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Validating the Vietnamese version of wearing – Off 19 questionnaire for patients with Parkinson's disease

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ABSTRACT

Background: One of the most common complication of the progression of Parkinson's disease (PD) is the wearing off phenomenon. A validated Vietnamese version of Wearing off 19 (WO19) questionnaire is necessary to optimize the Vietnamese PD treatment.

Objectives: This study was undertaken to determine the quality attribute of the questionnaire as a tool for early detection of wearing off (WO) in Vietnamese population with PD. We also sought the relationship between the WO phenomenon and factors concerning the clinical condition and course of the disease.

Subjects and methods: This is an observational, cross-sectional study. Patients diagnosed with PD under dopaminergic treatment came to University Medical Center Ho Chi Minh city for a regular appointment were sequentially asked to complete the Vietnamese WO19 questionnaire. A neurologist specialized in movement disorders assessed the patient and determined whether he had experienced wearing off or not. The questionnaire results were then compared to the clinical opinion of the expert which is considered the gold standard for diagnosing wearing off. The reliability of the questionnaire is evaluated by Cronbach'α and Cohen's kappa coefficient. The validity is measured by the sensitivity and the specificity of the instrument compared to the gold standard. The multivariate logistic regression analysis is used to learn the relations of associated factors and wearing off phenomenon.

Results: 98 patients with the mean age 59.12 ± 10.99 have joined our study; 58.2% are male; and the mean disease duration is 6.32 years. The Vietnamese version of the WO19 questionnaire has a good reliability (Cronbach'α = 0.778) and the agreement with the expert assessment (the diagnostic accuracy) is at a substantial level (Kappa value = 0.618). The sensitivity and specificity of the questionnaire resulted 89.28% and 71.43% respectively. The multivariate logistic regression analysis revealed a long disease duration ($\geq$ 6 years) (OR: 16.96; 95% CI: 2.17–132.57; p = 0.007), a high daily levodopa dosage ($\geq$ 400 mg/day) (OR: 6.31; 95% CI: 1.36–29.23; p = 0.019) and high score of MDS-UPDRS part IV ($\geq$ 4) (OR: 15.36; 95% CI: 2.13–110.58; p = 0.007) were independent predictive factors for wearing off in Vietnamese PD patients.

Conclusions: Vietnamese – WO19 is a reliable and effective tool which should be used in clinical practice for early detecting PD patients with wearing off.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder with median age standardized annual incidence rates in developed countries of 14 per 100,000 people, and 160 per 100,000 people aged 65 years or older [9]. Treatment with levodopa (L-dopa) for PD is complicated by subsequent development of motor complications, including motor fluctuations and dyskinesias later. The earliest type is the end of-dose wearing-off (WO), which is usually followed by complicated wearing-off, delayed-on, dose failures, and/or a random on-off effect [8,17]. Wearing off phenomenon, defined as generally predictable recurrence of motor and non-motor symptoms preceding scheduled doses of antiparkinsonian medication that usually improve postdosing. This is the earliest and the most frequent manifestation of fluctuations [2]. WO has a negative impact on quality of life in patients with PD. Early detecting WO and optimizing pharmacological therapy to limit WO is crucial to improve quality of life of PD patient [5]. In comparison to a delay in treatment, an early control over WO brings greater long term benefits for patients (Fig. 1, Tables 1–3) [13].
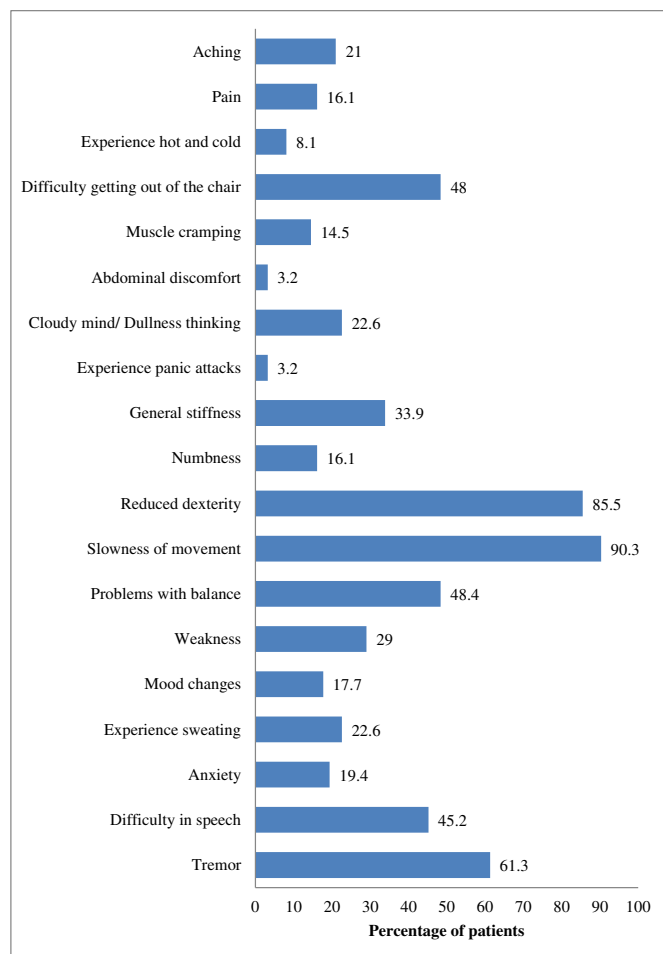
Fig. 1. Frequencies of motor and non-motor symptoms respecting to WO19 questionnaire results.

