นิพนธ์ต้นฉบับ – Original Article

ความชุกของภาวะซึมเศร้าในผู้ป่วยโรคพาร์กินสันชาวไทยและปัจจัยที่เกี่ยวข้อง

พาวุฒิ เมฆวิชัย, สุรินทร์ แซ่ตัง
สาขาประสาทวิทยา กลุ่มงานอายุรกรรม โรงพยาบาลมหาราชนครราชสีมา จังหวัดนครราชสีมา 30000

The Prevalence of Depression in Thai Parkinson's Disease Patients and Their Associated Factors

Pawut Mekawichai , Surin Saetang
Neurology unit, department of medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima THAILAND, 30000

วัตถุประสงค์: เพื่อศึกษาหาความชุกและปัจจัยที่เกี่ยวข้องกับการเกิดภาวะซึมเศร้าในผู้ป่วยพาร์กินสันชาวไทย ณ โรงพยาบาลมหาราชนครราชสีมา

วิธีการศึกษา: เป็นการศึกษาภาคตัดขวางในผู้ป่วยโรคพาร์กินสัน ณ คลินิกโรคระบบประสาท โรงพยาบาลมหาราชนครราชสีมา ระหว่างเดือนมกราคมถึงเดือนธันวาคม พ.ศ. 2553 โดยรวบรวมข้อมูลพื้นฐานผู้ป่วย เช่น อายุ เพศ ระยะเวลาดำเนินโรค ระดับความรุนแรงของโรค การรักษา และระดับเชาว์ปัญญา สำหรับภาวะซึมเศร้าประเมินโดยใช้แบบสอบถาม Thai geriatric depression scale (TGDS) ข้อมูลทั้งหมดจะนำมาวิเคราะห์เพื่อประเมินความชุกและปัจจัยที่เกี่ยวข้องกับการเกิดภาวะซึมเศร้าในผู้ป่วยโรคพาร์กินสัน

ผลการศึกษา: การศึกษานี้มีผู้เข้าร่วมจำนวน 87 ราย พบภาวะซึมเศร้าร้อยละ 63.2 (95%CI 52.9-73.5) และสามารถพบได้ในทุกระดับความรุนแรงของโรค โดยอยู่ในระดับซึมเศร้าเล็กน้อยร้อยละ 41.3 อยู่ในระดับซึมเศร้าปานกลางร้อยละ 18.4 และ 1.2 อยู่ในระดับซึมเศร้ารุนแรง ภาวะซึมเศร้าที่พบนั้นมีความสัมพันธ์กับระดับความรุนแรงของโรค และภาวะแทรกซ้อนทางด้านการเคลื่อนไหว (odds ratio 2.9 (95%CI 1.06-7.96) และ 5.3 (95%CI 1.35-20.54) ตามลำดับ)

สรุป: ความชุกของภาวะซึมเศร้าในผู้ป่วยพาร์กินสัน ณ โรงพยาบาลมหาราชนครราชสีมา เท่ากับ ร้อยละ 63.2 (95% CI 52.9 – 73.5%) โดยภาวะนี้สามารถพบได้ในทุกระดับความรุนแรงของโรค ปัจจัยที่เกี่ยวข้องในการเกิดภาวะซึมเศร้าได้แก่ ระดับความรุนแรงของโรคที่สูงและการเกิดภาวะแทรกซ้อนทางการเคลื่อนไหว

Objective: To evaluate the prevalence and identify the asso- ciated factors of depressive disorder in patients with Parkinson's disease (PD) at Maharat Nakhon Ratchasima Hospital (MNRH).

Methods: This is a cross sectional study which was performed in consecutive PD patients at neurological clinic, MNRH between January and December 2010. Depressive symptoms were assessed according to Thai geriatric depression scale (TGDS). The baseline characteristics as age, sex, duration and severity of disease, treatment and cognitive status were collected. All data were analyzed for determining the prevalence and factors that might correlate with depressive disorders in patients with PD.

Result: Eighty-seven patients were enrolled in the study. Sixty-three point two percents (95%CI 52.9-73.5%) of patients had depressive disorders, 43.7%, 18.4% and 1.1% had mild, moderate and severe degree of depressive disorders respectively. Depression can be found in any stage of PD. The advance stage of the disease and presence of motor complications were the factors that had influenced on developing of depression in patients with PD (odds ratio 2.9 (95%CI 1.06-7.96) and 5.3 (95%CI 1.35-20.54) respectively.

