Clinical Parkinsonism & Related Disorders 1 (2019) 21–24

Contents lists available at ScienceDirect

Clinical Parkinsonism & Related Disorders

journal homepage: www.elsevier.com/locate/prdoa

Philippine translation and validation of the Wearing-off Questionnaire-19

Katrina C. Remigio [a], Roland Dominic G. Jamora [b,*]

[a] Department of Neurosciences, Philippine General Hospital, University of the Philippines Manila, Manila, Philippines
[b] Department of Neurosciences, College of Medicine – Philippine General Hospital, University of the Philippines Manila, Manila, Philippines

ARTICLE INFO

Article history:
Received 8 May 2019
Received in revised form 19 July 2019
Accepted 22 July 2019
Available online 26 July 2019

Keywords:
Parkinson's disease
Translation
Validation
Wearing-off questionnaire
Filipino wearing-off

ABSTRACT

Introduction: The 19-item Wearing-Off questionnaire is used as a self-administered questionnaire assessing wearing-off (WO) in Parkinson's disease (PD) patients. Thus, we aim to translate and validate the WOQ-19 into Filipino (FWOQ-19).

Methods: We translated the WOQ-19 questionnaire into Filipino and used it to assess WO among Filipino PD patients. The original WOQ-19 was translated into Filipino using forward and backward translation by independent bilingual translators. WO is present if the patients checked at least 2 symptoms in the WOQ-19. Baseline demographic data, disease duration and medication use were collected. Internal consistency was measured using Cronbach's alpha. The Unified Parkinson's Disease Rating Scale (UPDRS) part IV and WOQ-32 were correlated with FWOQ-19 through Pearson's correlation coefficient to assess construct validity.

Results and discussion: The FWOQ-19 was answered by 46 patients. The mean age of the participants was 60.8 ± 10.0 years (range, 40–86 years). The mean duration of PD was 10.9 ± 3.1 years (range, 1–26 years). Majority (n = 38, 82%) of patients claimed that WO is predictable and only 2 of the patients claimed that WO is unpredictable. The rest of the patients (n = 6, 13%) said that they did not experience WO. The internal consistency of the FWOQ-19 is acceptable (Cronbach's alpha 0.7808). There is a high correlation between WOQ-32 and FWOQ-19 (r = 0.8191). The troublesome symptoms for the patients were tremor, insomnia, weakness and slowness.

Conclusion: The FWOQ-19 is a valid assessment tool for detecting wearing-off among Filipino-speaking PD patients.

1. Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder characterized by a constellation of symptoms, namely, bradykinesia, rigidity, tremor and loss of postural reflexes [1]. Levodopa/carbidopa (LD) remains to be the most effective medication for the symptomatic treatment of patients with PD. The use of LD, however, is associated with the development of motor complications such as wearing-off (WO) phenomenon and dyskinesias. A year after treatment of LD, 10% of patients develop motor fluctuations [2]. By the end of second year of LD treatment, 50% of patients develop complications. Majority of patients, 80–90%, may develop motor fluctuation after 5–10 years of LD therapy [3,4].

WO phenomenon is described as the reemergence of the motor and non-motor symptoms in patients with PD initially stable on treatment with LD [3]. The patients begin to notice the improvement in the symptoms only after taking their next dose of LD [5,6]. In essence, there is a decreasing benefit of therapeutic effects for each duration of each dosing cycle of LD.

Clinicians who are familiar with the problem of motor and non-motor fluctuations in PD may recognize the WO phenomena. Patient may have varying signs and symptoms making the WO phenomena to be underreported by patients thereby making it more difficult to be identified and diagnosed. WO symptoms have great impact on the neurological disability and quality of life of patients hence, management and early detection is essential to initiate proper therapeutic strategies [5,7]. Better recognition and timely intervention of WO symptoms in the early stages of PD may delay the progression and reduce the complications of this phenomenon thereby improving the quality of life by alleviating the patients' distress over their symptoms.