Table 1
Demographic and disease – related features of enrolled patients.

Characteristics	Overall (n = 98)	Clinical diagnosis of movement disorder specialists		
		WO (n = 56)	No WO (n = 42)	p
Sex				0.156
- Male	57 (58.2%)	36	21	
- Female	41 (41.8%)	20	21	
Age (years)	59.12 ± 10.99 (33–82)	59.46 ± 9.63	58.67 ± 12.7	0.072
Age at onset (years)	52.87 ± 11.95 (28–81)	51.41 ± 11.78	54.81 ± 12.48	0.165
Duration of disease (years)	6.32 ± 3.94 (1–19)	8.16 ± 3.97	3.86 ± 2.20	**0.000**
Levodopa treatment duration (years)	5.02 ± 3.59 (1–18)	6.71 ± 3.60	2.76 ± 1.99	**0.000**
Medications				0.190
- Levodopa monotherapy	14.3%	10.71%	19.05%	
- Adjunctive therapy	85.7%	89.29%	80.95%	
Daily levodopa dose (mg)	672.45 ± 444.85 (100–2400)	833.04 ± 490.11	458.33 ± 252.53	**0.003**
Hoehn and Yahr[a]				**0.000**
- Stage 1	24 (24.5%)	5 (8.93%)	19 (45.24%)	
- Stage 2	59 (60.2%)	37 (66.07%)	22 (52.38%)	
- Stage 3	12 (12.2%)	11 (19.64%)	1 (2.38%)	
- Stage 4	3 (3.1%)	3 (5.36%)	0 (0%)	
- Stage 5	0	0	0	
MDS – UPDRS[a]				
- Part 1		10.82 ± 5.94	7.10 ± 3.53	**0.006**
- Part 2		17.05 ± 8.06	8.14 ± 5.03	**0.002**
- Part 3		34.80 ± 17.82	20.69 ± 11.41	**0.018**
- Part 4		6.63 ± 4.24	1.1 ± 1.98	**0.000**

Bold items imply that the p is statistically significant (p < 0.05).
[a] The patients were evaluated in their most comfortable state.

Thought WO is reasonably common, it usually goes unrecognized and untreated, especially in patients suffering from non-motor wearing off phenomenon. Several self-assessed questionnaires including Wearing off 32 [20], Wearing off 19 [19], and Wearing off 9 [21] have been developed and proved to be useful in detecting WO phenomenon. Wearing off 19 (WO19) questionnaire has been adapted to several languages and was recommended by MDS for use to assess wearing off phenomenon [4].

We adapted the WO 19 questionnaire to optimize the detection of wearing off in Vietnamese Parkinson's disease patients and treatment of this complication.

Subjects and methods

This is an observational, cross-sectional study. The patients who were clinically diagnosed with PD based on IP-MDS, aged over 18, under dopaminergic treatment and signed the consent forms were consecutively enrolled in this study. Patients with psychiatric comorbidities (diagnosed by their attending physician), dementia (MMSE < 24) and with a history of previous neurosurgery for PD were excluded from the study. The patients were evaluated in their most comfortable state.

The major aim of this study is to adapt WO19 questionnaire into Vietnamese and to evaluate the quality attribute of the instrument. Sample size was calculated to allow the estimation of sensitivity and specificity of a diagnostic tool [6,7]. Based on the assumption of a minimum acceptable value of 75% and an expected value of 90% for both sensitivity and specificity, a minimum of 42 PD patients with WO and a minimum of 42 PD patients without WO were needed for an error = 0.1 and statistic power = 0.2.

