The Prevalence and the Associated Factors of Dementia in Patients with Parkinson's Disease at Maharat Nakhon Ratchasima Hospital

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Objective: *To evaluate the prevalence and the associated factors of dementia in Thai Parkinson's disease (PD) patients at Maharat Nakhon Ratchasima Hospital (MNRH), Nakhon Ratchasima Province, Thailand.*
Material and Method: *A cross sectional study in consecutive PD patients at the neurological clinic, MNRH between January and August 2011 was performed. The baseline characteristics such as age, sex, duration and severity of disease, education level, and medications were collected. Dementia was assessed according to Thai Mini Mental State Examinations (TMSE). The data were analyzed for determining the prevalence and factors that might correlate with dementia in patients with PD.*
Results: *One hundred forty three PD patients with mean age of 65.8±10.5 years and 49% males were enrolled in the present study. The prevalence of dementia was 35.0% in all subjects and 39.4% with education level adjustment. Dementia was found in any severity of PD. The advanced age and the later age at PD onset were the associated factors that had influenced on developing of dementia.*
Conclusion: *The prevalence of dementia in PD patients at MNRH with education level adjustment was 39.4% and could be found in any stage of disease. The advanced age and later age at PD onset were the significant associated factors for this condition. TMSE with cut-off score below 24 points was suitable for using to define dementia in Thai PD patients.*

Keywords: *Dementia, Thai Parkinson's disease, Prevalence and associated factors*

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The patients with Parkinson's disease (PD) have about five-fold increase risk for developing dementia than that of age-matched healthy control[1]. Dementia is associated with more rapid progression of disability in PD, so called PD dementia (PDD). The prevalence of PDD is ranging from eight to 41% (mean 24.5%) in a review of 12 studies that represent 1,767 patients with PD[2]. This variation depends on diagnostic criteria, methodology, duration of PD, and severity of the patients.

The early detection of PDD has a significant impact on the course of PD. This condition is associated with more rapid progression of disability, increased risk for nursing home placement, increased mortality[3], and reduced the quality of life in both patients and care givers[4]. In addition, recent evidence suggests that choline esterase inhibitor is effective for treatment of PDD[5].

In Thailand, Poungvarin et al[6], reported the prevalence of PDD in Thai PD patients at about 25%. However, the associated factors such as age, age at onset of PD, duration and severity of disease, medications, and education level were not mentioned in the study. The aim of the present study was to determine the prevalence and to identify the associated factors of PDD in Thai PD patients at Maharat Nakhon Ratchasima Hospital (MNRH), the tertiary care hospital in northeastern region of Thailand.

Material and Method

This is a cross sectional study. The data were collected from consecutive PD patients that attended the neurological Clinic, MNRH between January and August 2011. Every subject was diagnosed as PD by neurologists according to the United Kingdom Parkinson's disease society brain bank criteria[7]. After informed consent was obtained, the baseline characters such as age, sex, education level, medications and

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dosage, duration of treatment, and presence of motor complications were collected. The severity of PD was categorized following Modified Hoehn and Yahr (MHY) stage[8] and Unified Parkinson's Disease Rating Scale (UPDRS) part three (motor part)[9]. The average of the last three times of UPDRS motor score was used in the study for reducing the clinical variation between each time of visit.

Thai Mini Mental State Examinations (TMSE) was used to assess the cognitive status in the study. This test was proved to be equivalent to Mini Mental State Examination (MMSE) from the previous research[10]. The subjects whose score was below 24 points were defined as dementia.

The study protocol was approved by MNRH Institutional Review Board in accordance with ethical standards on human experimentation and with the Helsinki Declaration.

Statistical analysis

The data were presented as mean and standard deviation for continuous variables with normal distribution (according to Kolmogorov-Smirnov test) and as median and ranges for non-parametric distribution. Categorical data were expressed as frequency and percentage. The data analyses were performed by using student t-test, Man-Whitney U test, Chi-squares test or Fisher's exact test as appropriate. The p-value less than 0.05 was considered to have statistical significance.