The Wearing-Off Questionnaire-19 (WOQ-19), a sensitive self-rated questionnaire developed in 2007, has been translated in various languages such as Italian, Japanese, Spanish and Portuguese and has been subsequently validated [7–10]. It contains nine motor symptoms and ten non-motor symptoms. For every item in the questionnaire, the patient is asked to tick whether the patient experiences the symptom and whether it improved after the following dose of LD. This questionnaire has been recognized and recommended for use in clinical practice for the detection of WO [6].

The use of a translated questionnaire will be useful in enhancing the detection of WO symptoms by general practitioners and even neurologists in

* Corresponding author at: Department of Neurosciences, College of Medicine – Philippine General Hospital, University of the Philippines Manila, Taft Ave., Ermita, 1000 Manila, Philippines.
E-mail address: rgjamora@up.edu.ph. (R.D.G. Jamora).

http://dx.doi.org/10.1016/j.prdoa.2019.07.005

clinical practice. Also, the availability of these translated questionnaires in the vernacular will be helpful in reaching out to patients not familiar with the English language. In this light, this study aims to translate the WOQ-19 into Filipino (FWOQ-19) and validate the translated questionnaire.

2. Methodology

2.1. Target population, subject sampling, sample size calculation

Using Epi Info & software, the minimum sample size requirement was estimated to be at least 42 patients based on a specificity = 80% [6] with confidence level = 95% and margin error = 5%. The patient recruitment was done via consecutive sampling. Individuals diagnosed to have idiopathic PD according to the UK PD Society Brain Bank Clinical Diagnostic Criteria and has fulfilled the following were included in this study: (1) at least 40 years old, (2) the duration of disease is at least 1 year with the use of levodopa or dopamine agonist, (3) with a Hoehn and Yahr scale score of less than 5 and have signed the informed consent. We excluded patients with severe cognitive impairment or severe psychiatric co-morbidity and patients with secondary causes of parkinsonism such as structural and drug-induced.

2.2. Translation of the WOQ-19 into Filipino

The WOQ-19 was translated into Filipino using the forward and backward translation. An independent bilingual translator from the Sentro ng Wikang Filipino – Unibersidad ng Pilipinas Manila (Center for the Filipino Language – University of the Philippines Manila) translated the original version of WOQ-19 into Filipino (FWOQ-19). Modifications were done to the translated questionnaire by the investigators. The Filipino version was then translated back into English by another bilingual translator who was not familiar with the original version. A consensus meeting between the investigators was done prior to the approval of the final Filipino version of the questionnaire. Modifications were included in the final version of the translated questionnaire.

2.3. Data collection method, instruments used

The authors conducted the assessment of subjects coming in at the Neurology Outpatient Clinic of the Philippine General Hospital (PGH). The recruited patients were asked to answer the FWOQ-19. WO is present if the patients checked at least 2 symptoms in the FWOQ-19. Afterwards, the investigators assessed the patients using the Unified Parkinson's disease Rating Scale (UPDRS) and interviewed them about their symptoms using the Wearing-Off Questionnaire-32 (WOQ-32) as a checklist. WO is present if the patients answered at least 2 symptoms using the WOQ-32 checklist. The WOQ-32 has effectively identified symptoms of WO more frequently than routine assessments and was used in this study as a guide to standardize the interview conducted by the investigators [3]. The WOQ-32 checklist was used as the gold standard in this study due to lack of other Filipino screening tools for the detection of WO in PD.

Patients were debriefed after answering the questionnaire to verify that all items have been completed and to inquire about items that they had difficulty understanding. On follow-up, the patients were asked to answer the FWOQ-19 again. This is to assess the test-retest reliability over a time interval of 14 days.

The demographic data of the patients were recorded including age, sex, education, PD disease duration, total levodopa dose per day, modified Hoehn and Yahr (H&Y) stage and UPDRS part IV.

