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Effects of liraglutide in the treatment of severe obesity in a young patient with Parkinson's disease

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Abstract

Possible neuroprotective properties of Exenatide (a GLP-1 analog) have been described in patients with Parkinson's Disease (PD). In PD patients treated with Exenatide was reported not only significant improvement in motor performance, but also significant reduction in body weight, raising the issue of whether the improvement in motor performance was to be ascribed exclusively to treatment with Exenatide or whether it was also induced by body weight loss. We therefore decided to monitor a severely obese, young female PD patient on treatment with Liraglutide (GLP-1 analog used for the treatment of obesity in compliance with the relevant guidelines) for 6 months, to assess the effects of body weight loss both on efficacy of pharmacological treatment and on PD symptoms. The overall body weight loss of about 30 kg enabled improvement in the efficacy of medical treatment with levodopa, supported by the improvement in motor score and by the greater absorption of levodopa during the tests performed after body weight loss. Further studies are required to establish whether levodopa absorption is improved only by body weight loss or whether the GLP-1 analog can exert positive pharmacodynamic or pharmacokinetic effects

Case report

Possible neuroprotective properties of Exenatide (a GLP-1 analog) have been described in patients with Parkinson's Disease (PD) in The Lancet in 2017 [1]. In the group of PD patients treated with Exenatide the investigators reported not only significant improvement in motor performance, but also significant reduction in body weight. These findings raise the issue of whether the improvement in motor performance was to be ascribed exclusively to treatment with Exenatide or whether it was also induced by body weight loss. When PD is associated with obesity important complications may occur: dietary interference with levodopa absorption [2]; increase in levodopa requirements [3]; worsening of motor performance due to excessive body weight. We therefore decided to monitor a severely obese, young female PD patient on treatment with Liraglutide (GLP-1 analog used for the treatment of obesity in compliance with the relevant guidelines) [4] for 6 months, to assess the effects of body weight loss both on efficacy of pharmacological treatment and on PD signs and symptoms. The history of the patient is summarized in Figure 1.

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The patient (female, Italian, 43 years old) presented for the first time in October 2017. The onset of PD had occurred in March 2017 (at the age of 42 years) with resting tremor of the left upper limb and hyposmia. The diagnosis was confirmed by positive Datscan scintigraphy. She was on treatment with pramipexole PR 1 mg and weighed 138 mg (class III obesity-BMI 47 kg/m2).

She reported that she had been obese since childhood and that her obesity was resistant to all kinds of dietary and medical treatment. She had gained 7 kg since the diagnosis of PD and introduction of pramipexole. Weight gain may occur in patients on treatment with dopamine agonists, mainly on account of compulsive hunger [3]. We recommended an increase in anti-Parkinson pharmacological treatment (combining pramipexole with 400 mg levodopa in combination with benserazide daily), a low-calorie diet (1,600 kcal daily) with protein redistribution (0.9 g protein/kg ideal body weight) to optimize levodopa absorption [3] and increase in daily exercise to 10,000 steps daily.

January 2018: Partial improvement in resting tremor. Hematological and biochemical tests were within the normal range (blood sugar, lipid profile, thyroid, liver and renal function, CBC + differential). Body weight was unchanged. Poor compliance to recommended dietary and exercise regimen. Basal metabolic rate measured by indirect calorimetry (Fitmate, Cosmed): 2078 kcal (98% of predicted). Body composition (bioimpedentiometry): 67 kg fat body mass, 71 kg lean body mass. Liraglutide (0.6 mg daily for one week, then 1.2 mg daily) was introduced to assess its efficacy both on body weight and motor performance. Liraglutide was used according to obesity management guidelines. It is not contraindicated in PD and is generally well tolerated.

February 2018: Hospital stay for one week. Body weight down to 129 kg, body weight loss amounted to 9 kg (-7% body weight), BMI 44.2 kg/m2. 6,000 steps daily. The patient reported satiety. Plasma dopa level was measured to assess levodopa absorption (AUC 119 ug/ml * min) and the Levodopa Test was carried out to assess the efficacy of therapy using UPDRS scale scores (this is the international validated scale for the assessment of PD symptoms - 5). The levodopa test disclosed 20% motor improvement after ingestion of the drug. Recommendations: no change in anti-Parkinson treatment, increase in Liraglutide dosage regimen to 1.8 mg daily.

March 2018: Body weight 126 kg, body weight loss amounted to 12 kg (- 9% body weight), BMI 42 kg/m2. She did not tolerate Liraglutide 1.8 mg. Its daily dose was reduced to 1.2 mg on account of nausea

April 2018: Body weight 122 kg, - 16 kg since beginning of treatment (- 11.7% body weight), BMI 41 kg/m2. 8,000 steps daily. Body composition (bioimpedentiometry): 57 kg fat body mass (- 14,6% initial fat body mass), 65 kg lean body mass. The recommendation was to continue alternating 1.2 mg with 1.8 mg daily Liraglutide i.e. taking 1.8 mg every other day.

