (Table 5).

The authors used the multivariate logistic model, a backward stepwise procedure to identify factors associated with the adverse events in subjects using antidementia drugs. Age, presence of BPSD, and the use of antihypertensive, antipsychotics, and drugs that interacted with antidementia were introduced into a multivariate logistic model. The authors found that the only factor that was associated with adverse drug events was the presence of BPSD.

Discussion

The prescribing rates of antidementia drugs and the adverse drug events were high in the present study. The average prescribed daily dose of rivastigmine, galantamine and memantine were lower than their effective defined daily dose. At the one-year follow-up, the majority of the patients remained stable and/or improved in their functional level, BPSD, and cognitive functions, and the drug discontinuation was found in one quarter of the patients. Drugs with potential interaction with antidementia drugs were frequently prescribed concomitantly.

The proportion of patients receiving antidementia medications in the present study was high

	Cholinesterase inhibitors				Memantine
	Donepezil	Rivastigmine	Galantamine	Total	
Overall side effects (%)	26/61 (42.6)	13/27 (48.1)	1/4 (25.0)	40/92 (43.5)	2/16 (12.5)
Weight loss (%)	10/61 (16.4)	2/27 (7.4)	-	12/92 (13.0)	1/16 (6.3)
Gastrointestinal side effects (%)	23/61 (37.7)	10/27 (37.0)	1/4 (25.0)	34/92 (37.0)	1/16 (6.3)
Nausea and vomiting	10/61 (16.7)	5/27 (18.5)	1/4 (25.0)	16/92 (17.4)	-
Abdominal pain	1/61 (1.6)	-	-	1/92 (1.1)	-
Anorexia	14/61 (23.0)	2/27 (7.4)	-	16/92 (17.4)	1/16 (6.3)
Constipation	1/61 (1.6)	-	-	1/92 (1.1)	-
Diarrhea	4/61 (6.6)	1/27 (3.7)	-	5/92 (5.4)	-
Neurological side effects (%)	6/61 (9.8)	2/27 (7.4)	-	8/92 (8.7)	1/16 (6.3)
Dizziness	2/61 (3.3)	1/27 (3.7)	-	3/92 (3.3)	1/16 (6.3)
Headache	1/61 (1.6)	-	-	1/92 (1.1)	-
Confusion	-	1/27 (3.7)	-	1/92 (1.1)	-
Insomnia	2/61 (3.3)	-	-	2/92 (2.2)	-
Hallucination	-	-	-	-	
Agitation	4/61 (6.6)	1/27 (3.7)	-	5/92 (5.4)	-
Cardiac arrhythmia (%)	1/61 (1.6)	-	-	1/92 (1.1)	1/16 (6.3)
Urinary incontinence (%)	-	2/27 (7.4)	-	2/92 (2.2)	-
Drug discontinuation (%)	15/61 (24.6)	7/27 (25.9)	2/4 (50)	24/92 (26.1)	2/16 (12.5)

 Table 5.
 Adverse reactions of antidementia drugs in dementia patients in the Geriatric Clinic, Siriraj Hospital who were newly diagnosed with dementia between January 2007 and December 2009

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(83.3%) compared to that previously reported^(5,7,8,10-12). This difference might arise from several reasons. Firstly, three quarters of our patients could have their medical expenses reimbursed by the government. Differences in reimbursement rates and health policies could partly explain the variation in antidementia prescribing rates across countries. Secondly, as previously studied, factors that significantly predicted lower prescribing rates included female sex, perceptions of the antidementia drugs' effectiveness, and self-reported knowledge of the antidementia drugs⁽¹⁰⁾. The present study was conducted in a geriatric clinic where the geriatricians provided care for the patients. They are familiar with dementia and its treatment. In addition, the majority of the presented patients had mild to moderate severity of dementia where the ChEIs are indicated.

The most frequent initially prescribed drug in the present study was donepezil followed by rivastigmine. Donepezil was the preferred medication followed by galantamine and rivastigmine in most studies^(5,7). The difference in drugs dispensation may derive from the physicians' experience, differences in healthcare systems and health economics. Most patients in the present study had mild to moderate dementia and memantine is approved for patients with moderate to severe dementia. Thus, the use of memantine in the present study may be less than previously reported in other studies^(6,7). The average prescribed daily doses of rivastigmine, galantamine, and memantine were lower than the effective daily dose of all three drugs. The major cause was that the patients developed the adverse events before reaching the effective defined daily dose. This might be from the characteristics of the presented patients who were of relatively old age, had low body mass index and had multiple co-morbid diseases leading to the limitation in increasing doses of the medications.

