Long-term Apomorphine Infusion Users Versus Short-term Users: An International Dual-center Analysis of the Reasons for Discontinuing Therapy

Roongroj Bhidayasiri, MD, FRCP, Onanong Phokaewvarangkul, MD, PhD,* Kamolwan Boonpang, RN,* Thanatat Boonmongkol, MD,* Yuwadee Thongchuem, MD,* Nitinan Kantachadvanich, RN,* and Pedro J. García Ruiz, MD†*

Objectives: A retrospective analysis at 2 specialist centers was undertaken to determine the long-term efficacy of subcutaneous apomorphine infusion (APO), rates and reasons for discontinuation, and factors that might contribute to discontinuation.

Methods: Demographics, clinical outcomes data, and reasons for discontinuation were collected for patients treated with APO at Chulalongkorn Centre of Excellence for Parkinson's Disease and Related Disorders, Bangkok, Thailand (n = 36) and Fundacion Jimemez Diaz Universidad Autonoma de Madrid, Spain (n = 16).

Results: There were 19 (52.7%) patients in the Thai cohort and 10 (62.5%) patients in the Spanish cohort who discontinued treatment within around 6 months of initiation, most commonly due to skin nodules (Thai cohort) and perceived lack of efficacy (Spanish cohort). Those who continued APO tended to stay on treatment. In both cohorts, APO resulted in significant reductions in Unified Parkinson's Disease Rating Scale 3 motor scores, daily OFF time, and levodopa-equivalent dose in patients who subsequently stopped therapy, suggesting APO is clinically effective even when "lack of efficacy" is stated as a reason for discontinuing. Daily OFF hours after APO therapy was found to be a significant predictive factor for APO discontinuation with an odds ratio of 5.952 ($P = 0.040$). The cutoff point that determined APO discontinuation was calculated to be 1.75 or more OFF hours (sensitivity, 84.6%; specificity, 63.2%).

Conclusions: Apomorphine infusion is a minimally invasive therapy and therefore very easy to discontinue if difficulties arise. This fact might explain the high dropout rate of this technique. Successful long-term adherence to APO therapy requires a multidisciplinary health care team approach including regular patient follow-up and assessment and prompt resolution of queries and concerns.

Key Words: Parkinson's disease/parkinsonism, apomorphine infusion, retention in treatment

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For patients with Parkinson disease (PD), experiencing persistent, uncontrolled motor and nonmotor symptoms and frequent OFF periods, despite taking multiple antiparkinsonian therapies, can have a significant impact on their quality of life and daily functioning.[1–3] When patients reach this stage of their disease, and repeated adjustment of their intermittent oral or transdermal medication is insufficient to reliably restore them to the ON state after each dose, a continuous, device-aided dopaminergic drug delivery option may need to be considered[4–6]: either apomorphine infusion (APO), where the drug is administered subcutaneously using a removable mini-pump[7,8]; deep brain stimulation (DBS); or levodopa/carbidopa intestinal gel (LCIG) infusion delivered directly into the jejunum. All options have been shown to be highly effective in clinical trials for the management of these types of patients with PD and symptoms, but both DBS and LCIG require a surgical procedure.[9,10] Apomorphine infusion offers patients equivalent motor symptom efficacy to the other device-aided therapies but is a reversible option without the need for surgery.[11] Apomorphine infusion initiation can be undertaken either during inpatient hospitalization or on an outpatient day-case basis.[12] Various publications have debated the types of patients best suited to each of these 3 device-aided therapies, and the risks and benefits of each treatment, with the aim of assisting clinicians and patients in the best choice of therapy for their personal circumstances.[8,11,13–16]

Apomorphine infusion has been used in clinical practice around the world for many years, and its efficacy, safety, and tolerability for the relief of motor fluctuations and dyskinesias, as well as allowing a reduction in oral PD medications, have been proven in a range of open-label studies and, more recently, in a randomized, controlled, double-blind phase 3 trial, the TOLEDO study.[7,8,17–20] The clinical benefits of APO on motor function have also been shown to be sustained with long-term use.[21–27] Despite this accumulated experience and evidence of clinical benefit, APO remains underprescribed by clinicians,[28] and studies have suggested that there is a relatively high rate of treatment discontinuation by patients over the long term.[21] Patient preference is an

*Chulalongkorn Center of Excellence for Parkinson's Disease and Related Disorders, Chulalongkorn University Hospital, Bangkok, Thailand; and †Movement Disorders Unit, Department of Neurology, Fundacion Jimenez Diaz, Universidad Autonoma de Madrid, Madrid, Spain.

