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Apomorphine Therapy for Advanced Parkinson's Disease: A Twenty Four Month Prospective Real-World Cohort Continuous Subcutaneous Infusion versus Intermittent Injection in One Hundred and Ninety-Eight Patients

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Abstract — Apomorphine remains the only dopamine agonist with potency comparable to levodopa, available in two delivery modes intermittent subcutaneous injection for rescue of off periods, and continuous subcutaneous infusion for sustained motor benefit in advanced disease. Real-world outcomes data from South Asian populations remain limited. We prospectively followed 198 patients with advanced Parkinson's disease initiated on apomorphine therapy at a tertiary movement disorders service over 24 months, comparing 98 patients on continuous infusion with 100 on intermittent injection. Mean UPDRS-III motor score fell from 42.4 to 23.8 at 24 months in the continuous infusion cohort and from 42.8 to 30.4 in the intermittent injection cohort. Mean daily off-time fell from 6.4 hours to 2.8 hours with continuous infusion and from 5.6 to 4.4 hours with intermittent injection. Therapy persistence at 24 months was 75% with continuous infusion and 65% with intermittent injection. Strongest independent predictors of sustained response included continuous infusion modality, levodopa responsiveness, shorter disease duration, absence of cognitive impairment, and documented caregiver support. The findings support apomorphine particularly in continuous infusion form as an effective and tolerated advanced PD therapy in this population.

Keywords — *Parkinson's Disease; Apomorphine; Motor Fluctuations; Subcutaneous Infusion; Dyskinesia; Off-Time; Advanced Therapy.*

1. Introduction

Advanced Parkinson's disease presents one of the most challenging management problems in modern neurology. Motor fluctuations the alternation between mobile 'on' periods and immobile 'off' periods punctuated by troublesome levodopa-induced dyskinesia develop in approximately 80% of patients within ten years of diagnosis and substantially impair quality of life. Oral medication adjustment alone often proves inadequate, with progressive shortening of individual dose effects and narrowing therapeutic windows. Advanced therapies deep brain stimulation, levodopa-carbidopa intestinal gel, and apomorphine offer alternatives for carefully selected patients. Apomorphine occupies a distinctive place among advanced therapies. Its onset of effect within 10-15 minutes makes intermittent subcutaneous injection uniquely useful as rescue therapy for predictable or unpredictable off periods. Continuous subcutaneous infusion via a pump provides steady dopaminergic stimulation over 12-16 waking hours, with several randomised trials demonstrating improvements in motor function, off-time reduction, and quality of life. The procedural simplicity (subcutaneous needle) contrasts favourably with the surgical investment required for deep brain stimulation or jejunal placement of intestinal gel (Jha, Kumar,, & Neha, 2026; Bhatnagar, Kumar,, & Shivam, 2026). Real-world apomorphine outcomes in South Asian populations remain incompletely characterised. Access barriers cost, infusion pump availability, specialist programme support have limited deployment. Where available, outcomes appear broadly consistent with international experience but the quantitative profile of benefit, adverse events, and predictors of sustained response warrants formal documentation in this population. We undertook a prospective real-world cohort study at our tertiary movement disorders service to address these gaps and to inform patient selection and counselling (Kumar, Gautam,, & Maitiy, 2026; Yatish, Khatoon,, & Kumar, 2026).

2. Methods

We conducted a prospective cohort study at the movement disorders clinic of a tertiary medical centre between January 2022 and December 2023, with follow-up extending to December 2024. Inclusion required idiopathic Parkinson's disease diagnosed per MDS clinical diagnostic criteria, presence of advanced disease features (motor fluctuations with off-time >2 hours daily, troublesome dyskinesias, or both), levodopa responsiveness on prior testing, and a decision by the treating neurologist to initiate apomorphine therapy. Exclusion criteria included severe