The adverse events from ChEIs occurred more frequently than memantine and the most common adverse events were gastrointestinal side effects including anorexia, nausea, vomiting, and weight loss. This finding was similar to a report from Cochrane Systematic Review 2006⁽¹⁶⁾. Pariente A et al found that the factors associated with serious adverse reactions to ChEIs were age, the use of antipsychotics, the drugs targeting the alimentary tract, and antihypertensive drugs⁽¹⁷⁾. However, the prevalence of cardiovascular and neurological adverse events were more frequent than that in the present study. Due to the small population of the present study, the authors might lack the power to determine these associations. The reason that BPSD was associated with adverse drug reactions in patients treated with antidementia drugs was unknown. The authors hypothesized that it might be because most patients with BPSD had a high severity of disease and abnormal behavior leading to the misuse of antidementia drugs. It may also be due to the baseline abnormalities of central nervous systems that increases the risk of side effects of antidementia drugs. Further study is needed to explore this relationship.

One-year risks of drug discontinuation were 26.1% in ChEIs and 12.5% in memantine treatments. These proportions were lower than previous studies, which were 30.8% at six months and 54.7 to 66.4% at one-year. Established risk factors for ChEIs discontinuation are female sex, age 80 years or over, lower MMSE scores, not receiving social assistance, paying at least 65% of total prescription costs, concomitant use of antidepressants/ anticholinergics, hospitalization, and weight loss. The two main factors that decrease the discontinuation risk in the presented patients might be the healthcare support costs for the majority of our patients and family assistance in caring for the patients. Concomitant use of drugs with potential ChEI interaction was 41%, which was similar to the report by Tavassoli N et al $(35.5\%)^{(13)}$. The reasons for the use of the drugs with potential interaction with ChEIs in the present study may be from co-morbidities (100%), polypharmacy (89%), and seeing multiple clinicians from different clinics. This highlights the need for increasing awareness and more prudent prescription.

The strength of the present study is that the diagnosis of dementia in this clinic was made by experts. The diagnosis, treatment and monitoring of adverse drug events are expected to be of a high standard. The assessment of the impact from dementia was entirely evaluated in respect of cognition, behavioral and psychological symptoms, Activities of Daily Living (ADL), and caregiver burden. Previous studies regarding prescribing patterns of the antidementia drugs did not measure the treatment outcomes^(5,7-10). To the authors' knowledge, this is the first study regarding prescribing practices of antidementia drugs that reports the treatment outcomes. There have been a few studies focusing on the prescribing patterns of these medications in less developed countries, particularly in Asia. The present study could be a valuable resource for clinicians to apply in their clinical practice.

The present study had some limitations. Because of the retrospective design of the present study, there were some missing values in the required data. As a result of the retrospective chart review, the authors might miss some information regarding the monitoring of compliance and adverse drug events. However, the data and assessments were complete despite the retrospective nature of the present study. The assessment of cognitive functions, BPSD, and functional ability was not based on standard assessment tools. Only some patients underwent standard assessment. Most patients received only clinical evaluation and TMSE rather than a full set of formal measurements to determine the treatment effect of antidementia drugs. However, this is similar to what is routinely performed in daily clinical practice where there are limited resources and time. Another limitation is that the small population could lead to insufficient power to determine the factors associated with adverse drug reactions from antidementia drugs and, finally, the estimates from the relatively rarely prescribed medications such as galantamine are subjected to imprecision. Notably, the present study was conducted in the geriatric clinic of a tertiary medical center located in a metropolitan area. It is therefore unclear whether the results are generalizable to other clinical or community settings among different levels of healthcare centers and different specialties of clinicians where the prescribing policies and healthcare systems are different. However, antidementia drugs are usually available in large medical centers and special clinics where medical specialties are available. The patients in those centers and the practice of those clinicians should not be much different from the authors' setting.

Previously, there had been only rare studies of utilization patterns of antidementia drugs in less developed countries despite the fact that, in the near future, the majority of the world's elderly population will be living in such countries. Although this is a small study in a specific patient population, which has some limitations, it could be a resource for clinicians to consider when they are faced with dementia patients in their clinical practice. In addition, it could be used to generate future research questions and studies.

Potential conflicts of interest

None.

References

 Rees G, Chye AP, Lee SH, editors. Dementia in the Asia Pacific region. Proceedings of the 15th Asia Pacific member organisations of Alzheimer's Disease International (ADI) conference; 2005 May; Singapore. Canberra: Access Economics; 2006.