Results

One hundred forty three consecutive PD patients with a mean age of 65.8 years (standard deviation ±10.5 years), including 70 males (49.0%) participated in the study. The mean age at onset of PD was 60.2±11.3 years. The median duration of PD was 59.0 months (range 12-257 months). Almost all patients (98.6%) received levodopa with mean dosage of 525.4±316.9 mg/d. Thirty-five patients (24.5%) received anticholinergic medication with mean dosage of 4.3±1.7 mg/d. The median MHY stage was 2.0 (1.0-5.0) and the median of UPDRS motor score was 12.2 points (0.2-55.5 points). The motor complications were found in 40 patients (28.0%). The median duration of education was 4.0 years (0-18 years), which 104 patients (72.7%) had four years of education. The other baseline characteristics were presented in Table 1.

Fifty PD patients (35.0%) were diagnosed as dementia. That was found in any stage of PD as in Table 2. In the analyses, the significant difference in education time between demented and non-demented subjects was documented (4.4±2.5 years vs. 6.3±4.2 respectively, $p<0.01$).

To avoid the effect of education level, the subgroup analysis in subjects with 4-year-education (104 patients) was performed to identify the true associated factors for PDD. Regarding this analysis, PDD was found in 41 patients (39.4%). The comparisons of factors between demented and non-demented PD

Table 1. The baseline characteristics of 143 Parkinson's disease patients

Characters	Mean±SD or n (%)	Median	Range
Age, year	65.8±10.5	67.0	33-91
Age at onset, year	60.2±11.3	61.0	28-84
Disease duration, month	67.5±47.2	59.0	12-257
Treatment duration, month	55.4±45.1	46.0	12-239
Daily dose of levodopa, mg	525.4±316.9	500.0	0-2,000
Modified Hoehn and Yahr stage	2.1±0.8	2.0	1.0-5.0
UPDRS motor score	14.5±10.3	12.2	0.2-55.5
Education, year	5.7±3.8	4.0	0-18
TMSE score	23.8±4.4	25.0	2-30
Male	70 (49.0)		
Motor complications	40 (28.0)		
Receive anticholinergic	35 (24.5)		
Dementia (TMSE <24)	50 (35.0)		
Dementia (TMSE <26)	91 (63.6)		

UPDRS = unified Parkinson's disease rating scales; TMSE = Thai mini mental state examination

patients with 4-year-education were presented in Table 3. The advanced age and the later age of PD onset were significant associated factors for PDD ($p<0.01$ and 0.01 respectively). However, sex, duration of disease, duration of treatment, PD severity, presence of motor complications, and medications were not significant factors.

Discussion

PDD can be easily detected in routine clinical practice[11]. The international diagnostic criteria for detecting PDD were purposed by Movement Disorder Society (MDS) Task force in 2007[12]. In these criteria, MMSE was used to assess the cognition. Dementia was defined in subjects with MMSE score below 26 points. The criteria had showed 100% specificity and 46.7% sensitivity in clinical validation study[13] but the high cut-off MMSE score (less than 26 from 30 points) might be in doubt for application in Thai population.

In a Thai population, persons with age over 60-year-old (as in the PD patients), the mean education duration is not more than eight years (5.7±3.8 years in the present study), whereas the mean education duration in the confirmatory study for the MDS Task force criteria were 14.5 years[13]. In another study, only 13.7% of subjects had education level less than eight years[11] (compared with 81.8% in the present study). In addition, if the cut-off TMSE scores below 26 points was used, there were 91 patients (63.6%) including 50 persons with TMSE score more than 23 points, being documented as dementia. That was very high and out of the proportion from the previous data[2].

In fact, low education is one of the powerful risk factor for dementia[14] and higher education can delay accelerated decline a memory test in persons who develop dementia[15]. From these reasons, the cut-off MMSE scores below 26 points as in MDS task force criteria was not suitable for the Thai population. TMSE with cut-off scores below 24 points was proper to determine PDD in Thai population because this test was validated in Thai elderly population who had the same education level as in PD patients. This conclusion was confirmed by O'Bryant et al, who found that the MMSE cut-off scores below 26 points had a high sensitivity and specificity for detecting dementia in a person who had more than 12-year-education[16].