2.4. Statistical analysis

Data analysis was done using Stata SE version 13. Quantitative variables were summarized as mean and standard deviation, while qualitative variables were reported as frequency and percent distribution. Internal consistency of the questions was measured using Cronbach's alpha while the consistency of the patients' responses in the test-retest were measured using paired *t*-test. The content validity of the translated questionnaire was perused by a movement disorder specialist. Criterion-related validity e.g. concurrent validity was measured by obtaining the correlation between the WOQ-32 checklist and FWOQ-19. The correlation was graphically presented in a scatterplot and analyzed using Pearson's Product-Moment Correlation. Comparison of the WOQ-32 checklist and FWOQ-19 scores with and without WO based on UPDRS were analyzed using independent *t*-test. The level of significance was set at 0.05.

2.5. Ethical consideration

This study [(NEU)2015-337-001] was approved by the University of the Philippines Manila Research Ethics Board.

3. Results

3.1. Demographic data

The FWOQ-19 was answered by a total of 46 patients. The mean age of the patients was 60.8 ± 10 years. Majority (n = 26, 57%) of the patients were male. The mean duration of the disease was 10.9 ± 3.1 years (range 1–26 years). The demographics and disease-related characteristics are shown in Table 1. A total of 38 (82.6%) patients claimed that WO is predictable while 2 (4.34%) of the patients claimed that WO is unpredictable. The rest of the patients (n = 6) said that they did not experience WO.

Recruited patients were on a total LD dose of 366.3 ± 170.39 mg/day. Majority (n = 24, 52%) of patients were taking LD only. Eight patients (17%) had additional two add-on medications, and 14 patients (30%) had one add-on medication to LD. The add-on medications of the patients were a combination of dopamine-agonists, anticholinergic, MAO-B inhibitor and COMT-inhibitor.

3.2. Internal consistency of FWOQ-19 and test-retest reliability

The internal consistency of the 19-item questionnaire FWOQ-19 as measured by Cronbach's alpha was acceptable at 0.7808. Using the paired *t*-test, there was no significant difference between the initial (9 ± 3.18) and follow-up (7.67 ± 3.9) scores of patients who answered the FWOQ-19 (p-value = 0.2091). Only 15 patients were able to answer the FWOQ-19 on re-test as most of the patients did not follow-up after 14 days.

Table 1
Demographic and disease-related characteristics of patients in the study.

Characteristics	Mean (%) (n = 46)
Age, in years	60.8 ± 10.0
Male	26 (56.5%)
Disease duration, in years	10.9 ± 3.1
Hoehn & Yahr (H&Y) staging	
0	1 (2.17%)
1	5 (10.87%)
1.5	9 (19.57%)
2	16 (34.78%)
2.5	6 (13.04%)
3	9 (19.57%)
UPDRS score	
Part I	1.78 ± 1.56
Part II	10.35 ± 6.80
Part III	19.52 ± 12.92
Total score (I–III)	31.65 ± 18.88
Total Levodopa dose, in mg per day (mg/day)	366.3 ± 170.39
Educational level	
Less than 6 years of studies	4
7–10 years of studies	21
More than 10 years of studies	21

3.3. Criterion-related validity

The correlation between the WOQ-32 checklist and FWOQ-19 was high at 0.8191 as measured by the Pearson's Product-Moment Correlation (see Fig. 1).

3.4. Comparison of WOQ-32 checklist and FWOQ-19 scores with UPDRS part IV scores on wearing-off

The UPDRS part IV scores for the recruited patients were recorded and compared with their respective WOQ-32 checklist and FWOQ-19 scores using the independent *t*-test (see Table 2). Patients who reported "With Wearing-off" in the UPDRS part IV had significantly higher WOQ-32 scores than those patients who reported "No Wearing-off". However, the mean score of 7.0 for those who reported "No Wearing-Off" in WOQ-32 would still indicate that there is WO as the cut-off for presence of WO is 2. The FWOQ-19 scores for those who reported "No Wearing-Off" was 6.2 and for those who reported "With Wearing-Off" was 8.3. Although there was no significant difference in the FWOQ-19 scores between the two groups, a mean score of 6.2 in the "No Wearing-Off" group would still indicate the presence of WO.