Conclusion: The prevalence of depressive disorders in PD patients at MNRH Hospital was 63.2% (95%CI 52.9-73.5). Depression could be founded in any stage of PD. The advance stage of the disease and presence of motor complications were the significant associated factors for the recognition of this condition.

Key word: Depressive disorder, Parkinson's disease

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Introduction

Parkinson's disease (PD) is a slow progressive neurodegenerative condition affecting about 1% of people over 60-year-old[1]. The clinical manifestations include motor symptoms such as slowness of movement, resting tremor, rigidity, postural instability[2] and non- motor symptoms[3]such as dementia, psychosis and depression. Depression is one of the common non-motor symptoms, other than sleep disturbance, cognitive impairment, psychosis and anxiety[4].

The prevalence of depression in persons with PD was reported very variably, ranging from 7% to 76%. This variation was due to inconsistence in sampling procedures, assessment techniques and definition of depression[5]. However, when compared with healthy age and sex matched control subjects that prevalence of depression about 10%[6], depression in PD patients had six times greater[7]. Moreover, depression in PD patients was still higher than patients who had chronic disabling conditions (except PD)[8]. Factors relating with depression in PD patients were advanced disease, anxiety, cognitive impairment and psychosis[7].

Depression may occur at any stage of PD and relate with poor quality of life of patients and caregivers[9]. In general, depression remains untreated in PD population. Nearly two-thirds of patients who had depression did not received antidepressant therapy[10] due to the under recognition of this condition. The prevalence and the associated factors for the detected depression are necessity for the physician to improve health-care and quality of life in persons with PD.

This study had objective for determining the prevalence of depressive disorder in Thai PD patients at Maharat Nakhon Ratchasima Hospital, and identifying factors that might correlate with this condition.

Patients and methods

This is a cross sectional study. The data were collected from consecutive PD patients that attended in Neurological Clinic at Maharat Nakhonratchasima Hospital between January 2010 and December 2010. Every subject was diagnosed as PD by neurologists according to the United Kingdom Parkinson's disease society brain bank criteria[11]. The baseline characters as age, sex, medication (dosage of levodopa and dopamine agonist used), duration of treatment and presence of motor complications were collected. The severity of disease was categorized, regarding Modified Hoehn and Yahr Stage (MHYS), into two groups, mild and severe group. Mild group was defined as MHYS less than 2.5, whereas MHYS equal or more than 2.5 was referred severe group. The cognitive impairment was evaluated by using Thai mini-mental state examination (TMSE). This test was referred to Mini- mental state examination (MMSE) in Thai language[12]. The cutoff score of 24 from 30 points was defined as cognitive impairment[13].

After informed consent was obtained, Thai geriatric depression scale (TGDS) questionnaire was administrated to each patient for evaluating depressive disorder. This test was validated to geriatric depression scale (GDS)[14] in Thai language from the previous study[15]. TGDS has thirty simple questions for detecting the depression. The score of this test ranges from 0 to 30 points. The score 0 to 12 points refers no symptom of depression, 13 to 18 points as mild degree, 19-24 points as moderate and 25-30 points as severe degree of depression. Every question of the test was asked by the physician or well trained nurse for reducing confounding factors among each subject.

At least of 95 patients from sample size calculation were required to obtain in the study with a 95% confidence interval (95% CI) and 10% of allowable error. The continuous data were analyzed as mean and standard deviation or median and range as appropriate. The categorical data were analyzed as counts and percentages. The test for the difference in continuous data was done by using t-test or Mann-Whitney U test and Chi-squared or Fischer-Exact test for categorical data. The statistical significant was defined as p value equal or less than 0.05.

Results

There were one-hundred and five consecutive PD patients in the study duration, but 18 patients were

excluded due to inappropriate status to complete the test such as aphasia, severe psychosis and severe dyskinesia. Eighty-seven subjects with a mean age of 64.1+9.8 years and 45 males (51.1%) were recruited. Mean MHYS was 2.3+0.9. The mean duration of disease was 3.7+2.1 years. Almost all of the patients (99.9%) received levodopa with mean dosage of 575.6+318.9 mg/day. Forty-four (50.6%) patients were received dopamine agonists. Patients took more than one antiparkinsonian medications in 27.6%. Cognitive impairment was found in 34.5% and motor complications were developed in 29.9% of the patients. The others baseline characteristics were demonstrated in table 1.

