Neurology Asia 2018; 23(4) : 327 – 331

Non-motor symptoms in Thai Parkinson's disease patients: Prevalence and associated factors

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Abstract

Background & Objective: To identify the prevalence, pattern, associated factors of non-motor symptoms (NMS) in a cohort of Thai Parkinson's disease (PD) patients from the Surin province, Northeast Thailand. *Methods:* A cross-sectional study of 110 patients was conducted at neurological clinic in Surin Hospital from June to September 2017. NMS were assessed according to Thammasat University Non-Motor Symptoms Questionnaire 40 (TU-NMSQuest). The data on age, sex, duration and severity of disease, treatment and cognitive status were collected. All data were analyzed to determine the prevalence and factors that might correlate with severity of NMS. *Results:* All the PD patients have at least one NMS symptoms. Nocturia was the commonest symptom (81.8%), followed by insomnia (74.5%), pain (73.6%) and fatigue (71.8%). The number of NMS significantly increased with severity of disease, depression, duration of disease and dementia.
Conclusion: All the PD patients in a cohort from rural Northeast Thailand have at least one NMS symptoms. TU-NMSQuest was found to be a useful instrument for screening NMS.

Keywords: Non-motor symptoms, Parkinson's disease, TU-NMSQuest, associated factors

INTRODUCTION

Parkinson's disease (PD) is the common neurodegenerative disease characterized by rest tremor, rigidity, bradykinesia and postural instability.[1] PD has been mainly recognized for its motor symptoms. The clinical spectrum of PD is now known to include neuropsychiatric symptoms, sleep disorders, cognitive impairment, autonomic dysfunction, fatigue, impulse control disorders and others problems, which are called the non-motor symptoms (NMS). Motor symptoms can be treated with dopaminergic therapy but NMS are often poorly recognized and inadequately treated.[2] In Thailand, the prevalence of PD patients is 0.24%, which means approximately 170,000 Thai citizens with PD, and the prevalence of NMS is 97-100%.[3-5] The aim of the present study was to determine the prevalence and identify the associated factors of NMS in a cohort of Thai PD patients from the rural Surin province, Northeast Thailand.

METHODS

This is a cross-sectional study of 110 patients seen from June to September 2017 at the neurological clinic of Surin Hospital. All the patients were diagnosed with idiopathic PD by neurologists according to the United Kingdom Parkinson's Disease Society Brain Bank criteria (UKPDSBB). Patients with severe cognitive impairment were excluded. After informed consent was obtained, the baseline characteristic of the patients including sex, age, age of onset, duration of disease, duration of treatment, family history, educational level, medications, levodopa-related motor complication and disease severity were collected. All patients were evaluated with modified Hoehn and Yahr (MHY) stage, Thammasat University Non-Motor Symptoms Questionnaire-40 (TU-NMSQuest), Thai-Mental State Examination (TMSE) and Thai-Geriatric Depression Scale-30 (TGDS-30). The study protocol was approved by Surin Hospital Institutional Review Board in accordance with ethical standards on human experimentation and with Helsinki Declaration.

Thammasat University Non-Motor Symptoms Questionnaire (TU-NMSQuest)

The TU-NMSQuest consists of 40 questions. The questionnaire was modified from the 30-item Non-Motor Symptoms Questionnaire (NMSQuest). The TU-NMSQuest added 10 questions to the standard 30-item NMSQuest. Four questions were added to identify fatigue, multitasking deficits,

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seborrheic dermatitis, sense of presence and 6 questions were added to screen for impulse control disorders (ICD).

Statistical analysis

Statistical analyses were conducted using the SPSS version 16. The prevalence of each NMS was calculated for the total sample by summing positive responses by TU-NMSQuest scores. Statistical analysis methods used included; unpaired t-test, analysis of variance, correlation coefficient and linear regression. Linear logistic regression models were constructed to examine the relationship between NMS, and the factors of interest. A P-value of <0.05 was considered significant.

RESULTS

The TU-NMSQuest was completed by 110 PD patients consisting of 56 females (50.9%), with mean age ± standard deviation of 65.7 ±11.1 years. The mean of disease duration was 7.0±4.7 years. The mean dosage of levodopa was 493.0±255.5 mg/d. All the PD patients received levodopa, with 33.6% also receiving treated with dopamine agonist. The mean Modified H&Y stage was 2.1±0.7 which was classified into mild (74.5%), moderate (21.8%) and severe (3.7%). Motor complications were seen in 83 PD patients with predominant motor fluctuation (67.3%), freezing of gait (19.1%) and dyskinesia (11.8%). PD with dementia, defined by TMSE < 24 was presented in 34.5% of patients. Forty three patients (39%) were found to be depressed with TGDS-30 > 12. The baseline features for the other variables is summarized in Table 1.

