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Usefulness of Enteral Nutritional Intake Containing Median-Chain Fatty Acids in Parkinson's Disease Patients with Weight Loss: A Pilot Study

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Abstract

Background: No solution has yet been found for the nutritional issues of Parkinson's disease (PD) patients with weight loss, which affects their prognosis. The objective of the present study was to investigate whether a defined-formula diet rich in $\omega 3$ fatty acids improved nutrition through the effect of ghrelin in PD patients with weight loss. Method: Weight, serum total protein, albumin, lipids, serum ghrelin, serum acylghrelin, leptin, and the Unified Parkinson's Disease Rating Scale were monitored for approximately 3 months in 11 subjects given a defined-formula diet rich in $\omega 3$ fatty acids for 3 months and 5 control subjects who received no such treatment. Results: No significant changes from baseline in serum ghrelin, acylghrelin, and leptin levels were noted after administration of the nutritional product. Meanwhile, compared with the control, changes from baseline in the levels of albumin and weight were significant after the nutritional therapy rich in $\omega 3$ fatty acids ($P < 0.05$). Conclusion: Administration of a medium-chain fatty acid-rich product has few effects on motor functions and activities of daily living in PD patients with weight loss, but it is expected to offer effective ghrelin-mediated nutritional improvement.

Keywords

Parkinson's Disease, Weight Loss, Ghrelin, Leptin

1. Introduction

More than a quarter of the Parkinson's Disease (PD) population was found to be at risk of malnutrition necessitating more attention towards nutritional assess-

ment in PD [1]. Digestion and absorption disorders are suspected in patients with weight loss, but the causes and pathophysiology of weight loss remain poorly understood. Appetite in PD cases may be decreased, unchanged, or even apparently increased. Weight loss, occurring in about half of PD patients [2], has long been a common problem [3] [4] [5] [6]. In recent years, ghrelin has become noted for its applications in the treatment of not only gastrointestinal disorders, but also dementia [7]. Nevertheless, there have been no studies of the role of serum ghrelin-mediated pathophysiology in gastrointestinal dysfunction in PD patients who have lost weight.

High levels of *ω*3 fatty acids have shown anti-inflammatory, immunomodulatory, and anti-dementia effects in humans [8]. Essential fatty acids are not synthesized by the body and must be supplied by the diet. Nutritionally, *ω*3-containing essential fatty acids have become useful nutritional products in terms of energy intake in patients with a chronic progressive disease, and ghrelin is expected to effectively improve nutrition. As such, we hypothesized that the administration of an *ω*3 fatty acid-rich product in PD patients would lead to a good nutritional status through ghrelin, the "hunger hormone," and the effects of the *ω*3 fatty acid product on motor functions and activities of daily living were investigated in PD patients in this study.

2. Material and Methods

2.1. Subjects

The subjects selected met the following criteria: 1) PD patients with an unintended weight loss of 5% or more within 6 to 12 months before study entry; 2) a diagnosis of PD based on the British Brain Bank criteria; 3) undergoing treatment with oral administration of a combination of L-dopa and a dopa decarboxylase inhibitor for 6 consecutive months or longer; 4) ability to personally provide consent to receive the nutritional product; 5) treatment with an anti-PD agent with the same dosage and administration regimen in the 2 weeks before the start of observation; 6) ability to comply with the study schedule.

2.2. Evaluations

An open-label prospective study of Racol®-NF liquid (Otsuka Pharmaceutical Factory, Japan) for enteral use was conducted for 12 weeks, with a control group given regular dietary therapy, in subjects who met the above criteria and who gave consent. The planned duration of study participation was 16 weeks. Daily oral administration of Racol®-NF 400 ml was selected. In patients with poor oral ingestion, nasal or gastric fistula administration was allowed. In principle, the subjects were to continue treatment with an anti-PD agent under the same dosage and administration regimen from the beginning to the end of the treatment period. However, in the event that PD-affected motor symptoms worsened, adjustments of the anti-PD agent were permitted. Upon initiation and after 12th week visit, patients were examined according to the Unified Parkinson's disease