June 2018: Admittance to day hospital to reassess plasma dopa levels and levodopa absorption kinetics after body weight loss (AUC increased up to 235 ug/ml * min) (Figure 2). The Levodopa Test was also repeated: motor improvement in response to the drug increased from 20% to 70% (levodopa efficacy improvement by 35%) (Figure 2). Excellent compliance to low-calorie diet alternating Liraglutide daily dose (1.2/1.8 mg) i.e. taking 1.8 mg every other day. She continued to walk 8,000 steps daily. Body weight 116 kg, -22 kg since beginning of treatment (-16% body weight), BMI 39 kg/m2 (shift from class III to class II obesity).

August 2018: Body weight 109 kg, -29 kg since beginning of therapy (-21% initial body weight), BMI 37.2. Bioimpedentiometry was repeated: 49.5 kg fat body mass (-25.9% initial fat mass), 59.5 kg lean body mass. No change in daily dose of levodopa+benserazide. The decision was taken to reduce pramipexole on account of eating compulsion and to introduce safinamide, which does not have this adverse effect. Motor function control was excellent. The patient reported marked subjective improvement with body weight loss and greater efficacy of levodopa.

Conclusions

Liraglutide has proved to be effective in the treatment of severe obesity responding poorly to dietary treatment alone. The overall body weight loss of about 30 kg (21% initial body weight) enabled improvement in the efficacy of medical treatment with levodopa. This was supported both by the improvement in UPDRS motor score and by the greater absorption of levodopa during the tests performed after body weight loss (Figure 2). In literature, data reported that severe loss of weight may reduce the need for oral levodopa intake by parkinsonian subjects [6]. Moreover, recently has been reported a potential positive effect of Liraglutide on microbiota and on gut permeability in rats and mice [7,8], that might improve levodopa absorption also. Further studies are required to establish whether levodopa absorption is improved only by body weight loss or whether the GLP-1 analog can exert positive pharmacodynamic or pharmacokinetic effects.

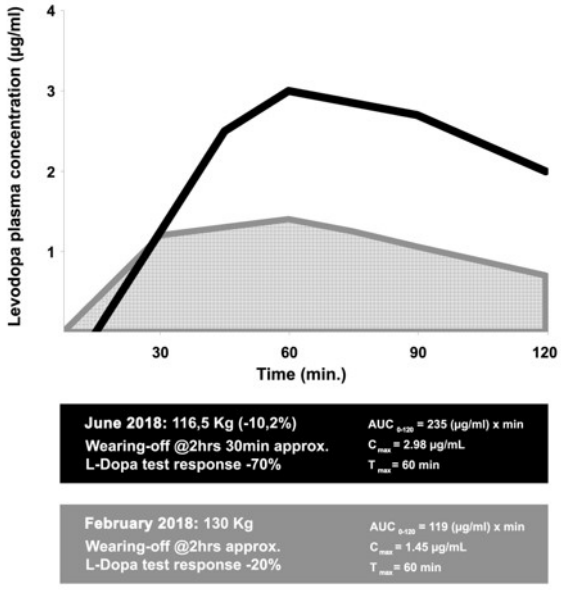

Table display variation of metabolic parameters, diet therapy and pharmacological therapy

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Table 1: The table display variation of metabolic parameters, diet, therapy and pharmacological therapy

Year of visit	2017	2018					
Month of visit	October	January	February	March	April	June	August
WEIGHT kg	138	138	129	126	122	116	109
Δ Weight from 1st visit	-	-	-9kg (-7%)	-12 kg (-9%)	-16 kg (-11.7 %)	-22 kg (-16 %)	- 29 kg (-21%)
BMI kg/m^2 Δ kg/m^2	47 obesity III	47 - obesity III	44.2 (-2.8) obesity III	42 (-5) obesity III	41 (-6) obesity III	39 (-9) obesity II	37.2 (-9.8) obesity II
FM kg (BIA) Δ kg Δ %	-	66.8	-	-	57 (-9.8 kg) (-14.6 %)	-	49.5 (-17.3 kg) (-25.9 %)
DIET Kcal Kjoule	 1600 1690	 1600 1690	 1600 1690	 1600 1690	 1600 1690	 1600 1690	 1600 1690
LIRAGLUTIDE mg	-	1.2	1.8	1.2	1.2/1.8 on alternate day	1.2/1.8 on alternate day	1.2/1.8 on alternate day
CALORIMETRY	-	MB= 2078 Kcal/die	-	-	-	-	-
LEVODOPA/BENSERAZIDE mg	100+25 x 4	100+25 x 2 150+37.5 x 2	150+37.5 x 4	150+37.5 x 4	150+37.5 x 4	150+37.5 x 4	150+37.5 x 4
PRAMIPEXOLE RP	1 mg	1 mg	1 mg	3 mg	3 mg	202 mg	2.2 mg
SAFINAMIDE	-	-	-	-	-	-	50mg
L- DOPA PHARMACOKINEETICS	-	-	done	-	-	done	-

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