- Cummings JL. Alzheimer's disease. N Engl J Med 2004; 351: 56-67.
- Gauthier S, Thal LL, Rossor MN. Future diagnosis and management of Alzheimer's disease. In: Gauthier S, editor. Clinical diagnosis and management of Alzheimer's disease. 3rd ed. Abingdon: Informa Healthcare; 2007: 379-82.
- Mamdani M, Rapoport M, Shulman KI, Herrmann N, Rochon PA. Mental health-related drug utilization among older adults: prevalence, trends, and costs. Am J Geriatr Psychiatry 2005; 13: 892-900.
- Hollingworth SA, Byrne GJ. Prescribing trends in cognition enhancing drugs in Australia. Int Psychogeriatr 2011; 23: 238-45.
- Prasad K, Gupta H, Bharath S, Prakash O, Sivakumar PT, Kumar CN, et al. Clinical practice with antidementia and antipsychotic drugs: Audit from a geriatric clinic in India. Indian J Psychiatry 2009; 51: 272-5.
- Truter I. Prescribing of drugs for Alzheimer's disease: a South African database analysis. Int Psychogeriatr 2010; 22: 264-9.
- Jeschke E, Ostermann T, Vollmar HC, Tabali M, Schad F, Matthes H. Prescribing patterns in dementia: a multicentre observational study in a German network of CAM physicians. BMC Neurol 2011; 11: 99.
- Rattinger GB, Mullins CD, Zuckerman IH, Onukwugha E, Delisle S. Clinic visits and prescribing patterns among Veterans Affairs Maryland Health Care System dementia patients. J Nutr Health Aging 2010; 14: 677-83.
- Hillmer M, Krahn M, Hillmer M, Pariser P, Naglie G. Prescribing patterns for Alzheimer disease: survey of Canadian family physicians. Can Fam Physician 2006; 52: 208-9.
- Pariente A, Helmer C, Merliere Y, Moore N, Fourrier-Reglat A, Dartigues JF. Prevalence of cholinesterase inhibitors in subjects with dementia in Europe. Pharmacoepidemiol Drug Saf 2008; 17: 655-60.
- Herrmann N, Gill SS, Bell CM, Anderson GM, Bronskill SE, Shulman KI, et al. A populationbased study of cholinesterase inhibitor use for dementia. J Am Geriatr Soc 2007; 55: 1517-23.
- 13. Tavassoli N, Sommet A, Lapeyre-Mestre M, Bagheri H, Montrastruc JL. Drug interactions with

cholinesterase inhibitors: an analysis of the French pharmacovigilance database and a comparison of two national drug formularies (Vidal, British National Formulary). Drug Saf 2007; 30: 1063-71.

- Bentue-Ferrer D, Tribut O, Polard E, Allain H. Clinically significant drug interactions with cholinesterase inhibitors: a guide for neurologists. CNS Drugs 2003; 17: 947-63.
- Train the Brain Forum Committee. Thai mental state examination (TMSE). Siriraj Hosp Gaz 1993; 45: 359-74.
- Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev 2006; CD005593.
- 17. Pariente A, Sanctussy DJ, Miremont-Salame G, Moore N, Haramburu F, Fourrier-Reglat A. Factors associated with serious adverse reactions to

cholinesterase inhibitors: a study of spontaneous reporting. CNS Drugs 2010; 24: 55-63.

- Kroger E, van Marum R, Souverein P, Egberts T. Discontinuation of cholinesterase inhibitor treatment and determinants thereof in the Netherlands: A retrospective cohort study. Drugs Aging 2010; 27: 663-75.
- Amuah JE, Hogan DB, Eliasziw M, Supina A, Beck P, Downey W, et al. Persistence with cholinesterase inhibitor therapy in a populationbased cohort of patients with Alzheimer's disease. Pharmacoepidemiol Drug Saf 2010; 19: 670-9.
- Pariente A, Pinet M, Moride Y, Merliere Y, Moore N, Fourrier-Reglat A. Factors associated with persistence of cholinesterase inhibitor treatments in the elderly. Pharmacoepidemiol Drug Saf 2010; 19: 680-6.