Based on by TU-NMSQuest, all of PD patients reported having at least one item of NMS. The mean total NMS score was 17.2 ± 8.3. The most common symptom was nocturia (81.8%), followed by insomnia (74.5%), pain (73.6%) and

Table 1: Baseline features of 110 Parkinson's disease patients

	Mean ±SD	Range	Percent
Age-years	65.7 ±11.1	32-87	
Sex, female			50.9
Age of onset	59.5 ±11.2	24-83	
Duration disease-years	7.0 ±4.7	1-20	
Duration treatment-years	5.2 ±4.2	1-15	
MHY stage	2.1±0.7	1-4	
-Mild (H&Y:1-2)			74.5
-Moderate(H&Y:2.5-3)			21.8
-Severe(H&Y:4-5)			3.7
Tremor dominant subtype			88.1
Family history of PD			10.9
UPDRS motor score	25.3±14.1	4-60	
Levodopa dose-mg/d	493.0 ± 255.5	100-1000	
Dopamine agonist			33.6
Anticholinergic drugs			25.5
COMT inhibitor			79.1
Motor complication			75.5
- Motor fluctuation			67.3
- Freezing of gait			19.1
- Dyskinesia			11.8
TU-NMSQuest score	17.2±8.3	1-36	
TMSE (TMSE<24)	23.6±4.4	10-30	34.5
Education	5.6±4.7	0-20	
TGDS-30 (TGDS>12)	8.6±8.0	0-24	39
-Mild (13-18)			24.5
-Moderate (19-24)			14.5
-Treatment for depression			37.3

H&Y = modified Hoehn & Yahr stage, PD = Parkinson's disease, UPDRS = Unified Parkinson's Disease Rating Scale, COMT = catechol-O-methyltransferase, TU-NMSQuest = Thammasat University Non-Motor Symptoms Questionnaire, TMSE = Thai Mental State Examination, TGDS = Thai Geriatric Depression Scale

fatigue (71.8%). ICD was identified in about 48% of the patients (Table 2).

There was a significant association between TU-NMSQuest score and severity of disease, H&Y (r=0.474, P<0.001) and UPDRS III (r=0.561, p<0.001). A significant positive correlation was also seen between TU-NMSQuest score and TGDS-30 (r =0.602, p<0.001), duration of disease (r=0.449, p<0.001) and TMSE (r= -0.445, p<0.002) (Table 3).

DISCUSSION

TU-NMSQuest questionnaire was used in this study to identify the prevalence, pattern, associated factors of NMS in a cohort of Thai PD patients from a rural Northeast province.[5] We found that all the PD patients had at least one NMS symptoms. This is similar to previous studies, and NMS has been found in all stages of disease. The most common symptoms previously reported were nocturia, insomnia, pain, fatigue and restless legs syndrome.[4-6]

Nocturia was the most common urinary tract dysfunctions and followed by urgency, similar to previous Thai and Chinese studies.[4-7] The spectrum of PD related autonomic symptoms is complex and includes urogenital, gastrointestinal, cardiovascular and sexual dysfunctions. The effect of autonomic disorders, especially nocturia, constipation and orthostatic hypotension have a significant effect on quality of life in PD patients. Urinary dysfunction in PD is caused by detrusor over activity.[8-9] Nocturia results in disturbance in sleep pattern; it may account for some overestimation of the sleep disorder.[10]

Pain is also a very common symptom in PD, it may be an important reason for dissatisfaction and patients' cause of unhappiness. This is seen in 73.6% of PD patients in the current study.

Table 2: The prevalence of non-motor symptoms (NMS) in 110 Parkinson's disease patients according to Thammasat University Non-Motor Symptoms Questionnaire-Thai version (TU-NMSQuest)

NMS	N (%)	NMS	N (%)
Sleep disorder and fatigue		**Urinary tract**	
Insomnia	82(74.5)	Urinary urgency	68(61.8)
Daytime sleepiness	60(54.5)	Nocturia	90(81.1)
Intense vivid dreams	49(44.4)	**Sexual disorder**	
Acting out dreams	66(60.0)	Loss of sex drive	41(37.4)
Restless legs	77(70.0)	Sex difficulty	29(26.4)
Fatigue	79(71.8)	**Others**	
Cardiovascular and falls		Pains	81(73.6)
Dizziness	67(60.9)	Sweating	43(39.1)
Falling	27(24.5)	Dry eyes	64(58.2)
Mood and apathy		Taste/smelling	43(39.1)
Sad, depressed mood	65(59.1)	Seborrheic dermatitis	33(30.0)
Anxiety	61(55.5)	Swelling legs	30(27.3)
Loss of interest	40(36.4)	Weight changes	28(25.5)
Perception and hallucinations		**Impulse control disorders**	
Diplopia	35(31.8)	Gambling	5(4.5)
Hallucinations	37(33.6)	Hypersexuality	11(10.0)
Sense of presence	30(27.3)	Buying	10(9.1)
Delusions	34(30.9)	Eating	21(19.1)
Memory and concentration		Hobbyism/punding	24(21.8)
Remembering	64(58.2)	Medication overuse	39(35.5)
Concentrating	51(46.4)		
Multitasking	65(59.1)		
Gastrointestinal tract			
Constipation	62(56.4)		
Bowel incontinence	64(58.2)		
Vomiting, acid reflux	37(33.6)		
Dribbling	52(47.3)		
Swallowing	43(39.1)		