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Address correspondence and reprint requests to Professor Roongroj Bhidayasiri, MD, FRCP, Chulalongkorn Center of Excellence for Parkinson's Disease and Related Disorders, Chulalongkorn University Hospital, 1873 Rama 4 Rd, Pathumwan, Bangkok 10330, Thailand; E-mail: rbh@chulapd.org

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important consideration and is a significant factor in both choice of therapy and continued adherence to treatment.

This article describes a retrospective analysis of the efficacy of APO (apomorphine hydrochloride; APO-go Solution for Infusion, Britannia Pharmaceuticals Ltd., Reading, UK) in patients who stopped therapy at 2 specialist PD treatment centers, 1 in Thailand (Chulalongkorn Center of Excellence for Parkinson's Disease and Related Disorders, Bangkok) and 1 in Spain (Movement Disorders Unit at Fundacion Jimenez Diaz, Universidad Autonoma de Madrid), and analyzes the reasons that patients discontinue treatment. We also evaluate factors that might contribute to treatment discontinuation.

MATERIALS AND METHODS

Participating Centers

Chulalongkorn Center of Excellence for Parkinson's Disease and Related Disorders, Bangkok, is a tertiary center, affiliated with Chulalongkorn University and the Thai Red Cross Society, providing specialist care to patients with PD (www.chulapd.org). All 3 device-aided treatment options (APO, DBS, and LCIG) are available to patients with PD if they meet the standard selection criteria for each therapy. The center's selection criteria for APO have been published previously.[17] An APO treatment program commenced at the center in 2015 when the product became available in Thailand. Currently, the center undertakes APO initiation on a day-case basis.

The Movement Disorders Unit at the Fundacion Jimenez Diaz (Universidad Autonoma de Madrid) is a tertiary center for the care of patients with PD and other movement disorders, including treatment with all 3 device-aided therapies. The unit undertakes APO initiation on a day-case basis.

Patients, Data Collection, and Analysis

A total of 36 patients treated with APO at the Chulalongkorn Centre of Excellence for Parkinson's Disease and Related Disorders in Bangkok (Thai cohort) and 16 patients at the Universidad Autonoma de Madrid (Spanish cohort) were included in the analysis. Data on demographics, clinical outcomes, and reasons for discontinuing treatment were collected retrospectively from patient electronic records. The Human Subject Ethics Committee of both Chulalongkorn University and Universidad Autonoma de Madrid approved this study.

Statistical Analyses

The Mann-Whitney *U* test was used for comparative analysis of continuous data between those patients who stopped and those who continued APO therapy. The Wilcoxon signed rank test was used for comparative analysis of continuous data before and after APO treatment. The reasons for stopping treatment were reported as numbers of cases and percentages of the patient cohort. To identify predictors that might determine APO discontinuation, binary logistic regression analysis was undertaken in which the prevalence of APO discontinuation was a dependent variable and participant-related variables were selected to run into the logistic model as independent variables. The logistic model was undertaken using the all enter method technique to select the most predicable variables to determine APO discontinuation, and the predictors were reported as odds ratios. Receiver operating characteristics (ROC) analysis was performed and calculated for cutoff points for factors that might determine APO discontinuation, in addition to determination of sensitivity and specificity. The confidence interval was 95% for all analyses. The results of the ROC analysis with higher area under the curve values had greater diagnostic accuracy for the possible predictive factors and included estimates of sensitivity and specificity. A P value less than 0.05 (2 tailed) was considered statistically significant. All statistical analysis was performed using SPSS version 22.0 software.

RESULTS

The demographic and baseline characteristics for the Thai and Spanish cohorts, as well as combined data for both patient cohorts, are shown in Table 1, stratified according to whether patients stopped APO therapy or continued APO therapy.

Within each individual cohort, and when data for both cohorts were combined, there were no statistically significant differences in baseline characteristics between patients with PD who stopped APO therapy and those who continued in terms of age, disease duration, disease severity at baseline and after commencing APO therapy [determined using the Hoehn and Yahr (H&Y) scale], Unified Parkinson's Disease Rating Scale (UPDRS) motor score during ON and OFF times before APO therapy, and daily levodopa-equivalent dose (LED) before and after APO therapy ($P > 0.05$ in each case).