rating scale (UPDRS) [9]. The endpoints were percent change in weight, changes in the scores of the PD clinical assessment scale, and percent changes in levels of serum albumin, serum pre-albumin, serum acylghrelin, serum des-acylghrelin, and leptin. The discontinuation criteria selected for this study were diarrhea, a common adverse drug reaction associated with the administration of Racol®-NF, lasting for 1 month or longer, and absence of improvement in nutritional status with weight loss of 3 kg or more over a 1-month period despite the administration of Racol®-NF.

3. Results

The clinical characteristics of the 11 subjects in the group who received the nutritional product containing ω3 fatty acids and the 5 subjects in the control group are shown in **Table 1**. Concentration-time profiles of serum ghrelin, leptin, and des-acylghrelin levels in the subjects at baseline and after administration of the nutritional product are shown in **Figure 1**. Of the 11 subjects in the group who received the nutritional product, 9 completed the 3-month treatment. The levels of leptin in 5 subjects in the treated group were below the measurement sensitivity both at baseline and after treatment. The level of serum ghrelin showed an increasing trend after treatment with the nutritional product, but the differences were not significant; the levels of des-acylghrelin and leptin also showed no significant changes after the treatment (**Figure 1**). The increase from baseline in weight after 3 months of treatment with the nutritional product was significant compared with the control, but the level of serum pre-albumin remained unchanged. Changes over time in levels of serum albumin, total cholesterol, and serum cholinesterase showed no significant differences within the same group, but the change in serum albumin was significantly greater in the group that received the nutritional product containing ω3 fatty acids than in the control group ($P < 0.05$). No other changes were noted. (UPDRS) scores showed no significant differences from baseline after the intervention in and between the two groups (**Table 2**).

4. Discussion

The present study is unique in that it investigated changes from baseline in the level of ghrelin, nutritional status, and motor functions after treatment with a nutritional product rich in ω3 fatty acids in PD patients with weight loss. The profiles of ghrelin used in the present study provided no evidence of any significant change in the level of either active ghrelin or desacyl-ghrelin, but the group received the nutritional product containing ω3 fatty acids had significant increases in the nutritional indices of body weight and serum albumin compared with the control group. The level of serum acylghrelin showed an increasing trend, even though the differences were not significant, suggesting it may have promoted dietary intake, thereby resulting in weight gain. Dietary counseling for PD patients has been considered to play a major role in maintaining patients'

quality of life [10], but there has been no definitive, evidence-based outcome obtained from a nutritional approach. The results from the present study suggest the potential usefulness of medium-chain fatty acid-rich nutritional products as a nutritional therapy for PD patients with weight loss or cachexia.

Table 1. Demographic information.

	Treatment group (n = 11)	Control (n = 5)	P value
Age	74	58	0.33
Sex (male)	5	4	0.44
Disease duration (years)	8.5	5.8	0.22
Height (cm)	154	166	0.01
Weight (kg)	44	61	0.001
BMI	18.8	21.1	0.009
Hoehn and Yahr stage (on)	3.5	2.4	0.019
UPDRS I	5.4	1.8	0.003
UPDRS II	15.7	6.4	0.001
UPDRS III	25.5	9.8	0.003
UPDRS IV	2.5	1	0.15
MIBG early	1.66	1.60	0.41
MIBG delay	1.43	1.38	0.80
Medication			
Carbidopa-Levodopa (mg)	482	320	
Entacapone (mg)	450 (n = 2)		
Pramipexole hydrochloride hydrate (mg)	1.5 (n = 3)	1.6 (n = 4)	
Ropinirole hydrochloride (mg)	12.2 (n = 6)		
Selegiline hydrochloride (mg)	4.2 (n = 2)	5 (n = 1)	
Amantadine hydrochloride (mg)	130 (n = 2)	100 (n = 1)	
Zonisamide (mg)	25 (n = 3)		

Table 2. Changes in each UPDRS score at baseline and 12th week.