Sixty-three point two percents (63.2%) PD patients had depressive disorder with the mean age of 64.6+10.1 years. Male to female ratio was nearly 1:1 (27 and 28 subjects respectively). The severity of this symptom was as follows, 38 (43.7%) patients had mild, 16 (18.4%) had moderate and one (1.1%) had severe degree of depression. The mean duration of disease in depressive PD patients was 3.7+2.1 years compared with 3.6+2.0 years of non depressive PD patients and was no difference. Mean MHYS was 2.6+0.8 and it was significantly different (p=0.0026) from that of non depressive patients. Moreover, depression could be found in any stage of PD as demonstrated in table 2. The patients with severe symptom of PD (MHYS > 2.5) were higher rate of depression when compared with mild symptom of PD patients (MHYS < 2.5) (75.0% and 38.8% respectively) and significantly difference at p=0.01. The mean dosage of levodopa was 618.6+339.3 mg/day which was higher than that of non depressive subjects (499.2+267.4 mg/day), but not difference. Depressive disorder developed in 68.1% of PD patients who received dopamine agonist medication, it was not different from those who did not take this medication. Eighty percent (24 from 30) of PD patients with cognitive impairment had depressive disorder. The statistical significance was found when compared with PD patients without cognitive impairment (p=0.03). Eighty percent (21 from 26) of PD patients who had motor complications had depression. The statistical significance with p=0.03 was found when compared with PD patients without motor complications (34 from 61 subjects, 55.7%). The comparison between each factor was shown in table 3.

The results by using multivariate logistic regression analysis were demonstrated in table 4. The PD patients with MHY > 2.5 were had significant more depressive disorder than that MHY < 2.5 (p = 0.04) with odds ratio = 2.91 (95%CI 1.06-7.96). The similar result was shown

Table 1 The baseline characteristics of the patients with Parkinson's disease (n=87)

Characters	**Mean+SD**	**Median** (IQR)	**n (%)**
Age (year)	64.1+9.8	65 (15)	
Disease duration (year)	3.7+2.1	4 (5)	
Dosage of levodopa (mg/day)	575.6+318.9	500 (450)	
Modified Hoehn and Yahr stage > 2.5			48 (55.1)
Male			45 (51.7)
Received dopamine agonists			44 (50.6)
Presence of motor complications			26 (29.9)
Cognitive impairment			30 (34.5)
Depressive disorder			55 (63.2)
Mild depressed			38 (43.7)
Moderate depressed			16 (18.4)
Severe depressed			1 (1.1)

SD = standard deviation, IQR = interquartile range

Table 2 Number of patients with depressive disorder (classified stage of disease)

Modified Hoehn and Yahr stage	Number of patients n (%)	Number of depressive disorder patients n (%)
0	2 (2.3)	0 (0)
1	14 (16.1)	5 (35.7)
1.5	2 (2.3)	1 (50.0)
2	21 (24.1)	13 (61.9)
2.5	17 (19.5)	11 (64.7)
3	23 (26.4)	18 (78.3)
4	8 (9.2)	7 (87.5)
total	**87 (100.0)**	**55 (63.2)**

Table 3 The factors concerned between Parkinson's disease patients with and without depressive disorder

Factors	Depression			
	Presence (n=55)	Absence (n=32)	Crude OR(95% CI)	p-value
Age (year)	64.6+10.1	63.2+9.3		0.52
Duration of disease (year)	4.0 (5)	4.0 (5)		0.88
Dosage of levodopa (mg/day)	618.6+339.3	499.2+267.4		0.08
Disease severity: n (%)				
Severe (MHYS > 2.5)	36 (75.0)	12 (25.0)	3.16	0.01*
Mild (MHYS < 2.5)	19 (48.7)	20 (51.3)	(1.28, 7.82)	
Sex: n (%)				
Male	27 (60.0)	18 (40.0)	0.75	0.52
Female	28 (66.7)	14 (33.3)	(0.31, 1.80)	
Received dopamine agonists: n (%)				
Yes	30 (68.2)	14 (31.8)	1.54	0.33
No	25 (58.1)	18 (41.9)	(0.64, 3.71)	
Cognitive impairment: n(%)**				
Yes	24 (80.0)	6 (20.0)	3.10	0.03*
No	31 (56.4)	24 (43.6)	(1.09, 8.77)	
Motor complications: n(%)				
Yes	21 (80.8)	5 (19.2)	3.34	0.03*
No	34 (55.7)	27 (44.3)	(1.11, 10.00)	

The values present in mean+standard deviation or median (interquartile range) as appropriate.
OR = odds ratio, MHYS = Modified Hoehn and Yahr stage, * significant at p < 0.05, ** n=85

in PD patients with motor complication when compare with which without motor complication (odds ratio = 5.26 (95%CI 1.35-20.54), p=0.02).