Among the Thai cohort, the number of daily OFF hours after APO therapy of those patients who continued APO treatment was significantly lower than that of those patients who stopped APO treatment [2.09 (SD, 1.29) hours vs 1.11 (SD, 0.29) hours; $P = 0.004$]. Similar results were observed for the combined data, which showed that OFF hours after APO therapy of those who continued APO treatment were significantly lower than for those who stopped APO treatment [2.25 (SD, 1.11) hours vs 1.45 (SD, 0.59) hours; $P = 0.003$].

In addition, and as expected, the follow-up period of those patients who continued APO therapy was significantly higher than that of those patients who stopped APO therapy: Thai cohort, 27.00 (SD, 17.6) months versus 5.50 (SD, 3.8) months ($P = 0.001$); Spanish cohort, 88.83 (SD, 96.2) months versus 44.67 (SD, 57.87) months ($P < 0.001$); combined data, 44.67 (SD, 57.87) months versus 5.12 (SD, 3.39) months ($P = 0.005$).

Of the 36 patients in the Thai cohort, 16 (52.8%) discontinued APO therapy compared with 10 (62.5%) of 16 patients in the Spanish cohort. In both cohorts, APO discontinuation usually occurred within 6 months of initiation. A total of 17 patients in the Thai cohort continued APO therapy with a mean follow-up period of 27 (SD, 17.6) months, and 6 patients in the Spanish cohort continued APO therapy with a mean follow-up period of 88.83 (SD, 96.2) months. The significantly shorter follow-up time for the Thai cohort compared with the Spanish cohort reflects the fact that APO only became available as an option for PD treatment in Thailand in 2013.

A comparison of parameters before and after APO treatment in patients who stopped therapy and reasons given for treatment discontinuation in each cohort are shown in Table 2. For patients who subsequently chose to stop therapy in the Thai cohort, APO treatment resulted in a significant reduction compared with pretreatment values in UPDRS 3 motor scores during ON [28.29 (SD, 15.80) vs 25.36 (SD, 16.08); $P = 0.006$], daily OFF time hours [4.27 (SD, 2.32) vs 2.09 (SD, 1.29); $P < 0.001$], and daily LED [1102.12 (SD, 356.73) mg vs 608.53 (SD, 302.74) mg; $P < 0.001$]. Similar results were observed in the Spanish cohort, in which APO therapy resulted in a significant reduction compared with pretreatment values in UPDRS 3 motor scores during ON [19.9 (SD, 6.77) vs 17.7 (SD, 5.66); $P = 0.011$], daily OFF time hours [4.6 (SD, 1.17) vs 2.50 (SD, 0.71) hours; $P < 0.001$], and daily LED [748 (SD, 181.83) mg vs 506.33 (SD, 125.61) mg; $P = 0.002$].

Although significant clinical benefits were experienced by patients after commencing APO treatment, a variety of reasons were

TABLE 1. Comparison of Demographic and Clinical Parameters for Patients With PD Who Stopped APO Therapy and Current APO Users

