

PROtein, LEucine And vitamin D Enhancing Rehabilitation (PRO-LEADER) in patients with Parkinson's disease or parkinsonism: a RCT

Emanuele Cereda ^{a*} MD, PhD, Michela Barichella ^{b*} MD, Giovanna Pinelli ^c MD, PhD, Laura Iorio ^d MD, Diana Caroli ^b ScD, Irene Masiero ^b ScD, Valentina Ferri ^b MD, Erica Cassani ^b MD, Carlotta Bolliri ^b ScD, Serena Caronni ^b ScD, Paola Ortelli ^c PsyD, Davide Ferrazzoli ^c MD, Antonios Maras ^d MD, Giulio Riboldazzi ^d MD, Giuseppe Frazzitta ^c MD, Gianni Pezzoli ^b MD

a. Clinical Nutrition and Dietetics Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy.

b. Parkinson Institute, ASST G.Pini-CTO, ex ICP, Milan, Italy.

c. Dipartimento Riabilitazione Malattia di Parkinson e Disturbi del Movimento, Ospedale Classificato Moriggia Pelascini di Gravedona, Gravedona, Italy.

d. U.S. Riabilitazione Parkinson, Fondazione Gaetano e Piera Borghi di Brebbia, Brebbia, Italy.

OBJECTIVES

Physical rehabilitation is an important strategy for treating motor disability in patients with Parkinson's disease (PD) or parkinsonism. Studies in old adults have shown that muscle-targeted nutritional support can positively influence muscle mass and physical performance but no evidence is available in parkinsonian syndrome which are characterized by high rates of muscle dysfunction, particularly muscle weakness. We evaluated the efficacy of a muscle-targeted nutritional support on the functional outcomes of a multidisciplinary intensive rehabilitation treatment (MIRT) in patients with PD or parkinsonism.

METHODS

We conducted a randomized (1:1), controlled trial (NCT03124277) in patients suffering from PD or parkinsonism and undergoing a MIRT. Patients (n=150) (Figure 1) received a standard hospital diet with or without a vitamin D and leucine-enriched whey protein-based nutritional supplement twice daily for 30 days. The primary efficacy end point was the increase in the distance walked during a 6-minute walking test (6MWT). Secondary outcome variables were changes in: gait speed, timed up and go test (TUG), Berg balance scale, handgrip strength, Self-assessment Parkinson's Disease Disability Scale, body weight and skeletal muscle mass (SMM).