Our study composed of 3 stages: (i) performing translation and cultural adaptation of the WO19 questionnaire into Vietnamese by following required steps in Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures (ISPOR) [22]; (ii) delivering a survey on a group of 5 PD patients to investigate the intelligibility and feasibility of the questionnaire to modify the translated instrument; (iii) recruiting patients and executing the main study on Vietnamese version of WO19.

During regular appointment at the clinic, after informed consent, PD patients were instructed to complete the Vietnamese WO19 questionnaire before interviewed by the physician. All the participants completed the questionnaire on their own or along with the caregivers without help from the investigators. They need <5 min to finish. It were noted that whether the patients finished the task with or without the investigators' assistance. The time needed to answer the questionnaire was also noted. The patients were considered "patients with WO" when they had at least 1 out of 19 symptoms listed in the questionnaire improving after next dose of medications. Subsequently, a neurologist specialized in movement disorders evaluated the patient and determined whether he had experienced wearing off or not. In addition, the physician documented the reason (s) for a diagnosis of WO: type of symptoms, symptom response to medication, timing of symptom response to medication, time of day that symptoms occur in relation to medication. The physician had no access to the questionnaire results. The questionnaire results were then compared to the clinical opinion of the expert which is considered the gold standard for diagnosing wearing off.

The reliability of the questionnaire is evaluated by Cronbach'α and Cohen's kappa coefficient. The validity is measured by the sensitivity and the specificity of the instrument compared with the gold standard. The multivariate logistic regression analysis is used to learn the relations of associated factors and wearing off phenomenon. We conducted univariate analysis to explore the relationships of all factors such as age, gender, age

Table 2
Dispositions of patients by the specialists' clinical diagnosis and the WO19 questionnaire result.

		Clinical diagnosis of movement disorder specialists		Total
		Yes	No	
Vietnamese	Yes	50	12	62
WO19	No	6	30	36
Total		56	42	98

at onset, disease duration, L-dopa treatment duration, H&Y and MDS-UPDRS with wearing off. Subsequently, we included those variables in the multivariate analysis model.

This study was reviewed and approved by the Ethics committee of University of Medicine and Pharmacy Ho Chi Minh city.

Results

The process of translating and adapting into Vietnamese following steps of IPSOR completed in 2017 November. The survey on group of 5 patients revealed that the Vietnamese version of WO19 is clear, comprehensible and feasible.

98 patients meeting the inclusion criteria participated in this study.

According to the clinical diagnosis of the specialists, there are 56 patients with WO, accounting for 57.1% and 42 patients without WO, accounting for 42.9%. In patients diagnosed with wearing off, the most frequent characteristics used to determine WO is symptom response to medication (92.9%). Vietnamese version of WO19 detected 62 patients with WO (63.3%). The instrument has Cronbach'α = 0.778 and the agreement with the expert Kappa value = 0.618 ($p = 0.000$).

The sensitivity and specificity of the questionnaire are 89.28% and 71.43% respectively. The positive predictive value and negative predictive value were calculated to be 80.65% and 83.33% respectively.

Identified by WO19, the most frequent motor sign of WO was slowness in movements (90.3%). Besides, the most frequent non-motor symptoms reported by WO19 included sweating and dullness thinking (22.6%).

The multivariate logistic regression analysis revealed a long disease duration (≥ 6 years) (OR: 16.96; 95% CI: 2.17–132.57; $p = 0.007$), a high daily levodopa dosage (≥ 400 mg/day) (OR: 6.31; 95% CI: 1.36–29.23; $p = 0.019$) and high score of MDS-UPDRS part IV (≥ 4) (OR: 15.36; 95% CI: 2.13–110.58; $p = 0.007$) has a significant and positive association with wearing off in Vietnamese PD patients.

Discussions

Wearing off 19 questionnaires has been adapted following IPSOR [22] which is an internationally recognized procedure including: preparation, translation, forward translation, reconciliation, back translation, back translation review and harmonization. Additionally, the back translated version was accepted by the author of the original version. That secured

Table 3
Results of multivariate regression analysis.