	Patients Who Stopped APO Therapy			Patients Who Continued APO Therapy			
Parameter	**Thai Cohort (n = 19)**	**Spanish Cohort (n = 10)**	**Combined Data (n = 29)**	**Thai Cohort (n = 17)**	**Spanish Cohort (n = 6)**	**Combined Data (n = 23)**	***P***
Age, y	62.58 ± 9.91	56.9 ± 7.33	60.62 ± 9.38	66.47 ± 10.09	64.2 ± 11.48	65.87 ± 10.25	$p_a = 0.196$ $p_b = 0.220$ $p_c = 0.060$
Duration of PD, y	10.95 ± 3.22	8.00 ± 3.40	9.93 ± 3.53	11.53 ± 4.38	9.83 ± 2.71	11.09 ± 4.02	$p_a = 0.876$ $p_b = 0.220$ $p_c = 0.275$
H&Y score at baseline	3.63 ± 0.68	2.70 ± 0.35	3.31 ± 0.74	3.23 ± 0.44	2.67 ± 0.41	3.09 ± 0.49	$p_a = 0.107$ $p_b = 0.958$ $p_c = 0.198$
Before APO: OFF time, h/d	4.27 ± 2.32	4.6 ± 1.17	4.39 ± 1.97	5.38 ± 2.58	5.17 ± 0.75	5.32 ± 2.21	$p_a = 0.224$ $p_b = 0.368$ $p_c = 0.122$
Before APO: UPDRS 3 during ON	28.29 ± 15.80	19.9 ± 6.77	25.19 ± 13.66	28.47 ± 12.25	21.4 ± 5.46	26.86 ± 11.37	$p_a = 0.973$ $p_b = 1.000$ $p_c = 0.647$
After APO: OFF time, h/d	2.09 ± 1.29	2.50 ± 0.71	2.25 ± 1.11	1.11 ± 0.29	2.17 ± 0.41	1.45 ± 0.59	$p_a = 0.004$* $p_b = 0.428$ $p_c = 0.003$*
After APO: UPDRS 3 during ON (last day of initiation)	25.36 ± 16.08	17.7 ± 5.66	22.17 ± 13.17	26.00 ± 14.68	19.2 ± 2.28	24.45 ± 13.18	$p_a = 0.922$ $p_b = 0.859$ $p_c = 0.559$
Follow-up period, mo	5.50 ± 3.8	4.5 ± 2.80	5.12 ± 3.39	27.00 ± 17.6	88.83 ± 96.2	44.67 ± 57.87	$p_a = 0.001$* $p_b < 0.001$* $p_c = 0.005$*
LED before APO, mg	1102.12 ± 356.73	748.00 ± 181.83	980.01 ± 348.97	1315.34 ± 658.17	731.67 ± 242.69	1163.08 ± 630.17	$p_a = 0.219$ $p_b = 0.792$ $p_c = 0.189$
LED after APO, mg	608.53 ± 302.74	506.00 ± 113.16	573.17 ± 255.92	777.06 ± 630.22	528.33 ± 125.61	712.17 ± 552.19	$p_a = 0.827$ $p_b = 0.492$ $p_c = 0.234$
LED reduction (before – after), mg	493.59 ± 373.29	242.00 ± 147.33	406.84 ± 333.72	538.28 ± 610.71	203.33 ± 285.98	450.90 ± 558.97	$p_a = 0.876$ $p_b = 0.428$ $p_c = 0.726$

All statistics were performed using the Mann-Whitney *U* test. Values are mean ± SD.

*Significant difference between groups.

p_a represents *P* value of the comparison in the Thai cohort between those patients who stopped and continued APO therapy; p_b, *P* value of the comparison in the Spanish cohort between those patients who stopped and continued APO therapy; p_c, *P* value of the comparison of combined data between those patients who stopped and continued APO therapy.

TABLE 2. Comparison of Parameters Before and After APO in Patients Who Stopped Treatment and the Reasons for Treatment Discontinuation

	Before APO	After APO	*P*
Thai cohort (n = 19)			
UPDRS 3 during ON	28.29 ± 15.80	25.36 ± 16.08	0.006*
OFF time, h/d	4.27 ± 2.32	2.09 ± 1.29	<0.001*
LED, mg	1102.12 ± 356.73	608.53 ± 302.74	<0.001*
Reason for stopping treatment, n (% of total cohort of 36 treated patients)†			
Skin nodules	7 (36.8)		
Perceived lack of efficacy	3 (15.8)		
Hallucinations	3 (15.8)		
Dyskinesia	2 (10.5)		
Hypotension	1 (5.3)		
Difficulty with device	1 (5.3)		
Financial problems	1 (5.3)		
Other reason	1 (5.3)		
Spanish cohort (n = 10)			
UPDRS 3 during ON	19.9 ± 6.77	17.7 ± 5.66	0.011*
OFF time, h/d	4.6 ± 1.17	2.5 ± 0.71	<0.001*
LED, mg	748.00 ± 181.83	506.33 ± 125.61	0.002*
Reason for stopping treatment, n (% of total cohort of 16 treated patients)†			
Perceived lack of efficacy	7 (43.8)		
Insufficient dexterity to handle device	1 (6.3)		
Nausea	1 (6.3)		
Hemolytic anemia	1 (6.3)		
Other reason	1 (6.3)		

All statistics were performed using the Wilcoxon signed rank test. Values are mean ± SD for the Thai cohort and mean for the Spanish cohort.
*Significant difference between groups. †Patients may have given more than 1 reason for stopping treatment.

given for stopping treatment. In the Thai cohort, the development of skin nodules (36.8%) was the most common reason given for APO discontinuation, followed by hallucinations (15.8%) and dyskinesia (15.8%). Conversely, in the Spanish cohort, perceived lack of efficacy was the most common reason stated for APO discontinuation.

