

## ENDOTHELIAL PROGENITOR CELLS: A CARDIOVASCULAR PROTECTIVE FACTOR IN PARKINSON'S DISEASE?

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### BACKGROUND

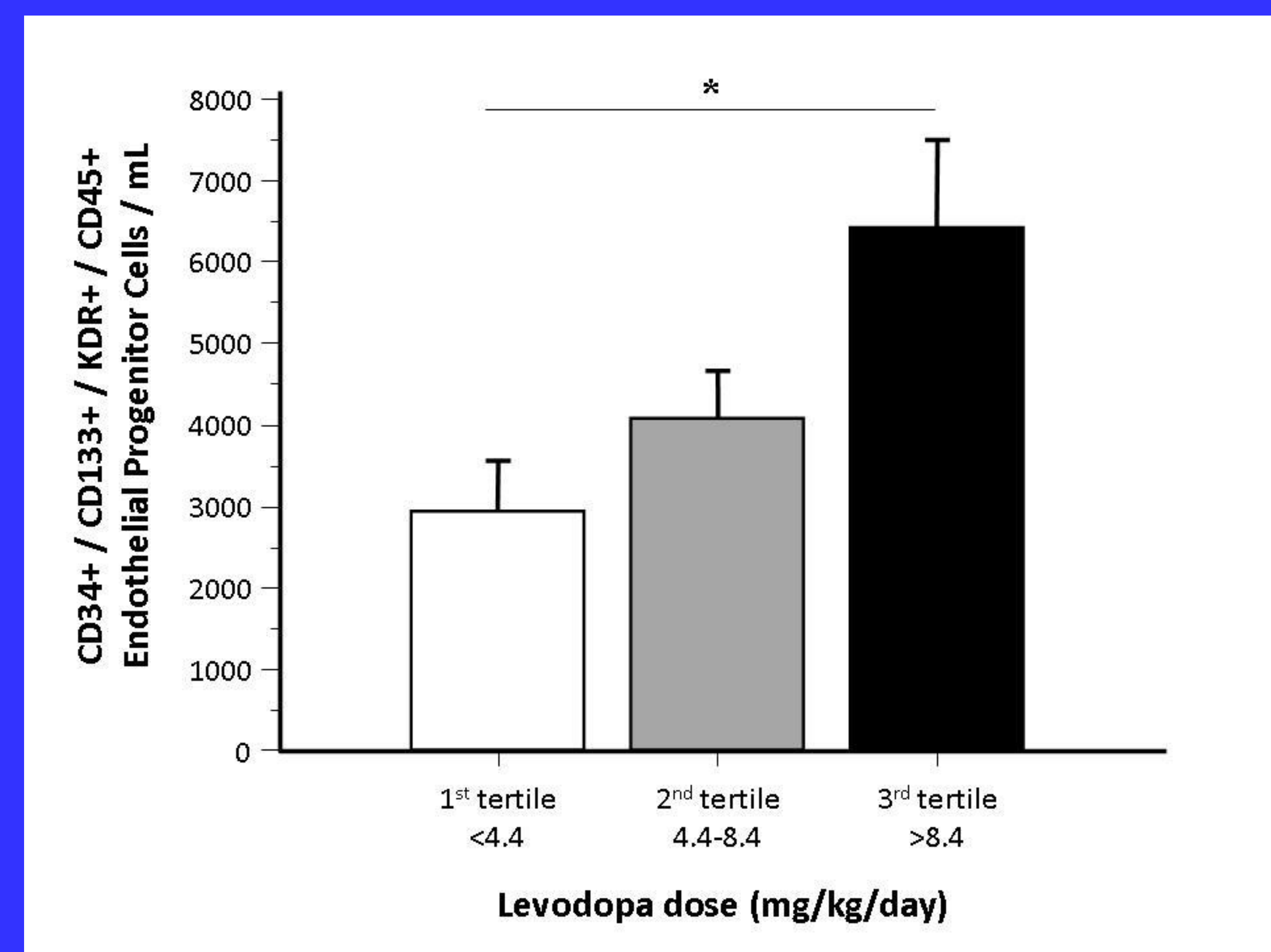
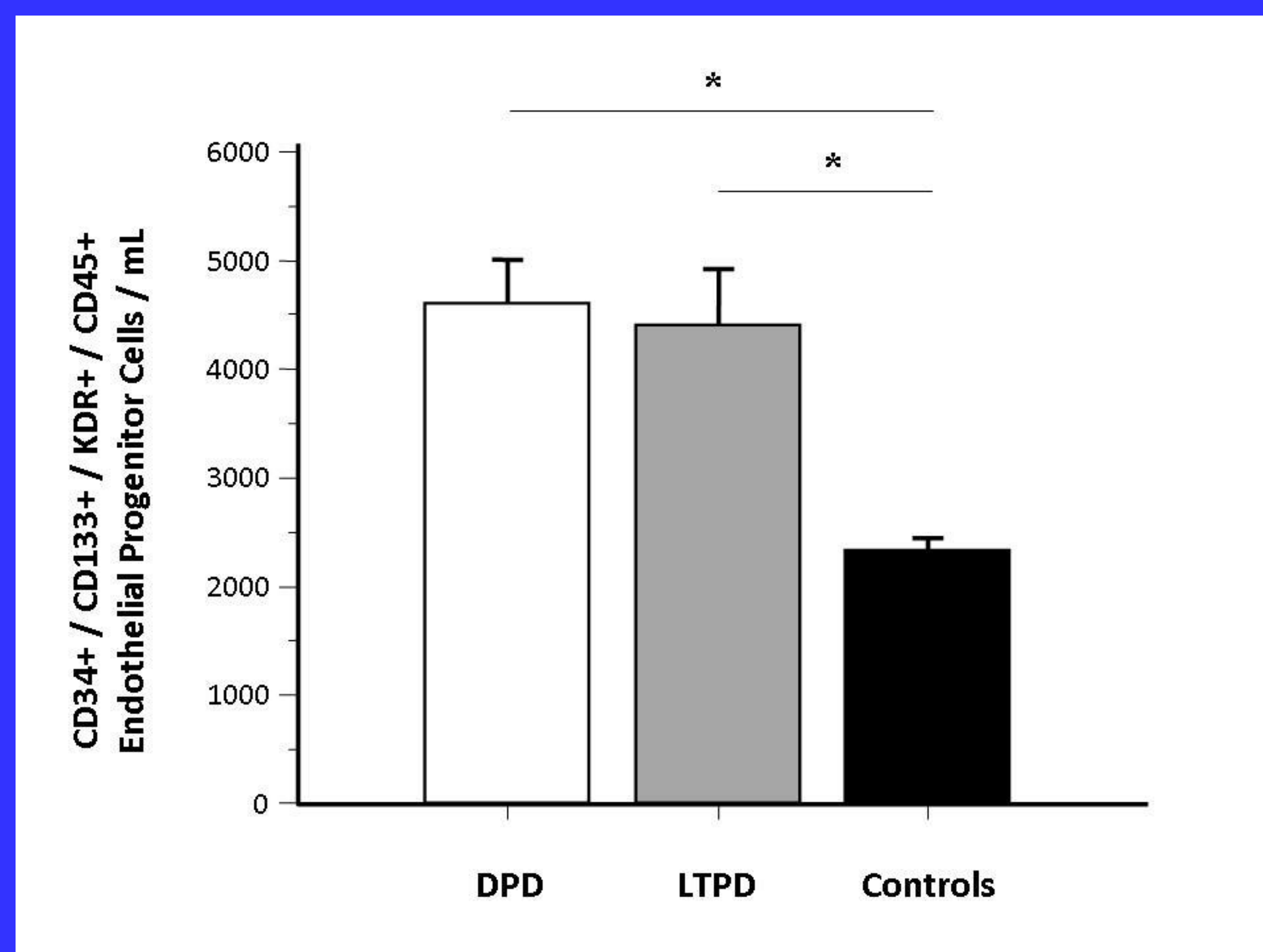
Parkinson's disease (PD) patients have a favourable cardiovascular risk profile. Cardiovascular risk factors are inversely associated with circulating endothelial progenitor cells (EPCs). These cells are involved in the recovery of endothelial integrity, and their function and mobilization from the bone marrow are negatively affected by dopamine.