Discussion

The prevalence of depression in patients with PD was widely varied. That was depended on assessment techniques. In this study, TGDS was used for determining depression, because this test is the one of standard

Table 4 The factors concerned between Parkinson's disease patients with and without depressive disorder (multivariable logistic regression)

Factors	Depression		Crude OR (95% CI)	Adjusted OR (95%CI)	p-value
	Presence (n=55)	Absence (n=32)			
Disease severity					
Severe (MHYS > 2.5)	36 (75.0)	12 (25.0)	3.16	2.91	0.04*
Mild (MHYS < 2.5)	19 (48.7)	20 (51.3)	(1.28, 7.82)	(1.06, 7.96)	
Cognitive impairment**					
Yes	24 (80.0)	6 (20.0)	3.10	2.65	0.09
No	31 (56.4)	24 (43.6)	(1.09, 8.77)	(0.86, 8.15)	
Motor complications					
Yes	21 (80.8)	5 (19.2)	3.34	5.26	0.02*
No	34 (55.7)	27 (44.3)	(1.11, 10.00)	(1.35, 20.54)	

tests for depression that can be used in mild to moderate cognitive impairment subjects and was validated into Thai language. This test is simple (yes or no question), does not need lots of time to complete and can be used in every level of health-care in Thailand. In a previous study, that depression was assessed in PD by using GDS, depressive disorder was present in 57.0% of patients, with 40.2 % considered mild to moderate and 16.7% classified as moderate to severe depression[16]. These results were similar to this study that depressive disorder was found in 63.2% of patients whereas 43.7% and 19.5% of these were classified as mild and moderate to severe depression respectively. This finding may be suggests that, if the same test was used for detecting depression in person with PD, the same result would be found.

The severity of PD in this study was classified into two groups follow MHYS, less than 2.5 and equal or higher than 2.5. The reason of this classification was with and without gait involvement. The meaning of MHYS = 2 is "symptoms appear on both sides without impairment of balance", whereas impairment of balance has show in MHYS > 2.5.

In this study, the severity of PD and presence of motor complications were found to be the factors correlated with depression in PD subjects. These were consistent with the previous studies which suggest that depression in PD could be resulted from reaction to disability and stress of the illness which linked with movement problems[17].

Medications for treatment of motor symptoms in PD may be the cause of depression. Some studies had even suggested that levodopa might produce depression[18], but other research failed to confirm this finding[19]. The explanation for this result was that the degeneration of norepineprine and serotonin systems may be play as major role in the manifestation of PD-related depression more than that in dopaminergic system[20]. In this study, dosage of levodopa did not influence the depression. Dopamine agonists had been chosen for management of motor symptoms in PD patients who had co-morbid depression[21]. This finding may be due to an antidepressant affect of dopamine agonists. Pramiprexole is one of the dopamine agonists that had been demonstrated to have antidepressant activity in PD and non-PD population[22], but there is a lack of controlled study in this finding. In this study there was no different of depressive disorder between dopamine agonist-treated patients and the patients did not receiving dopamine agonists. This finding could be explained by the main dopamine agonist medication in this study was bromocriptine (83%), which had no evidenced in antidepressant activity. The small population in patients who treated with pramiprexole leaded to the limitation of our ability to detect between-group difference for exploring the antidepressant effect of this medication. It is very interesting to explore this effect in the future study which focus in pramiprexole treated patients.

PD is the condition that can present with motor and non-motor symptoms. This study had not included some non-motor symptoms (anxiety, sleep disorder, psychosis and orthostatic hypotension) and the functional capacity of patients such as activity of daily living, the patients who had a regular job or could perform only household work into the study. These factors may have related to depressive disorder in PD patients. So, the future controlled study that has included these factors for determine the correlate with depressive disorder is necessity.

Conclusion

Depressive disorder was found in about 60% of persons with PD. It can happen in every stage of the disease and it is under-recognized by the physician. The advanced stage of disease and presence of motor complications were the significant associated factors. The physicians must highly concern about this disorder for health-care improvement and the best quality of life for the patients and care givers.

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