The items were tallied for the troublesome and most troublesome symptoms for PD patients in the study. The troublesome symptoms were tremors, insomnia and slowness. The most troublesome symptoms for the recruited patients were tremors, weakness and slowness.

4. Discussion

Currently there is no gold standard in diagnosing WO in PD patients. Patients have to be educated about this phenomenon and have to be asked about their symptoms regularly as the symptoms differ among patients. However, this is prone to recall bias as the symptoms may fluctuate in between consultations. Similarly, not all clinicians and neurologists are familiar with WO symptoms decreasing the detection rate of WO in PD. In addition, direct observation of patients during consults to observe the response to levodopa and re-emergence of symptoms is time consuming and is not practical [3]. Several attempts have been made to provide a more objective way of detecting WO and one of these is the UPDRS, specifically items 36 and 37 [6]. Despite that, WO can include a variety of motor and non-motor symptoms making it difficult for clinicians to recognize and manage this complication. To increase the detection rate, attempts have been made to develop a more specifically designed WO questionnaire.

The WOQ-32 was constructed based on a review of literature and a consensus from movement disorder specialists of the most common motor and non-motor symptoms that are associated with wearing-off. It was designed to include redundant situations for symptoms to incorporate the full spectrum of a certain symptom. The questionnaire, however, was only intended for investigators and not intended for use during routine clinic visits [3]. The WOQ-19 was developed from the results of the evaluation of the

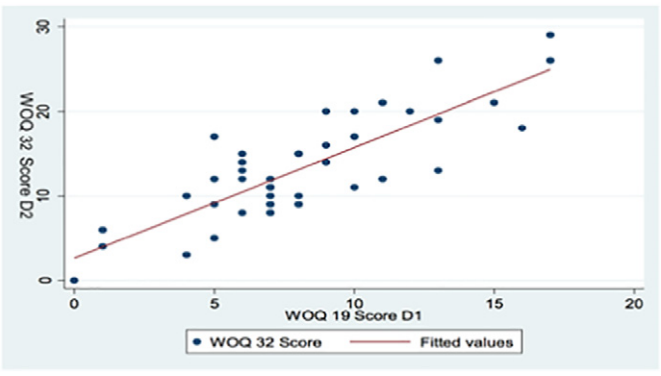

Fig 1. Scatterplot showing the correlation of WOQ-32 checklist and FWOQ-19.

Table 2
Comparison of WOQ-32 checklist and F-WOQ-19 Scores with UPDRS IV Score on WO using independent *t*-test.

	UPDRS Part IV		*p*-Value
	No WO (n = 6)	With WO (n = 40)	
WOQ-32 checklist	7.0 ± 5.0	14.1 ± 5.9	0.0073
FWOQ-19	6.2 ± 4.1	8.3 ± 3.8	0.207

WOQ-32. It was composed to provide a simpler and more suitable tool for routine clinic use [6]. A systematic approach was used to determine which symptoms were the best predictors of WO by removing redundant symptoms [3]. A review of the diagnostic screening questionnaires by the MDS Task Force showed that WOQ-32 is a "Suggested" diagnostic screening tool and the WOQ-19 is a "Recommended" screening tool for the presence of WO in PD. The WOQ-19 was labeled as a "Recommended" screening tool because it fulfilled the following criteria: (1) applied to PD population; (2) used in studies other than the developers; and (3) has undergone clinimetric studies. WOQ-32 is a "Suggested" screening tool as it has been applied to PD populations and has fulfilled only 1 of the other criteria [11].

A 2-item cut-off for the detection of WO was used in this study as it increases the accuracy of the questionnaire compared to a 1-item cut-off [6]. The WOQ-32 checklist guide of the investigators and the UPDRS were used as comparison in this study due to lack of other Filipino scales available for the detection of WO in PD. Several studies have shown that the clinician assessment on the detection of WO has been consistently lower when compared with the use of WO questionnaires [7,13]. The clinic visits may fail to detect WO and that its position as the gold standard should be reevaluated as it could vary depending on the physician's expertise [12].