Table 2. Number of dementia patients and mean Thai mini mental state examinations (TMSE) according to modified Hoehn and Yahr (MHY) stage

MHY stage	Number (%)	Mean TMSE score	Dementia n (%)
1	30 (21.0)	24.3±3.8	5 (16.7)
1.5	12 (8.4)	24.2±3.6	5 (41.7)
2	44 (30.8)	24.2±5.0	11 (25.0)
2.5	26 (18.2)	22.1±4.4	12 (46.1)
3	22 (15.4)	22.4±4.7	11 (50.0)
4	6 (4.2)	19.5±5.8	4 (66.7)
5	3 (2.1)	18.3±7.4	2 (66.7)

Table 3. Factor comparisons between Parkinson's disease patients with and without dementia with education level adjustment (n = 104)

Factors	Dementia		OR (95% CI)	p-value
	With (n = 41)	Without (n = 63)		
Age, year	69.6±8.3	64.3±9.8		<0.01
Age at onset, year	63.8±8.6	58.7±11.5		0.01
Disease duration, month	71.8±47.2	65.8±47.6		0.54
Treatment duration, month	56.1±39.5	54.3±44.8		0.84
UPDRS motor score	14.8 (0.2-55.5)	12.0 (0.7-52.3)		0.06
MHY stage	2.0 (1.0-5.0)	2.0 (1.0-2.0)		0.08
Daily dose of levodopa, mg	525.6±301.3	590.2±319.2		0.31
Male, n (%)	19 (38.8)	30 (61.2)	1.0 (0.4-2.1)	0.90
Anticholinergic use, n (%)	12 (46.2)	14 (53.8)	1.4 (0.6-3.6)	0.42
Motor complications, n (%)	11 (36.7)	19 (63.3)	0.8 (0.4-2.0)	0.71

Values are means ± standard deviations (SD) or medians (range) as appropriate.
UPDRS = unified Parkinson's disease rating scales; OR = odds ratio; CI = confidence interval

For reducing the effect of education level, one of the risk factor for dementia, the subgroup analyses in 4-year-education subjects (104 patients) were performed to verify the associated factors that might correlate with PDD. The advanced age and the later age of PD onset were the associated factors for PDD in the study which results were consistent with the former study[17]. Normally, advanced age is one of risk factor for dementia but the prevalence of PDD in many studies was higher than that of normal age-matched subjects (18.5%)[18]. The reason of this finding was likely to be related with the PD pathology. Lewy bodies, the PD pathology that extends into the cerebral cortex which leads to atrophy of the nucleus basalis of Meynert resulting in a cholinergic deficit more than that in normal aging process[19,20].

Hobson et al, found the correlation between PD severity and dementia, but the mean UPDRS motor score in the study was higher than the score in the present study (36.6 points in demented subjects and 22.9 points in non-demented subjects compared with 14.8 points in demented subjects and 12.0 points in non-demented subjects in the present study)[1]. In another study, which mean UPDRS motor score (16.8 points) was similar to the result of the present study (14.5 points), PD severity had only minimal effect on dementia (hazard ratio = 1.05 with 95% CI = 1.02-1.08)[21]. Although this association was not documented in the study due to the difference in the degree of PD severity, the increasing proportion of demented patients were established in high stage of disease (25.0%, 46.2%, 50.0%, and 66.7% in MHY stage 2, 2.5, 3, and 4 in that order). The hypothesis that the obvious effect of PD severity on dementia shown in more severe PD subjects might be a concern arising from this finding. The further study comparing the PDD between mild and severe PD patients should be performed to clear out this hypothesis.