การใช้ยารักษาโรคสมองเสื่อมในคลินิกผู้สูงอายุ

ทิพรัตน์ รังสรรค์ปัญญา, วีรศักดิ์ เมืองไพศาล, รุ่งนิรันดร์ ประดิษฐสุวรรณ

ภูมิหลัง: ปัจจุบันยา cholinesterase inhibitor (ChEIs) และ N-methyl-d-aspartate (NMDA) receptor antagonist ได้มีการถูกสั่งใช้มากขึ้นตามลำดับ ยารักษาภาวะสมองเสื่อมส่วนใหญ่มีราคาแพง และก่อให้เกิดมีผลข้างเคียงได้ อย่างไรก็ตามมี รายงานการศึกษาถึงลักษณะการสั่งใช้ยานี้ในประเทศกำลังพัฒนาไม่มากนัก ทั้งที่ผู้ป่วยภาวะสมองเสื่อมจำนวนมากจะอยู่ในประเทศ เหล่านี้ ผู้นิพนธ์ด้องการศึกษาถึงลักษณะการสั่งใช้ยา ผลข้างเคียง และค่าใช้จ่ายดังกล่าวในคลินิกผู้สูงอายุ โรงพยาบาลศิริราช วัสดุและวิธีการ: เก็บรวบรวมข้อมูลจากเวชระเบียนผู้ป่วยสมองเสื่อมที่เพิ่งได้รับการวินิจฉัยใหม่ในช่วงระหว่างเดือนมกราคม พ.ศ. 2550 ถึง ธันวาคม พ.ศ. 2552 ในคลินิกผู้สูงอายุ โรงพยาบาลศิริราช กรุงเทพมหานคร การวินิจฉัยภาวะสมองเสื่อมใช้เกณฑ์ DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-IV)

ผลการสึกษา: ผู้ป่วยสูงอายุ 96 คนได้รับการวินิจฉัยใหม่ว่ามีภาวะสมองเสื่อมในช่วงเวลาดังกล่าว ผู้ป่วย 80 คน (ร้อยละ 83.3) ซึ่งมีอายุเฉลี่ย 80.6 ปี (ส่วนเบี่ยงเบนมาตรฐาน 7 ปี) ได้รับยารักษาภาวะสมองเสื่อมโดยยา donepezil เป็นยาที่ถูกสั่งใช้มากที่สุด (ร้อยละ 70) ตามมาด้วยยา rivastigmine (ร้อยละ 22.5) ผู้ป่วยได้รับยาตัวอื่นร่วมด้วยที่อาจมีปฏิกิริยากันกับยารักษาภาวะ สมองเสื่อมถึงร้อยละ 41.3 ขนาดยาโดยเฉลี่ยของยา rivastigmine, galantamine, และ memantine ที่ผู้ป่วยได้รับต่ำกว่า ขนาดยาที่กำหนดว่าได้ผล ค่าใช้จ่ายยาสูงสุดต่อปี ได้แก่ galantamine (60,020.5 บาท/ปี) และต่ำสุดได้แก่ rivastigmine (45,857.7 บาท/ปี) ผู้ป่วยที่ได้รับยา cholinesterase inhibitor ร้อยละ 43.5 เกิดผลข้างเคียงขึ้นอย่างน้อย 1 อย่าง โดย ร้อยละ 37 เกิดผลข้างเคียงทางด้านทางเดินอาหาร ในขณะที่ร้อยละ 12.5 ของผู้ป่วยที่ได้รับ memantine เกิดผลข้างเคียงจากยา ในระยะเวลา 1 ปี มีผู้ป่วยที่ได้รับ cholinesterase inhibitor และ memantine หยุดยาร้อยละ 26.1 และ 12.5 ตามลำดับ จากการวิเคราะห์การถดถอยพหุโลจิสติกส์ ปัจจัยที่มีความสัมพันธ์กับการเกิดผลข้างเคียงจากยารักษาภาวะสมองเสื่อมคือ การที่มี อาการความผิดปกติทางพฤติกรรมและอารมณ์ของผู้ป่วย

สรุป: ผู้ป่วยสมองเสื่อมในการศึกษานี้ส่วนใหญ่ได้รับยารักษาภาวะสมองเสื่อมและเกิดผลข้างเคียงเกือบครึ่งหนึ่งของผู้ป่วย อย่างไรก็ตามการหยุดยาสมองเสื่อมที่ระยะเวลา 1 ปี ไม่สูงมากนัก ขนาดยาเฉลี่ยที่ผู้ป่วยได้รับต่ำกว่าขนาดยาที่แนะนำ ในอนาคต ควรมีการศึกษาไปข้างหน้า เพื่อศึกษาถึงความคุ้มค่าของยาและกำหนดแนวทางการปฏิบัติสำหรับการดูแลผู้ป่วยสมองเสื่อมโดยใช้ หลักฐานเชิงประจักษ์เหล่านี้