	OR	CI 95%	p
Disease duration $\geq$ 6 years	16.96	2.17–132.57	**0.007**
Levodopa treatment duration $\geq$ 2 years	2.56	0.38–6.42	0.538
Daily levodopa dose $\geq$ 400 mg	6.31	1.36–29.23	**0.019**
MDS – UPDRS part 1 > 10[a]	2.47	0.56–10.85	0.23
MDS – UPDRS part 2 > 12[a]	0.40	0.05–3.03	0.38
MDS – UPDRS part 3 > 32[a]	2.30	0.35–15.32	0.39
MDS – UPDRS part 4 > 4[a]	15.36	2.13–110.58	**0.007**
Hoehn – Yahr $\geq$ 2	1.19	0.08–18.45	0.90

[a] We used the proposed MDS-UPDRS cut off points for mild/moderate PD. [11]

the conceptual equivalence of the Vietnamese version. All participants could finish answering the questionnaire in <5 min without help of a health professional. That assured the feasibility of the instrument.

Our study showed that the Vietnamese version of the WO19 questionnaire has a good internal consistency (Cronbach'α > 0.7). This result is consistent with that in earlier studies. For instance, the Cronbach's α of Italian WO19 was 0.868 [1], and that of Filipino WO19 is 0.781 [16]. The agreement of WO19 results with the expert assessments (the diagnostic accuracy) is at a substantial level (Kappa value = 0.618). This is consistent with previous studies of the Spanish WO19 with Kappa value of 0.68 [10].

The Vietnamese WO19 detected signs and symptoms of WO in 63.3% of patients comparing with 57.1% diagnosed by neurologists and the sensitivity of the instrument was quite high (89.28%). The high sensitivity in our study is consistent with previous reported sensitivity of 82% [18] 91.52% [1], and 95% [10]. WO19 is a highly sensitive tool in early detecting wearing off phenomenon.

In agreement to the results from other studies, the specificity of Vietnamese WO19 is low, <75% [1,10,18]. This is acceptable for a screening tool. The patients identified by WO19 should be referred to a movement disorders specialist for further examination.

The most frequent motor signs of WO detected by Vietnamese WO19 were slowness in movements, reduced dexterity and tremor. This finding is similar to results in some other studies [3,10,12]. Regarding non-motor signs, the most common ones include dullness thinking and sweating. According to previous study sweating is the most frequent sign associated with fluctuations, in 64% cases [23]. Sweating is more common and more severe in patients with wearing off [15]. In other studies using WO19, the dominant non-motor sign presented as wearing off was anxiety [1,3,10,12]. Whether the tropical climate of Vietnam results in increase sweating of wearing off cannot be answered with the current study.

Many studies have been conducted to seek for the risk factors or the predictors of wearing off. The results from those studies were inconsistent. The most common mentioned factors were disease duration and daily levodopa dose [14,17]. Our study also showed the association of these two factors with WO. Furthermore, our study shows the association of WO with the score of MDS – UPDRS part IV. MDS – UPDRS part 4 is the scale used by physician to assess fluctuations. The relation between WO19 and MDS-UPDRS part 4 exhibited congruence between a self-rating scale and a physician-administered scale.

Conclusions

Vietnamese Wearing off 19 is a feasible and reliable instrument. Vietnamese WO19 showed to be a highly sensitive and effective tool for early detection of WO in clinical settings.

Conflict of interest

Uyen Le Ngoc Ha has nothing to declare Tai Ngoc Tran has received honoraria/lecture fees from Abbott, Boehringer-Ingelheim, Ipsen Pharmaceuticals, Medtronic, and Novartis. Minh Le has nothing to declare Thuong Huyen Thi Dang has nothing to declare Nhi Anh Vu has nothing to declare Daniel Truong serves as an editor in chief for the Journal of Clinical Parkinsonism and Related Disorders, as an associate editor for the journal of Neurological Sciences and on the editorial board of Parkinsonism Related Disorders, Journal of Neural Transmission, Translational Neurodegeneration and eNS. Daniel Truong has research grants from Ipsen, Merz, Auspex, Daiichi Sankyo Pharma, AbbVie, Kyowa, Lundbeck Ltd., Neurocrine, Sunovion Pharmaceuticals Inc., Acadia, Accorda, Cynapsus, Neuroderm, Prexton Therapeutics, and Intec. He receives honoraria for services as a consultant or advisory committee member for Alexza Pharmaceuticals, Inc.; Adamas Pharmaceuticals; Merz and US World Meds. He has received speaking fees from Neurocrine, Teva and Accorda. He receives royalties from Cambridge University Press, Wiley Publishing and Demos Publishing Company and honoraria from Elsevier publishing company.

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