There were many medications being used to treat PD, such as anticholinergic that can cause cognitive impairment[22,23] but these relationships were not found in the present study. This result was clarified from the usage of these medications. In general, clinical practice, anticholinergic drug has limited use in young and early stage of PD patients. In the study, the subjects who received anticholinergic had significantly younger age (62.9±10.1 years vs. 67.7±9.2 years) and lower age at PD onset (55.4±10.7 years vs. 62.5±10.1 years) than the subjects who did not receive this medication.

There were a number of limitations in the present study. The neuropsychological tests were not performed, probably leading to miss some cases of mental depression, a common associated clinical syndrome that might come up in any stage of PD. The other related factors for PDD such as baseline cognitive status and postural hypotension were not determined due to a cross-sectional study design. The further prospective study design that includes all factors should be conducted to determine the risk for PDD.

Conclusion

The prevalence of PDD at MNRH with education level adjustment was 39.4% and could be found in any stage of disease. The advanced age and later age at PD onset were the significant associated factors for this condition. TMSE with cut-off score below 24 points was suitable for using to define dementia in Thai PD patients.

Potential conflicts of interest

None.

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ความชุกและปัจจัยที่เกี่ยวข้องกับภาวะสมองเสื่อมในผู้ป่วยพาร์กินสันในโรงพยาบาลมหาราชนครราชสีมา

พาวุฒิ เมฆวิชัย, ลัดดาพร เชยคำแหง

วัตถุประสงค์: *ศึกษาถึงความชุกและปัจจัยที่เกี่ยวข้องกับภาวะสมองเสื่อมในผู้ป่วยพาร์กินสันในโรงพยาบาลมหาราชนครราชสีมา*

วัสดุและวิธีการ: *เป็นการศึกษาภาคตัดขวางในผู้ป่วยพาร์กินสัน ณ คลินิกโรคระบบประสาท โรงพยาบาลมหาราชนครราชสีมา ในช่วงเวลาระหว่าง เดือนมกราคม พ.ศ. 2554 ถึงเดือนสิงหาคม พ.ศ. 2554 โดยรวบรวมข้อมูลพื้นฐาน ได้แก่ อายุ เพศ ระดับความรุนแรงของโรค ระยะเวลาที่เป็นโรค ชนิดและขนาดของยาที่ได้รับ และระดับการศึกษา ภาวะสมองเสื่อมวินิจฉัยโดยแบบทดสอบ Thai Mini Mental State Examinations (TMSE) ข้อมูลทั้งหมดจะถูกนำมาวิเคราะห์เพื่อหาความชุกและปัจจัยที่เกี่ยวข้องกับภาวะสมองเสื่อม*

ผลการศึกษา: *การศึกษานี้มีผู้ป่วยพาร์กินสันเข้าร่วมจำนวน 143 ราย เป็นเพศชายร้อยละ 49 มีอายุเฉลี่ย 65.8±10.5 ปี พบภาวะสมองเสื่อมร้อยละ 35.0 โดยพบในทุกระดับความรุนแรงของโรคพาร์กินสัน ผู้ป่วยร้อยละ 39.4 มีภาวะสมองเสื่อมหลังจากวิเคราะห์โดยตัดปัจจัยเรื่องระดับการศึกษาออก ปัจจัยที่เกี่ยวข้องกับภาวะนี้ได้แก่ ผู้ป่วยสูงอายุ และผู้ป่วยที่เริ่มมีอาการของโรคพาร์กินสันเมื่ออายุมาก*

สรุป: *ความชุกของภาวะสมองเสื่อมในผู้ป่วยพาร์กินสันในโรงพยาบาลมหาราชนครราชสีมาหลังจากตัดปัจจัยเรื่องระดับการศึกษาเท่ากับร้อยละ 39.4 โดยมีปัจจัยที่เกี่ยวข้องคือผู้ป่วยสูงอายุ และผู้ป่วยที่เริ่มมีอาการของโรคพาร์กินสันเมื่ออายุมาก การวินิจฉัยภาวะสมองเสื่อมในผู้ป่วยพาร์กินสันชาวไทยโดยใช้คะแนนของแบบทดสอบ TMSE น้อยกว่า 24 คะแนน มีความเหมาะสม*