### OBJECTIVE AND METHODS

To investigate EPC counts in PD and establish whether their count is affected by dopamine-replacement therapy. We studied de novo (DPD; N=27) and levodopa-treated (LTPD; N=27) PD patients and control subjects (N=54) free of comorbidities and matched (1:1:2) by age, gender and body mass index.

### RESULTS

Both DPD and LTPD patients had higher EPC counts than controls ( $P < 0.001$ ). No difference was detected between groups of PD patients. After adjusting for age, gender, total serum cholesterol and protein intake the difference between patients and controls remained significant (DPD,  $P = 0.020$ ; LTPD,  $P = 0.045$ ). High serum cholesterol and protein intake were also significant independent predictors of a reduced number of EPCs. In LTPD patients levodopa dosage (mg/kg/day) was directly associated with circulating EPC counts ( $P = 0.014$ ).



### CONCLUSIONS

PD patients have higher EPC counts than controls, independently of cardiovascular risk profile and dopamine-replacement therapy. A major contributing factor is likely the peripheral sympathetic denervation characterizing these patients. The determinants of circulating EPC counts in PD deserve further investigation. Future studies should address also the functional properties of EPCs in PD. Prospective studies controlling for relevant confounders are required to clarify the role of EPCs as a new marker of cardiovascular disease and risk in PD.

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# DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL OF A FERMENTED MILK CONTAINING MULTIPLE PROBIOTICS STRAINS AND PREBIOTIC FIBER FOR CONSTIPATION ASSOCIATED WITH PARKINSON'S DISEASE: STUDY DESIGN.