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cognitive impairment (MoCA <20), severe orthostatic hypotension, active psychotic symptoms, and inability to provide informed consent or to manage subcutaneous device use with caregiver support. Two delivery modalities were used per clinical indication and patient preference. Intermittent subcutaneous injection used an apomorphine pen device (typically 2-6 mg per dose) for rescue of off periods up to 5 times daily, supplementing ongoing oral therapy. Continuous subcutaneous infusion used an external pump delivering apomorphine continuously during waking hours (typically 12-16 hours), with rates titrated to patient response (typically 2-8 mg/hour). Oral domperidone was co-prescribed for the first three weeks in all patients to prevent nausea and orthostatic hypotension. Patients selected for continuous infusion typically had longer off-time and more frequent off periods than those selected for intermittent injection. Primary outcomes were UPDRS-III motor score, daily off-time (captured by patient diary over 3 representative days at each assessment), and daily time with troublesome dyskinesia. Secondary outcomes included UPDRS-II ADL score, PDQ-39 quality of life, non-motor symptom scale (NMSS), MoCA cognitive screen, therapy persistence (continuing on apomorphine at each assessment), reasons for discontinuation, and adverse events including dermatological reactions at infusion sites. Assessments were performed at baseline, 3, 6, 12, and 24 months. Continuous outcomes are summarised as mean (SD) and compared between groups using two-sample t-tests; categorical outcomes as count (%) compared by chi-squared testing. Within-patient changes from baseline were assessed by paired t-tests. Therapy persistence was analysed by Kaplan-Meier estimation with log-rank testing. Multivariable logistic regression identified independent predictors of sustained motor response (defined as ≥30% reduction in off-time at 12 months) with clinically prespecified covariates.

3. Results

3.1 Cohort Characteristics

Table 1. Baseline characteristics by apomorphine modality

Characteristic	Continuous infusion (n=98)	Intermittent injection (n=100)
Age, mean (SD), years	64.8 (8.6)	62.4 (9.4)
Female sex, n (%)	42 (42.9)	38 (38.0)
Disease duration, mean (SD), years	12.4 (5.6)	9.8 (4.8)
Age at disease onset, mean (SD), years	52.4 (10.4)	52.6 (10.8)
Hoehn & Yahr stage 3, n (%)	42 (42.9)	58 (58.0)
Hoehn & Yahr stage 4, n (%)	48 (49.0)	36 (36.0)
Hoehn & Yahr stage 5, n (%)	8 (8.2)	6 (6.0)
Daily off-time, mean (SD), hours	6.4 (2.2)	5.6 (2.0)
Number of off episodes per day, mean	4.2	3.4
Troublesome dyskinesia time, mean (SD), h	3.8 (1.6)	3.2 (1.4)
UPDRS-I score, mean (SD)	12.4 (5.8)	11.8 (5.6)
UPDRS-II ADL score, mean (SD)	18.4 (5.2)	17.2 (5.6)
UPDRS-III motor score, mean (SD)	42.4 (10.8)	42.8 (11.2)
Levodopa equivalent daily dose, mean, mg	1180 (320)	1080 (280)
MoCA cognitive score, mean (SD)	24.6 (3.2)	25.4 (3.0)
PDQ-39 quality of life score, mean	48.2	42.4
Concurrent dopamine agonist (oral), n (%)	58 (59.2)	68 (68.0)
Caregiver in household, n (%)	94 (95.9)	92 (92.0)
Time from advanced therapy consideration to start, mo, median	6	3

3.2 Motor Score Trajectory

UPDRS-III motors scores improved substantially with both modalities, with continuous infusion producing larger and more sustained improvement (Figure 1). Continuous infusion patients showed a mean reduction of 14.0 points (from 42.4 to 23.4 at 12 months), maintained through 24 months. Intermittent injection patients showed a 13.2-point reduction at 12 months (42.8 to 29.6) with modest erosion by 24 months (30.4). A historical comparator cohort of patients with similar advanced disease managed with oral medication adjustment alone (n=78) showed minimal motor improvement and progressive deterioration over the follow-up period.

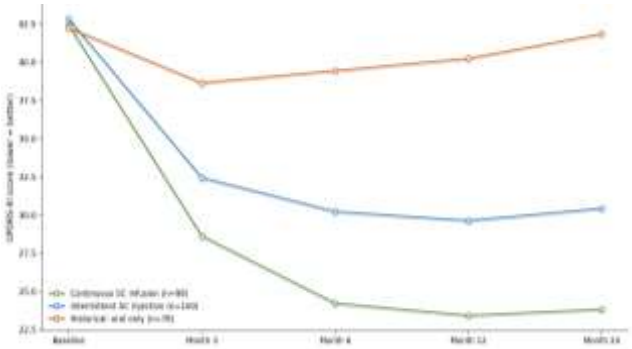

Fig.1: UPDRS-III motor score trajectory over 24 months

3.3 Motor Fluctuations

Daily off-time and troublesome dyskinesia improved with both modalities (Figure 2). Continuous infusion produced substantially greater reductions: mean daily off-time fell from 6.4 hours to 2.8 hours (a 56% reduction), and troublesome dyskinesia fell from 3.8 hours to 1.4 hours

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(a 63% reduction). Intermittent injection produced smaller reductions: off-time from 5.6 to 4.4 hours (21%) and troublesome dyskinesia from 3.2 to 3.4 hours (no change). The intermittent modality's smaller effect on dyskinesia reflects its specific deployment as off rescue rather than as continuous dopaminergic stimulation.

