LETTER TO THE EDITOR

To The Editor

Does Apomorphine Have an Effect on Body Weight? An Observational Study

Keywords: Apomorphine, Parkinson's disease, Continuous dopaminergic therapy, Body weight

Weight and nutritional changes are one of the core features in neurodegenerative disorders due to various pathophysiological mechanisms.[1] Weight changes in Parkinson's Disease (PD) have been attributed to both pathophysiological changes and therapeutic interventions.[2–4] Apomorphine, a potent dopamine agonist, is currently one of the standards of care for continuous dopaminergic therapies in patients with motor fluctuations. Till date, apomorphine's specific effects on body weight are sparsely addressed.[5–8] We present our observations of body weight in PD patients on continuous apomorphine pump therapy (APT).

After approval from the Institute Ethics Review Board, records of PD subjects who were on APT for at least 3 months were included. Clinical data regarding their demographic, clinical profile, medications, and weight were collected from a retrospective review of clinical record forms. A prospective semi-structured interview was conducted to understand various factors that could have played role in weight changes including change in appetite preferences, dyskinesias, physical activity levels, and other medical conditions after obtaining written consents. The weight changes in these subjects were classified as: (a) no change (up to 1 kg), (b) mild (1.1–5 kg), (c) moderate (5.1–10 kg), and (d) severe (>10.1 kg).

Twelve subjects (M:F = 4:8, mean age: 61 years) with a mean PD duration of 10.7 ± 2.7 years met inclusion criteria. They were on APT for 5.7 ± 2.7 months (range: 3–10 months). Among these, 10/12 (83%) subjects had body weight changes (weight loss – 7, weight gain – 3, and no change – 2). This change ranged from a loss of 12 kg to a gain of 5 kg (mean loss of −2.2 ± 5.1 kg) (Table 1).

Seven patients (M:F = 2:5, mean age: 57 years) had weight loss. They were on APT for 5.8 ± 2.4 months (range: 3–10 months). Among these, four were in mild category, two in moderate category (6 and 9 kg), and one in severe category (12 + kg) (Table 1). The semi-structured interview indicated loss of appetite in four and increased appetite in two. Mild nausea was noted in two patients and was managed with domperidone. No vomiting or other medical comorbidities were noted in this group during the assessment periods. 5/7 had dyskinesia, and among them, one had significant dyskinesia (Table 2). Two subjects discontinued pump therapy at 4th and 8th month. Reasons included significant weight loss in one and lack of social support for the other.

Three patients had weight gain (M:F = 0:3, mean age: 65 years). They were on APT for 5.6 ± 3.0 months (range: 3–9 months). All of them were in mild category (3, 4, and 5 kg, respectively). In this category, one patient (+5 kg) discontinued the therapy after 9 months. She had been diagnosed to have tuberculosis at the time of initiation of the apomorphine therapy with significant weight loss in preceding months. The weight gain could have been part of her response to tubercular treatment.

No significant weight changes were noted in two patients (M:F = 2:0) who were on APT for 6.5 ± 4.9 months (3–10 months). The whole cohort had a total cumulative weight loss of 27 kg (total weight loss = −39 kg; total weight gain = +12 kg). The weight loss category was more significantly affected group and had more concerns about the continuation of therapy.

The body weight changes in PD have been attributed to various factors involving increased energy metabolism, impaired homeostatic regulation of energy metabolism, impact of dopaminergic therapies, impairment of gastrointestinal function, impulse control disorders (ICDs), and other comorbid factors.[2] In one of the early documentations on the effect of dopaminergic therapies and body weight, *Vardi et al.* (1976) reported that patients treated with higher dosages of levodopa and elder age groups tend to have considerable weight loss.[9] A subsequent long-term assessment of initiating pramipexole versus levodopa in PD, involving 301 subjects over 6 years, no specific comments were provided about the effect of these medications on weight.[10] *Wills et al.* (2017) conducted an exploratory secondary analysis of 1619 PD patients to check the weight loss in treated cohorts. They noted that weight loss was significant in levodopa-treated patients as compared to dopamine agonists during the initial year. It was also noted that the weight loss linearly correlated with increasing levodopa dosages.[11]

Continuous dopaminergic therapies involving Levodopa–Carbidopa Intestinal Gel (LCIG), apomorphine pumps, and deep brain stimulation (DBS) are currently the mainstreams of treatment in PD. Data on these therapies in relation to body weight are more robustly available only for DBS. DBS surgery for PD has been associated with an increase in overall body weight gain. In a systematic review (n = 979), it was noted that body weight increased across the studies to a mean value of 5.71 kg and was higher with longer duration of follow-ups.[12] The literature is sparse in relation to pharmacological interventions including LCIG and apomorphine pumps. *Fabbri et al.* (2019), in their analysis, noted 30/44 patients of PD who were on LCIG, noted an average weight loss of 9.9% ± 10.5% (7.6 ± 7.1 kg) over a period of 51.6 ± 28.5 months of therapy. The reasons attributed were multifactorial including dyskinesia, disease severity, dysphagia, feeding difficulties, dosage of dopaminergic therapies, worsening of preexisting peripheral neuropathy, and possible interactions between LCIG and small intestinal bacterial growth.[13] However, data in relation to APT and weight are almost nonexistent. The robust data on APT are currently available through the Euroinf studies.[6,7] These are the studies where all continuous dopaminergic therapies have been compared head-to-head including APT, LCIG, and DBS. The information on weight changes is available only in relation to Non-Motor Symptoms Scale (NMSS). In the NMSS, the weight question forms part of the miscellaneous domain (Q29) and does not quantify whether the weight change was in relation to gain or loss. In the Euroinf 2 study, a post hoc analysis of NMSS showed significant weight change in the apomorphine pump group and the same was not noted in the