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## BACKGROUND



Constipation is the most frequent (prevalence, about 60%) dysautonomic non motor symptom affecting Parkinson's disease (PD) patients.

Unfortunately, limited treatment options have been investigated and are now available for the management of constipation in PD.

Preliminary data have suggested that probiotics could be help improving bowel habits but high-quality randomized trials are required in this area.

## OBJECTIVE

To evaluate whether the use of a fermented milk containing multiple probiotics strains and prebiotic fiber have a beneficial effect on constipation in PD.

## METHODS AND PATIENTS

**We designed a double-blind randomized, controlled trial.**

Table 1 – Rome III criteria for defining chronic functional constipation in adults

Adults
Diagnostic criteria*
1. Must include two or more of the following:
a. Straining during at least 25% of defecations
b. Lumpy or hard stools in at least 25% of defecations
c. Sensation of incomplete evacuation for at least 25% of defecations
d. Sensation of anorectal obstruction/blockage for at least 25% of defecations
e. Manual manoeuvres to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)
f. Fewer than three defecations per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome
* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis



After a 2-week run-in phase to confirm diagnosis of constipation according to Rome III criteria, PD patients will be randomized (2:1) to receive daily (at breakfast) a fermented milk (125 grams), containing multiple probiotics strains and prebiotic fiber, or placebo (pasteurized fermented milk without prebiotics) for 4 weeks.

Patients will be allowed continuing the use of anticonstipation medications but also advised to limit it as much as possible.

**The primary efficacy end point will be the increase in the number of complete spontaneous bowel movements (CSBMs) per week.**

**A**

Fermented milk

Probiotics

Prebiotic fiber

**B**

Placebo

Day	1	2	3	4	5	6	7
1	x						
2		x					
3							
4			xx				
5							
6			x				
7	xx						

Day	1	2	3	4	5	6	7
1	x						
2		x					
3							
4			xx				
5							
6			x				
7	xx						

## RESULTS

Using internal unpublished data, we calculated that for a p value of 0.05 and for a power of 0.9, 120 total patients (80+40) would be required to show a difference in the frequency of CSBMs between case patients (3.4±2.2 per week) and control subjects (2.2±1.7 per week) based on stool diaries.

## CONCLUSIONS

**Positive data from this trial would offer an effective adjuvant treatment options for constipation in PD.**



# SIMPLE AND LOW-COST MUCUNA PRURIENS PREPARATION FOR PARKINSON'S DISEASE PATIENTS IN LOW-INCOME COUNTRIES

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## BACKGROUND

In low income areas, such as Africa, most Parkinson's disease (PD) patients cannot afford pharmacological therapy : levodopa costs on average 1.5\$ daily and the average monthly wage is approx. 60\$ a month.

A therapeutic option for them is the use of a legume called *Mucuna Pruriens* var. *Utilis* (MP), which has seeds with a high levodopa content (5-6%). Seeds may be black, white or mottled. MP grows in South America, Africa and Asia.

## OBJECTIVE

Our objective is to develop a safe, simple, low-cost method for MP seed preparation. Furthermore, to quantify the dose of MP required to treat PD patients



## METHODS



We collected 29 different kinds of MP seeds, from Africa and Latin America. We measured the content in levodopa in the dried seeds and the change in levodopa content after cooking (roasting). The cooking method involves:



Roasting in a pan for 15 min. Waiting for all the teguments to burst (the noise resembles popcorn bursting)



Removing from the fire and hulling



The roasted seeds are ground in a little coffee grinder, passed through a sieve and added to water as a powder.



Then, the physician can calculate the quantity of levodopa required for each patient, weigh the corresponding dose of roasted powder, disperse it in water and administer it to patients.

## RESULTS

1

- The mean levodopa concentration in dried seeds is 5.1%.

2

- Roasting does not significantly reduce the content in levodopa (still about 5%).

3

- In the tropics the cost of the roasted powder prepared at home is negligible

4

- The roasted powder is easy to take and to store

**A 100+25 mg tablet of levodopa/DDCI corresponds to about 7.5-8 g of MP roasted powder (containing about 400 mg of DDCI-free levodopa)**

## CONCLUSIONS

All the types of MP (*Utilis* variant) contain levodopa, with a mean concentration of 5.1 %. We did not identify a more promising ecotype, hence the most easily available ecotype in the various geographical areas may be used 5.1%.

Roasting has no effect on levodopa concentration, which remains unchanged. Furthermore, roasting appears to be the best cooking method for a number of reasons: it is easy to standardize (it does not require the measurement of the amount of cooking or soaking water, the measurement of temperature and cooking time); it facilitates the removal of the teguments; it is easy, does not require any equipment except a pan, some fire and a little grinder that can be replaced by a mortar. Roasted powder is safe from a hygienic point of view and is easy to store even for a long time.

MP powder is very cheap (total annual cost for a PD patient: 10-15 US \$). It seems to be a sustainable alternative treatment for PD patients in low income countries

A double-blind, randomized, controlled trial is required to assess the use of MP in patients both in terms of safety and short and long-term efficacy