	Treatment group				Control group			
	Baseline	12th week	Rate of variability	P value	Baseline	12th week	Rate of variability	P value
UPDRS I	4.9	4.4	0.10	0.98	1.8	1.8	0	1.0
UPDRS II	14.9	12.5	0.16	0.68	6.4	6.2	0.03	0.32
UPDRS III	22.4	19.9	0.11	0.68	9.8	8.6	0.12	0.18
UPDRS IV	2.9	2.8	0.05	0.046	1.0	0.8	0.2	0.32

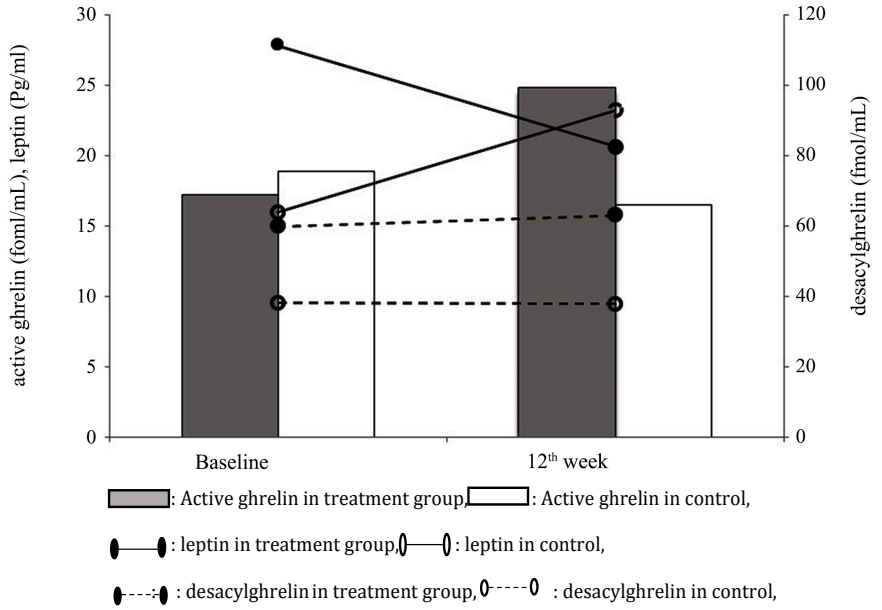

Figure 1. Changes of serum active ghrelin, desacyl-ghrelin, and leptin.

In the present study, the level of serum leptin was below the sensitivity of the assay in a large number of subjects, indicating the causes may include reduced leptin production due to decreased adipose tissue mass in PD patients with cachexia experiencing weight loss. The below-sensitivity levels can also be attributed to the dose load of the medium-chain fatty acid-rich nutritional product, and the level of serum leptin production can be interpreted as an absence of marked improvement in metabolic function.

Studies have long indicated increased energy metabolism [11] or a hypothalamic disorder [12] as the mechanism of weight loss in PD patients. Moreover, long-term L-dopa treatments, β-adrenaline receptor agonist have been reported to show the potential to increase muscle mass and strength and to improve quality of life in patients with Parkinsonism [13] [14] [15], suggesting the presence of diverse mechanisms. Dietary therapies for advanced PD patients with diurnal variations include low-protein and protein-redistribution diets, but they are poorly supported by evidence and may even exacerbate under nutrition due to excessive restriction of protein intake [16]. In the present study, the administration of a medium-chain fatty acid-rich product offered the potential of nutritional improvement via the intragastric-vagal-hypothalamic to central pathways. We expect that further follow-up and other studies of cases with poor appetite will shed more light in the future.

5. Conclusion

The administration of a medium-chain fatty acid-rich product in PD patients with weight loss has few effects on the PD-affected motor functions and activities of daily living, but it is expected to offer an effective ghrelin-mediated nutritional improvement.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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