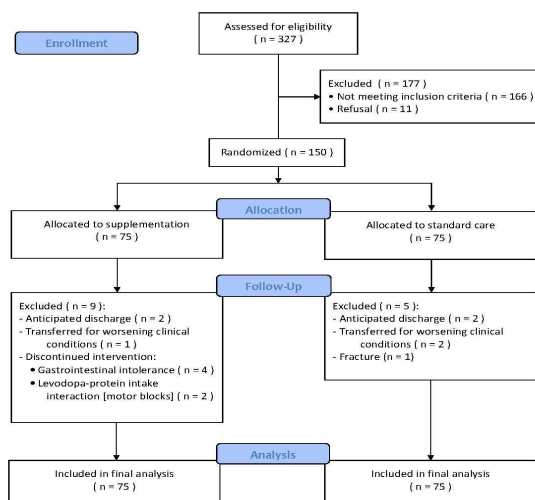


FIGURE 1. Flow diagram of patients identified and included in the study

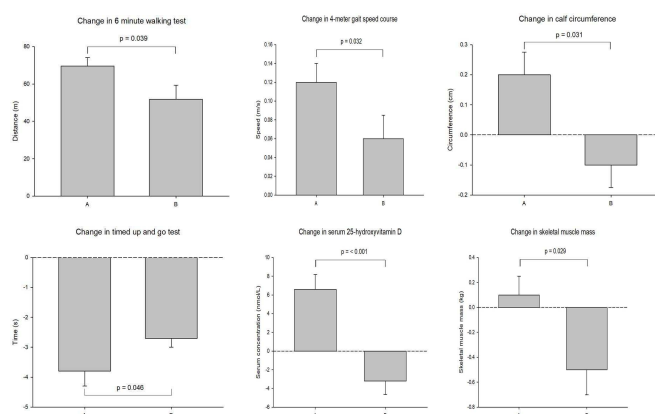
RESULTS

Nutritional support resulted in a greater increase in the distance walked during a 6MWT (mean, 69.6 meters [95%CI, 60.7-78.6]) than no support (51.8 meters [95%CI, 37.0-66.7]): center-adjusted mean difference, 18.1 meters [95%CI, 0.9-35.3] (P=0.039). Further adjustment for changes in dopaminergic therapy and SMM yielded consistent results: mean difference, 18.0 meters [95%CI, 0.7-35.2] (P=0.043). A significant effect was also found for the following secondary end points: 4-meter walking speed (0.07 m/s [95%CI, 0.01-0.13], P=0.032), TUG test (-1.1 s [95%CI, -2.2-0.0], P=0.046), SMM (0.5 kg [95%CI, 0.0-1.0], P=0.029) (Table 1- Figure 2).

ENDPOINTS	SUPPLEMENTED CHANGE* (N=75)	STANDARD CARE CHANGE* (N=75)	TREATMENT EFFECT† DIFFERENCE *	P-VALUE
Primary endpoint				
6-minute walking test distance (m)	69.6 (60.7, 78.6)	51.8 (37.0, 66.7)	18.1 (0.9, 35.3)	0.039
Secondary endpoints				
4-meter gait speed course (m/s)	0.12 (0.09, 0.16)	0.06 (0.01, 0.11)	0.07 (0.01, 0.13)	0.032
Timed up and go test (s)	-3.8 (-4.8, -2.8)	-2.7 (-3.2, -2.1)	-1.1 (-2.2, 0.0)	0.046
Berg balance scale (score)	6.4 (5.4, 7.4)	6.8 (5.7, 7.8)	-0.3 (-1.6, 1.1)	0.69
Handgrip strength (kg)	1.2 (0.3, 2.2)	-0.1 (-1.2, 1.1)	1.3 (-0.1, 2.7)	0.068
SPDDS (score)	-11.6 (-12.5, -10.6)	-12.1 (-13.5, -10.6)	0.5 (-1.1, 2.1)	0.52
Body weight (kg)	-1.3 (-1.9, -0.8)	-1.2 (-1.6, -0.8)	-0.1 (-0.8, 0.6)	0.78
Skeletal muscle mass (kg)	0.1 (-0.3, 0.4)	-0.5 (-0.8, -0.1)	0.5 (0.0, 1.0)	0.029
Skeletal muscle mass index (kg/m ²)	0.03 (-0.09, 0.14)	-0.15 (-0.27, -0.04)	0.18 (0.02, 0.34)	0.029
Post-hoc exploratory endpoints				
UPDRS total score	-14.4 (-15.7, -13.1)	-14.8 (-16.6, -13.1)	0.3 (-1.4, 2.0)	0.76
UPDRS part III score	-7.6 (-8.6, -6.6)	-7.6 (-8.8, -6.4)	-0.2 (-1.2, 0.8)	0.75
Calorie intake (kcal/kg/day)	2.6 (1.5, 3.7)	0.6 (-0.4, 1.6)	2.0 (0.6, 3.4)	0.007
Protein intake (g/kg/day)	0.43 (0.35, 0.51)	0.04 (-0.01, 0.08)	0.39 (0.30, 0.48)	<0.001
Calf circumference (cm)	0.2 (0.0, 0.3)	-0.1 (-0.2, 0.1)	0.2 (0.0, 0.4)	0.031
Serum 25-hydroxyvitamin D (nmol/L)	6.6 (3.4, 9.8)	-3.2 (-6.2, -0.3)	9.8 (5.5, 14.1)	<0.001

TABLE 1. Summary of study results

FIGURE 2. Effects of muscle-targeted nutritional support on the functional outcomes



CONCLUSIONS

In patients with PD or parkinsonism, the consumption of a whey protein-based nutritional formula enriched with essential amino acids and vitamin D improved the efficacy of a MIRT, particularly lower body physical function.

This work was supported by "Fondazione Grigioni per il Morbo di Parkinson" www.parkinson.it and "Brain and Malnutrition in Chronic Diseases Association Onlus" www.bm-association.it