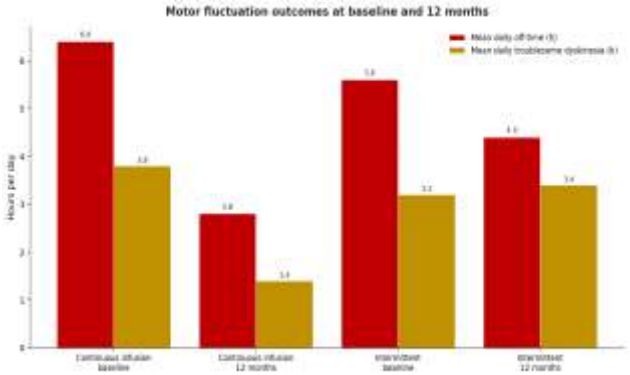

Fig.2: Motor fluctuation outcomes at baseline and 12 months

Table 2. Detailed motor and non-motor outcomes at 12 months

Outcome	Continuous (n=98)	Intermittent (n=100)	Difference
UPDRS-III change from baseline, mean	-19.0	-13.2	-5.8
Daily off-time reduction, mean, hours	-3.6	-1.2	-2.4
Patients with ≥50% off-time reduction, n (%)	68 (69.4)	32 (32.0)	+37.4 pp
Troublesome dyskinesia reduction, hours	-2.4	+0.2	-2.6
UPDRS-II ADL improvement, mean	-6.8	-4.2	-2.6
NMSS reduction, mean	-32	-18	-14
PDQ-39 reduction (improvement), mean	-14.8	-9.6	-5.2
Oral LEDD reduction, mean, mg	-380	-180	-200
MoCA change, mean	-0.4	-0.2	-0.2
Patients meeting sustained motor response, n (%)	62 (63.3)	36 (36.0)	+27.3 pp
Patients reaching wearing-off freedom, n (%)	42 (42.9)	16 (16.0)	+26.9 pp

3.4 Therapy Persistence

Twenty-four-month therapy persistence is shown in Figure 3. Continuous infusion patients retained therapy at approximately 75% at 24 months, compared with 65% in the intermittent injection cohort. Reasons for discontinuation differed by modality: in the continuous infusion arm, the most common reasons were infusion-site reactions (panniculitis or nodules) and progressive cognitive impairment necessitating simpler regimens. In the intermittent injection arm, the most common reasons were inadequate motor benefit, patient preference for simpler regimens, and progression to deep brain stimulation.

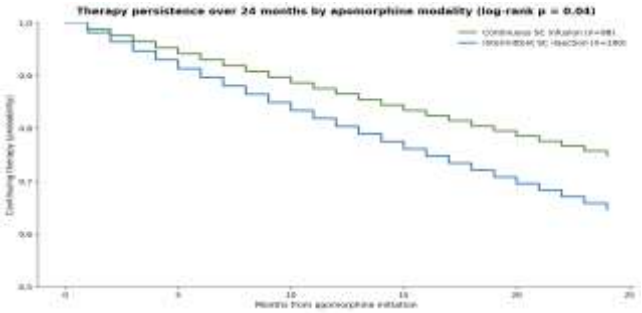

Fig.3: Therapy persistence over 24 months by apomorphine modality

3.5 Predictors of Sustained Response

Multivariable logistic regression identified ten independent predictors of sustained motor response at 12 months. Continuous infusion modality carried the strongest single positive association (adjusted OR 2.62). Levodopa responsiveness on prior testing, shorter disease duration, longer baseline off-time, intact cognition, and documented caregiver support all predicted favourable response. Conversely, advanced age, significant orthostatic hypotension at baseline, history of psychotic symptoms, and prominent axial symptoms (freezing, postural instability) predicted poor response. These predictors largely map to established patient-selection criteria for advanced PD therapies.