This study showed that WO is present in 86.94% (n = 40) PD patients which is very high in contrast to the study of Stacy where only 57% PD patients experience WO as detected by the WOQ [13]. The high detection rate for WO can be explained by the lack of expertise of clinicians previously treating the PD patients included in this study in comparison to the PD patients in the study of Stacy wherein they were recruited from Parkinson Centers. Consequently, the high frequency of WO is a reflection of lack of stabilization of symptoms of their current medications.

This study demonstrated a high correlation of the FWOQ-19 when compared with the WOQ-32 checklist (r = 0.8191) and an acceptable internal consistency for the FWOQ-19 (0.7808). The test-retest reliability was measured using the paired *t*-test showing no significant difference in the scores of the patients indicating consistency.

The comparison of the WOQ-32 checklist and FWOQ-19 with the UPDRS part IV items 36 and 37 score showed that patients who reported "No Wearing-off" actually have high scores for WO when both questionnaires were used. The predictable off-periods were probably not equated with wearing-off experiences, hence, the discrepancy in the scores. The lack of significant difference in the FWOQ-19 scores between the two groups makes the FWOQ-19 less sensitive in detecting WO; however, this can be explained by the higher absolute number of the items in the WOQ-32 and by the difference in the approach in answering the FWOQ-19 and WOQ-32.

The UPDRS was used in this study instead of MDS-UPDRS as the former showed higher sensitivity in detecting motor fluctuations (87.2%) when compared to the latter (74.3% for question 4.3 and 67.9% for question 4.5) [14,15].

Similar to the study of Stacy in 2005, the most common troublesome symptom for PD patients in this study was tremor [13]. The other common troublesome symptoms for the PD patients in this study were insomnia, weakness, and slowness. It is important to emphasize that one of these is a non-motor symptom.

Our study has several limitations. First, the study had a small population size and the study design did not allow computation for the sensitivity and specificity of the translated F-WOQ-19. Second, there was a difference in our gold standard when compared to previous studies as the clinician's

assessment may have questionable accuracy depending on the physician's expertise. Nevertheless, this is the first validation study of WOQ-19 in Filipino with acceptable values for parameters used in validation.

The high correlation ($r = 0.8191$) and acceptable internal consistency (0.7808) reinforces the eligibility of the FWOQ-19 to be administered to Filipino PD patients. At present, the country has limited number of neurologists and there are even less movement disorder specialists [16]. The utilization of the FWOQ-19 in addition to UPDRS will aid in the detection and management of WO among Filipino PD patients.

Funding

This study did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Drs. Remigio and Jamora declare that they do not have any disclosures.

Author roles

Dr. Remigio: study concept and design, acquisition of data, analysis and interpretation, writing of the initial draft and critical revision of the manuscript.

Dr. Jamora: study concept and design, acquisition of data, analysis and interpretation, critical revision of the manuscript for intellectual content, study supervision.

Declaration of competing interest

The authors does not have any conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.prdoa.2019.07.005.

References

[1] J. Jankovic, Parkinson's disease: clinical features and diagnosis, J. Neurol. Neurosurg. Psychiatry 79 (2008) 368–376, https://doi.org/10.1136/jnnp.2007.131045.

[2] C.C. Aquino, S.H. Fox, Clinical spectrum of levodopa-induced complications, Mov. Disord. 30 (2015) 80–89, https://doi.org/10.1002/mds.26125.

[3] M. Stacy, R. Hauser, Development of a patient questionnaire to facilitate recognition of motor and non-motor wearing-off in Parkinson's disease, J. Neural Transm. 114 (2007) 211–217, https://doi.org/10.1007/s00702-006-0554-y.

[4] M.C. Altavista, E. Cassetta, L. Brusa, F. Viselli, A. Denaro, M. Ventriglia, P. Pasqualetti, A. Peppe, Wearing-off detection in clinical practice: the wearing off real practice key (WORK-PD) study in Parkinson's disease, Parkinsonism Relat. Disord. 21 (2015) 95–100, https://doi.org/10.1016/j.parkreldis.2014.11.002.