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Table 1: Clinical and demographic profile of PD patients on apomorphine pump therapies

Subject	Gender	Age (years)	Duration of PD (years)	Weight (kg)					Final weight change (kg)	Apomorphine dosage (cumulative/day)	Total duration of pump therapy (months)	Current pump status
				Baseline	1 m	3 m	6 m	9 m				
Weight loss												
1	Male	52	10	46	40	38	34	–	−12	7 mg/hr (90 mg)	6	Discontinued
2	Female	43	11	64	61	57	55	53	−9	3 mg/hr (45 mg)	10	In use
3	Female	54	8	66	65	62	60	–	−6	6 mg/hr (90 mg)	7	In use
4	Male	64	20	65	63	63	–	–	−2	3 mg/hr (45 mg)	3	Discontinued
5	Female	75	12	57	55	55	–	–	−2	5 mg/hr (90 mg)	4	In use
6	Female	60	10	79	78	77	–	–	−3	3 mg/hr (45 mg)	4	In use
7	Female	54	9	60	59	55	–	–	−5	3.4 mg/hr (45 mg)	5	In use
Weight gain												
8	Female	65	7	65	66	68	–	–	+ 3	3 mg/hr (45 mg)	5	In use
9	Female	67	4	66	68	70.4	–	–	+ 4	3 mg/hr (45 mg)	3	In use
10	Female	64	19	46	47	50	50	51	+5	3.2 mg/hr (45 mg)	9	Discontinued
No change												
11	Male	66	8	70	70	71	70	–	0	5 mg/hr (90 mg)	10	In use
12	Male	68	10	58	58	58	–	–	0	5 mg/hr (90 mg)	3	In use

Table 2: Semi-structured interview analysis for possible factors affecting body weight

Subject	Appetite change	Food pattern change	Exercise pattern change	Nausea	Vomiting	Dyskinesia	Other factors contributing to weight changes	Non-PD medication changes	Other medical issues developed during this period
Weight loss									
1	Decreased	Yes	No change	Yes (+)	No	Yes (+++)	No	No	No
2	Increased	Yes	No change	No	No	Yes (+)	No	No	No
3	Decreased	Yes	Reduced	No	No	Yes (++)	No	No	No
4	No change	No	No change	Yes (+)	No	No	No	No	No
5	Decreased	No	No change	No	No	Yes (+)	No	No	No
6	Decreased	No	No change	No	No	No	No	No	No
7	Increased	Yes	Increased	No	No	Yes (+)	No	No	No
Weight gain									
8	No change	No	Increased	Yes (+)	No	No	No	No	No
9	No change	No	No change	No	No	No	No	No	No
10	No change	No	No change	No	No	Yes (++)	Tuberculosis	Yes	Tuberculosis
No changes									
11	No change	No	No change	No	No	Yes (+)	No	No	No
12	Increased	No	No change	No	No	No	No	No	No

+=Mild; ++=Moderate; +++=Severe.

LCIG and subthalamic nucleus-DBS groups.[7] Whether this significant change was due to weight gain or loss was not discussed. ICDs could be another important factor affecting the weight. It is well known that impulsivity has an effect on body weight[14] and dopamine agonists are known to induce ICD. Apomorphine being a potent dopamine agonist, it needs to be closely monitored for ICDs. None of our subjects showed features of ICD during this period.

We do acknowledge that the small cohort size and short duration of follow-up are limiting factors of the study. Our paper on APT gives an overview of the effect of apomorphine on the body weight. It is clear that apomorphine does have an effect on body weight; however, swing has been on either directions with brunt on the weight loss. It was noted that about 58% of patients (n = 7) had weight loss following initiation of apomorphine and about 25% had weight gain (n = 3). The cumulative changes in our group were a negative 27 kg loss. It was also noted that in regard to the management of APT, patients with weight loss had more concerns for the continuation of therapy as against those who had gained weight. Weight gains were milder in nature as against weight loss. The factors playing a role in weight gain and weight loss could be different in APT, which needs to be elucidated further. Weight loss is more deterrent for the continuation of a therapy as against weight gain. A more judicial clinical observation, tracking of ICD, monitoring of weight, appetite, and calorie expenses should also be a part of standard monitoring of continuous dopaminergic therapies. This would also help in long-term compliance of the therapy and better quality of life.

Conflict of Interest

The authors have no conflicts of interest to declare.

Statement of Authorship

Research project conception: PLK, SK, JR, RS, and RBI; organization: PLK, DKHS, and SK; execution: PLK, DKHS, and SK; statistical analysis: PLK; manuscript preparation: PLK; Manuscript review and critique: PLK, JR, RS, and 3B.

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