A comparison of data between the Thai and Spanish cohorts who stopped APO therapy (Supplementary Table 1, available online at http://links.lww.com/CNP/A7) found that the duration of PD at baseline was significantly longer [10.95 (SD, 3.22) years vs 8.00 (SD, 3.40) years; $P = 0.035$], and the H&Y score at baseline was significantly higher in the Thai cohort [3.63 (SD, 0.68) vs 2.70 (SD, 0.35); $P < 0.001$]. In addition, daily LED before patients received APO therapy was significantly higher in the Thai cohort [1102.12 (SD, 356.73) mg vs 748.00 (SD, 181.83) mg; $P = 0.003$]. There were no significant differences between the cohorts in daily OFF time before APO treatment or in UPDRS 3 motor scores during ON before or after APO treatment ($P > 0.05$ in each case).

As shown in Table 3, logistic regression analysis was conducted to identify possible predictive factors for discontinuation of APO, including age, Thai cohort, male sex, presence of postural instability or H&Y score of 3 or higher, UPDRS 3 motor score during ON before and after APO therapy, and OFF hours after APO therapy. Nagelkerke R^2 of 0.498 indicates a moderate relationship of 49.8% between the predictors and the prediction. Prediction success overall was 70.7%. The enter method criterion demonstrated the EXP(*B*) value and indicated that only OFF hours after APO therapy was a significant predictive factor of APO discontinuation with an odds ratio of 5.952 ($P = 0.040$).

Further ROC analysis was performed and calculated for cut-off points of OFF hours after APO therapy that might determine APO discontinuation, in addition to estimates of sensitivity and specificity (Fig. 1). The results of the ROC analysis revealed areas under the curves of 0.759 ± 0.074 ($P = 0.003$), suggesting that the number of OFF hours after APO therapy was able to distinguish between those patients who stopped and those who continued

TABLE 3. Predictors and Odd Ratios EXP(*B*) for the Determination of APO Therapy Discontinuation

Predictors	Model 1: Odd Ratios/EXP(*B*)
OFF hours after APO therapy	5.952*
Age	—
Thai cohort	—
Male sex	—
Presence of postural instability (H&Y ≥3)	—
Pre-APO UPDRS (ON period)	—
Post-APO UPDRS (ON period)	—
Model summary	—
Hosmer and Lemeshow test	0.331
Nagelkerke R^2	0.498

*Significant difference.

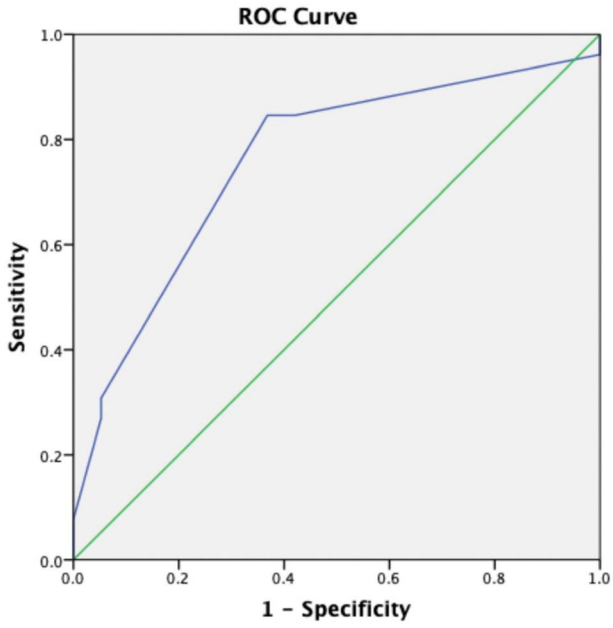

FIGURE 1. The ROC analysis for the cutoff scores of OFF hours after APO therapy that might determine discontinuation.

APO therapy. The calculated cutoff point for OFF hours that determined APO discontinuation was 1.75 hours or more (sensitivity, 84.6%; specificity, 63.2%).