[5] M. Stacy, J.M. Murphy, D.R. Greeley, R.M. Stewart, H. Murck, X. Meng, The sensitivity and specificity of the 9-item Wearing-off Questionnaire, Parkinsonism Relat. Disord. 14 (2008) 205–212, https://doi.org/10.1016/j.parkreldis.2007.07.013.

[6] P. Martinez-Martin, E. Tolosa, B. Hernandez, X. Badia, Validation of the "QUICK" Questionnaire - a tool for diagnosis of "wearing-off" in patients with Parkinson's disease, Mov. Disord. 23 (2008) 830–836, https://doi.org/10.1002/mds.21944.

[7] G. Abbruzzese, A. Antonini, P. Barone, F. Stocchi, T. Tamburini, L. Bernardi, M. Amboni, L. Vacca, V. Posocco, D. Colombo, Linguistic, psychometric validation and diagnostic ability assessment of an Italian version of a 19-item wearing-off questionnaire for wearing-off detection in Parkinson's disease, Neurol. Sci. 33 (2012) 1319–1327, https://doi.org/10.1007/s10072-012-0943-y.

[8] T. Kondo, K. Takahashi, Translation and linguistic validation of the Japanese version of the wearing-off questionnaires (WOQ-19 and WOQ-9), Brain Nerve 63 (2011) 1285–1292, https://doi.org/10.11477/mf.1416101064.

[9] P. Martínez-Martín, E. Tolosa, B. Hernández, X. Badia, The patient card questionnaire to identify wearing-off in Parkinson disease, Clin. Neuropharmacol. 30 (2008) 266–275, https://doi.org/10.1097/wnf.0b013e3180413da7.

[10] L.M. Melo, H.F. Chien, E.R. Barbosa, Identification of wearing-off manifestations (reduction of levodopa effect) in Parkinson's disease using specific questionnaire and comparison of the results with routine ambulatory evaluations, Arq. Neuropsiquiatr. 68 (2010) 506–510, https://doi.org/10.1590/S0004-282X2010000400007.

[11] A. Antonini, P. Martinez-Martin, R.K. Chaudhuri, M. Merello, R. Katzenschlager, P. Odin, M. Stacy, F. Stocchi, W. Poewe, O. Rascol, C. Sampaio, A. Schrag, G. Stebbins, C. Goetz, Wearing-off scales in Parkinson's disease: critique and recommendations, Mov. Disord. 26 (2011) 2169–2175, https://doi.org/10.1002/mds.23875.

[12] C.E. Mantese, A. Schumacher-Schuh, C.R. Rieder, Clinimetrics of the 9- and 19-item Wearing-Off Questionnaire: a systematic review, Parkinsons Dis. (2018) 1–5, https://doi.org/10.1155/2018/5308491.

[13] M. Stacy, Identification of motor and non-motor wearing-off in Parkinson's disease: comparison of a patient questionnaire versus a clinician assessment, Mov. Disord. 20 (6) (2005) 726–733, https://doi.org/10.1002/mds.20383.

[14] L. Raciti, A. Nicoletti, G. Mostile, R. Bonomo, V. Dibilio, G. Donzuso, G. Sciacca, C.E. Cicero, A. Luca, M. Zappia, Accuracy of MDS-UPDRS section IV for detecting motor fluctuations in Parkinson's disease, Neurol. Sci. (2019) 4–6, https://doi.org/10.1007/s10072-019-03745-2.

[15] L. Raciti, A. Nicoletti, G. Mostile, R. Bonomo, D. Contrafatto, V. Dibilio, A. Luca, G. Sciacca, C.E. Cicero, R. Vasta, M. Zappia, Validation of the UPDRS section IV for detection of motor fluctuations in Parkinson's disease, Parkinsonism Relat. Disord. 27 (2016) 98–101, https://doi.org/10.1016/j.parkreldis.2016.03.008.

[16] R. Jamora, J. Miyasaki, Treatment gaps in Parkinson's disease care in the Philippines, Neurodegener Dis Manag 7 (2017) 245–251, https://doi.org/10.2217/nmt-2017-0014.