Table 3: Multiple linear regression model of the TU-NMSQuest

	Adjusted Rs	Standardized beta	t	*p*-value
TU-NMSQuest	0.526			
(Constant)		8.917	6.584	0.000
UPDRS		0.332	4.517	0.000
TGDS-30		0.416	5.768	0.000
Duration of disease		0.449	5.220	0.000
TMSE		-0.229	-3.244	0.002

TU-NMSQuest = Thammasat University Non-Motor Symptoms Questionnaire, UPDRS = Unified Parkinson's Disease Rating Scale, TGDS = Thai Geriatric Depression Scale, TMSE = Thai Mental State Examination

Causes of pain in PD are multifactorial; it includes muscle rigidity, spasm and motor complication, if the occurrence of pain correlates with off phenomenon, increasing doses of anti-PD drugs may be helpful.[11]

Sleep disorders are other frequent NMS in PD patients. It includes insomnia, sleep fragmentation, excessive daytime sleepiness, REM sleep behavior disorder. The findings in this study (Table 2) is similar to the previous Thai studies.[4-6] The pathogenesis of sleep disorder are multifactorial, it include degenerative of central sleep regulation centers in the brain stem structures, depressive disorders, medication side effect, nocturia and hallucination.[10,11]

Fatigue was found in 71.8% of our PD patients. Causes of fatigue include physical causes (motor impairment, stiffness) and mental caused (depression, anxiety). Identification of the causes of fatigue may help in its further treatment.[11]

Cognitive impairment in PD's patients is said to be characterized by impairment of executive and visuospatial functions. In the current study, 58.2% of the patients complained of difficulties in memory. We assessed our patients' cognitive function using TMSE. When Parkinson's disease with dementia (PDD) is defined by TMSE < 24, the prevalence of PDD in our patients was 34.5%, a rate similar to previous studies.[11-13] We also found an association between TMSE and TU-NMSQuest in our patients. The association between severity of dementia and NMS has been noted in other study.[14] Impairment of concentration and multitasking ability are reported in close to half of our patients. These symptoms are common and associated with older age at the onset and longer duration of disease. The symptoms may also be the adverse drug reactions to anticholinergic, which should be avoided in the old PD patents.[12,18]

Depression and anxiety are common neuropsychiatric complication in PD patients. Depression can occur in any stages of PD and even before onset of the disease. Depression associated with PD is the result of damage to serotoninergic, noradrenergic and dopaminergic pathways.[11] TGDS-30 was used to evaluate severity of depression in our study. We found that depression was one of the strongest factors on high score of TU-NMSQuest in our study. As both depression and NMS impact quality of life in PD patients, the clinicians should look out for these symptoms.[15-17]

Psychological problems; defined as hallucinations, delusions and sense of presence, occurred in about 30% of our PD patients. Impulsive control disorders (ICD) was identified in about 48% of our patients, there was overall more common than the previous Thai study.[5] When interpreting the high prevalence of ICD, one should take into account the younger mean age of the Thai patients, who tends to take higher dose of DA.[19]

We have shown in this study that TU-NMSQuest is a useful screening questionnaire, to identify the NMS and ICD in Thai PD patients. In previous study in Thammasat University, Bangkok, NMS have greater impact on quality of life than motor symptoms and were important causes of disabilities in PD patients.[5,20] In the current study, we found the association of NMS with duration of disease, disease severity (H&Y), dementia and depression. Attention to both NMS and motor symptoms would provide a more comprehensive treatment, attending to both mind and body. TU-NMSQuest, by helping to screen for NMS, will help to enhance comprehensive approach to PD care.

There are some limitations in the current study. Firstly, the TU-NMSQuest is a screening test for NMS. The results depend on subjective awareness which do not necessary reflect the specificity and severity of NMS. Some of NMS such as nocturia, insomnia, and pains are common symptoms in geriatric population. Secondly, depressive scores

were assessed by using TGDS-30. TGDS-30 is useful in geriatric patients but its sensitivity and specificity in young onset PD patients is uncertain. Thirdly, the TU-NMSQuest consists of 40 items. However in many previous studies, the 30 items NMSQuest was used, it can thus affect statistical analysis of the data, and comparison with previous studies.

In conclusion, our study in a cohort of PD patients from a rural province in Northeast Thailand showed that all the patients have at least one NMS symptoms. Nocturia was the commonest symptom, followed by insomnia, pain and fatigue. The number of NMS significantly increased with the degree of severity of disease, depression disorder, duration of disease and dementia.

DISCLOSURE

Conflicts of interest: None

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