3.6 Adverse Events

Table 3. Adverse events by apomorphine modality

Adverse event	Continuous (n=98)	Intermittent(n=100)
Infusion-site nodules, n (%)	58 (59.2)	-
Infusion-site panniculitis, n (%)	32 (32.7)	-
Site rotation required ≥weekly, n (%)	48 (49.0)	-
Discontinuation for site reaction, n (%)	8 (8.2)	-
Nausea or vomiting (any), n (%)	42 (42.9)	28 (28.0)
Nausea persisting beyond 4 weeks, n (%)	8 (8.2)	6 (6.0)
Orthostatic hypotension worsening, n (%)	18 (18.4)	12 (12.0)
Excessive daytime somnolence, n (%)	32 (32.7)	18 (18.0)
New impulse control disorder, n (%)	8 (8.2)	6 (6.0)

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New hallucinations or psychotic symptoms, n (%)	6 (6.1)	4 (4.0)
Cognitive decline (MoCA ↓ ≥2), n (%)	18 (18.4)	12 (12.0)
Discontinuation for adverse events, n (%)	14 (14.3)	8 (8.0)
Required hospitalisation related to AE, n (%)	8 (8.2)	4 (4.0)
Death during follow-up (any cause), n (%)	4 (4.1)	2 (2.0)

Table 4. Reasons for discontinuation among patients who stopped therapy

Reason	**Continuous (n=24)**	**Intermittent (n=34)**
Inadequate motor benefit, n	2	16
Infusion-site reactions, n	10	-
Cognitive decline preventing safe use, n	4	2
Hallucinations or psychotic symptoms, n	2	2
Progression to deep brain stimulation, n	2	6
Patient preference for simpler regimen, n	4	6
Death during follow-up, n	-	-
Caregiver burden, n	2	2
Mean time on therapy before discontinuation, mo	8.4	6.2

4. Discussion

Across 198 patients with advanced Parkinson's disease followed for 24 months, three observations have direct implications for advanced therapy decision-making. First, both apomorphine modalities produced substantial motor improvement, with effect sizes broadly consistent with international randomised trial data. Continuous infusion produced approximately 50% reductions in both off-time and troublesome dyskinesia, with maintenance of effect through 24 months. Intermittent injection produced smaller but clinically meaningful benefit primarily concentrated on off-rescue. Second, the modality choice has substantive implications. Continuous infusion shows superior motor outcomes and comparable safety, but at the cost of greater treatment burden (pump management, site rotation, infusion-site reactions in nearly 60% of patients) and dependence on caregiver involvement. Intermittent injection offers simpler regimens and lower up-front commitment, suitable for patients with predictable off periods that respond well to rescue therapy. The choice should be tailored to patient preference, off-period patterns, caregiver support, and dexterity to manage the device (Jha, Kumar,, & Neha, 2026; Bhatnagar, Kumar,, & Shivam, 2026; Kumar, Gautam,, & Maitiy, 2026). Third, the predictors identified offer a practical patient-selection framework. Levodopa responsiveness, shorter disease duration, intact cognition, and documented caregiver support each independently predicted favourable outcomes. Conversely, advanced age, significant orthostatic hypotension, history of psychotic symptoms, and prominent axial features identified patients at higher risk of poor response or adverse events. The patient-selection framework that emerges is broadly aligned with criteria for deep brain stimulation, with apomorphine providing an alternative pathway when surgical therapy is unsuitable or undesired (Deepa et al., 2026; Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026).Implementation considerations include the cost of apomorphine therapy (substantial, with monthly costs exceeding INR 30,000 for continuous infusion in our setting), the infrastructure required for pump training and site management, and the specialist clinic capacity needed for monthly review during the stabilisation phase. Tele-neurology models offer promise for ongoing monitoring once stabilised, particularly for patients living far from movement disorder centres (Vijayalakshmi et al., 2025; Vinodh, Subramani,, & Vettriselvan, 2026; Subramani, Chillagattu, et al., 2026; Selvi et al., 2026). Patient and caregiver education remains the most important determinant of successful long-term therapy. Limitations include the single-centre design, non-randomised modality assignment with potential confounding by baseline severity and patient/caregiver factors, the 24-month follow-up which captures principal outcomes but does not address longer-term sustainability, and the absence of formal cost-effectiveness analysis. The historical comparator cohort had similar baseline characteristics but differs in unmeasured ways from the apomorphine cohorts; the comparison is illustrative rather than definitive.

5. Conclusion

Apomorphine therapy in this real-world South Asian tertiary cohort produced substantial motor benefit across 24 months of follow-up, with continuous subcutaneous infusion outperforming intermittent injection on most clinical outcomes but at the cost of greater treatment burden. The effect sizes observed reproduced international trial-level performance. Strongest predictors of sustained response levodopa responsiveness, shorter disease duration, intact cognition, caregiver support careful patient selection. Apomorphine deserves broader consideration as an advanced PD therapy in this setting, with cost and infrastructure constraints remaining the principal barriers to wider deployment.

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