DISCUSSION

Long-term APO therapy is proven to be effective and well tolerated in both clinical studies and clinical practice, and no reduction in efficacy has been observed over time. In this study, mean follow-up periods for patients on APO treatment were almost 27 months in the Thai cohort and almost 89 months in the Spanish cohort. Apomorphine infusion is relatively new in Thailand; therefore, patients were likely to have used oral medications for a longer period before switching to APO, compared with those in the Spanish cohort. However, this observation may also have a cultural aspect whereby Asian patients tend to prefer oral medications and are only willing to switch to a more advanced therapy if they have exhausted all oral treatment options. In addition, Thai patients may also have a misconception that infusion therapy is a "last resort" treatment and its use indicates that their disease has progressed beyond the control of oral medications, and so may be reluctant to switch. There were some differences in demographics observed among those patients who chose to stop therapy between the Thai and Spanish cohorts in terms of disease duration, H&Y score at baseline, and daily LED before APO treatment, which may be related in part to each center's particular practices.

Although previous published studies have reported APO discontinuation rates for their patients with PD cohorts, this is the first study to specifically evaluate the underlying reasons for discontinuation at 2 specialist PD centers. Previous retrospective and observational studies of APO-treated patients have reported discontinuation rates ranging from 41% to 67% of patients.[22,23,25,29] In a large study undertaken in Spain of 166 patients treated with APO for at least 3 months, 68 (41%) discontinued treatment for a variety of reasons including changing to another device-aided treatment (17 patients), insufficient response (8), lack of acceptance of APO therapy (9), and secondary adverse effects (19).[23] Another Spanish center reported their 10-year experience treating 230 patients with APO.[25] Over this time, 137 (60%) patients discontinued treatment, 27% dropped out of treatment within the first 6 months, and 37% had stopped after 1 year. The primary reason for discontinuation was adverse events (16% of patients). A 10-year observational study of long-term APO therapy at a single center in Australia found a discontinuation rate of 67% of patients, with the most common reasons for stopping treatment cited as adverse effects and inadequate motor benefit.[29] A further retrospective long-term study undertaken in the Netherlands of 45 patients with PD with cognitive dysfunction reported that 29 (64%) patients discontinued treatment over this time, although this included 17 deaths unrelated to therapy.[22] Six patients withdrew due to adverse events and 4 due to lessening of therapeutic effect after 9 months.

In our study, a shared reason for discontinuation in both cohorts was a perceived lack of efficacy. Other reasons given differed between cohorts. Local skin reactions, in particular the development of subcutaneous nodules, occur in virtually all patients receiving APO, but these can often be prevented or easily managed with instruction on needle insertion technique and good skin hygiene.[30] However, not all patients who develop subcutaneous nodules will discontinue treatment. In a large Spanish study, skin nodules were observed in 68% of patients, but only 4 (2%) of 166 patients discontinued APO as a result.[23]

In our study, it is interesting to observe that skin nodules were the main reasons for discontinuation in the Thai cohort, but not in Spanish cohort; however, the overall rate of discontinuation was comparable between the 2 centers. Part of the reason for this may be related to the technique or the type of needle used. In Thailand, Surflo winged infusion set 27G (Terumo Corp, Japan) was used, whereas the Neria soft infusion set 27G (Unomedical, Denmark) was used in Spain. Although both infusion sets use the same needle size, the Neria needle is soft, which may be more tolerable for APO patients. Other reasons given for discontinuation were known adverse effects of APO that have been observed in clinical practice in some patients.

Notably, at each center, we found that APO was, in fact, effective in reducing UPDRS 3 motor scores in patients who chose to stop therapy, even when perceived lack of efficacy was stated as a reason for discontinuation. There are likely to be a variety of reasons that contribute to patient's perception of lack of efficacy with APO treatment, including unrealistic expectations of the clinical effects of their new treatment due to the relative complexity of the device-aided option compared with oral therapy. There may also be misconceptions or a lack of knowledge about the drug, its benefits, and possible adverse effects.[31] A previous study has demonstrated that subjective ratings of patients with PD of their degree of improvement with medication do not always accurately reflect the degree of objective change in motor symptoms or disability.[32] As both study sites are well established and dedicated PD centers, staffed with experienced neurologists, PD nurses, and supporting staff, it is unlikely that a lack of adequately skilled staff or their unfamiliarity with APO treatment could be a contributing factor to the observed high discontinuation rates.

Analysis of the data from the 2 centers suggests that patients generally fall into 2 groups: early versus late discontinuation, which warrants further investigation. Prospective data collection via a registry would be likely to provide insights into this issue and help characterize these types of patients. Notably, analysis of pooled data from the 2 centers revealed that a higher number of OFF hours after APO therapy was predicative of discontinuation. From our analysis, those with OFF times of less than 2 hours were likely to stay on treatment. This finding suggests that patients who have better response with minimal daily OFF time were likely to stay on treatment, implying high expectations among our patients. Indeed, OFF time of more than 1.75 hours was identified

as a cutoff for those who discontinue treatment. This could be a potential OFF time target for physicians to consider for patients with APO infusion.

Patient adherence to therapy over the long term is a common challenge on many areas of medicine. The phenomenon is not limited to the more complex device-aided therapies and can be observed with many treatments that have documented efficacy, including oral agents. Tolerability and adverse effects have some part to play in this; however, other reasons such as perceived lack of efficacy and inconvenience are also cited. As examples, substantial rates of discontinuation have been reported for botulinum toxin, the treatment of choice for cervical dystonia,[33] and for cholinesterase inhibitors in the management of Alzheimer disease.[34] Similarly, in the management of PD, high rates of discontinuation have been reported within 3 years for patients taking the oral dopamine agonists ropinirole (51%) and pramipexole (60%).[35] In the case of device-aided PD treatments, several studies of LCIG therapy have reported discontinuation rates of up to 34%.[36–40] Discontinuation is most common within the first year, and elderly patients with longer PD duration are more likely to discontinue. Common reasons for discontinuation include device complications, such as infections at the stoma site, disease progression, worsening dyskinesias, and patient dissatisfaction with treatment.

As APO is a minimally invasive therapy and does not require any form of permanent surgery, it is relatively easy for patients to discontinue if difficulties arise or they decide to change treatment. This rapid and easy reversibility of APO is likely to be another contributing factor to the relatively high rate of discontinuation compared with LCIG or DBS, which require more aggressive, and irreversible, techniques. The easy reversibility of APO, however, can also be an advantage as patients can try APO therapy before they commit to a surgical option and easily discontinue if their treatment goals are not reached. Apomorphine infusion has also been shown to have a good ratio of clinical benefit to risks of treatment; although surgical options have also been shown to be effective for PD management in suitable patients, they are associated with relatively high risk of adverse events and complications associated with the surgical procedure.[11]

In some cases, patients will decide that APO treatment does not suit them, or they have tolerability issues and so select an alternative option. However, in many cases, their problems with APO are manageable or can even be prevented or at least minimized with good technique, for example, skin hygiene and rotating the site of injection to avoid the development of skin nodules. It is therefore important that any issues are identified and resolved promptly so treatment can be continued for optimum clinical benefit.

Health care teams should aim to use effective tools and strategies that help engage patients with PD with their treatment and therefore maximize adherence. These can include the use of PD nurse specialist in the regular assessment of patients, telephone follow-up, and the planning, evaluation, and implementation of treatment.[33] Their vital role in patient education, engagement, and follow-up is thought to be one of the keys to the long-term success of APO treatment.[17,41] Health care professionals should also recognize that there may be gaps in patients' knowledge about their disease and misconceptions about treatment. A recent survey of Asian patients with PD identified a range of misconceptions about PD diagnosis, therapeutic options, and disease course, which highlights the importance of identifying such patients and implementing appropriate educational interventions to correct these inaccuracies.[31]

At the Chulalongkorn Centre of Excellence for Parkinson's Disease and Related Disorders, Bangkok, in addition to delivering patient education at the start of treatment (eg, using videos), an "apomorphine hotline" has also been established at the center, and patients receive scheduled telephone follow-up calls and home visits by a home-care team to facilitate the early identification and management of any manageable adverse events. "Patient advocates" who are receiving APO treatment are also a useful source of advice to new patients. Clinicians also need to ensure that the patient's PD symptoms are being managed effectively throughout the full 24-hour period. In some patients, night-time symptoms, such as nocturnal hypokinesia, can be bothersome but can be effectively controlled with overnight APO.[30,42–44]

In conclusion, all members of the health care team involved in the care of patients with PD treated with APO should be aware of the importance of patient engagement and support, particularly in the initial few months of therapy, to ensure optimal treatment outcomes. Direct follow-up by telephone or e-mail may help resolve any minor concerns or problems the patients may experience and enable them to continue treatment.

An APO patient registry was launched for those who have initiated APO therapy in Thailand since 2015, and it is hoped that routine collection of data from all patients treated with APO will provide valuable information on patterns of treatment and patient adherence.

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