Peripheral neuropathies associated with levodopa-carbidopa continuous intestinal gel infusion: long-term prospective assessment

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Introduction: levodopa-carbidopa intestinal gel infusion (LCIG) is an effective treatment for advanced Parkinson's disease (PD) [1]. Peripheral neuropathy (PN) is a described complication of LCIG infusion, and both subacute and chronic forms have been reported [1-3]. Although prospective analyses are required to investigate the role of LCIG in the pathogenesis of PN, only few data are currently available [4].

Objectives: to prospectively evaluate the incidence of PN during LCIG treatment.

Methods: 33 consecutive PD patients underwent a battery of PN-specific scales (ONLS, INCAT-SSS, MRCSS), nerve conduction studies and a serum work-up including vitamin B12, folate and homocysteine. The assessment was performed before starting LCIG infusion and regularly thereafter. Only subjects with normal clinical-electrophysiological (EP) features at baseline were included in the long-term analysis.

Results: at baseline 9% (3/33) patients showed a symptomatic sensory-motor PN and 21% (7/33) showed asymptomatic EP alterations (subclinical PN).
Over a follow-up of 24.36 ± 12.18 months, among patients with normal clinical and electrophysiological features at baseline, 8.7% (2/23) subjects developed a subacute PN, 8.7% (2/23) developed a chronic PN and 30.4% (7/23) developed a subclinical PN. The onset of subacute PN was significantly more precocious compared to other PN phenotypes (*p: 0.001*). All patients who developed PN received folate, vitamin B1 and vitamin B12 supplementations; only subacute PN patients required LCIG suspension.
Patients with subacute or subclinical PN showed no significant differences in B12, folate, homocysteine or levodopa-equivalent daily dose (LEDD) variations over time compared to patients without clinical-EP alterations. On the contrary, patients who developed chronic PN showed a higher increase in homocysteine (*p: 0.024*) and LEDD (*p: 0.041*) compared to normal patients (Figure 1), while no differences in vitamin B12 or folate levels were observed.
A progressive body mass index (BMI) decrease compared to baseline was observed both in chronic PN subjects (from 26.9 ± 5.3 to 24.5 ± 5.2; *p: 0.049*) and in normal subjects (from 23.6 ± 2.7 to 21.9 ± 2.0; *p: 0.045*). The modification of BMI over time did not show significant differences between groups (Figure 1).
Patients with symptomatic PN at baseline showed a mild EP worsening. 1/7 patients (14.3%) with subclinical PN at baseline developed a symptomatic PN after 12 months of LCIG infusion, associated with a marked weight loss; folate and vitamin B12 supplementations were administered and subsequent evaluations showed a substantial clinical and electrophysiological stability.

Conclusion: PN is a relevant complication among PD patients undergoing LCIG [2,3]: follow-up protocols should include serial clinical-electrophysiological evaluations [3].
The pathogenesis of subacute PN might be related to immunological triggers on predisposed subjects. On the contrary, higher LEDD and homocysteine-mediated neurotoxicity could be implicated in chronic forms [5]. Weight loss seems not to represent a primary causative factor of PN.

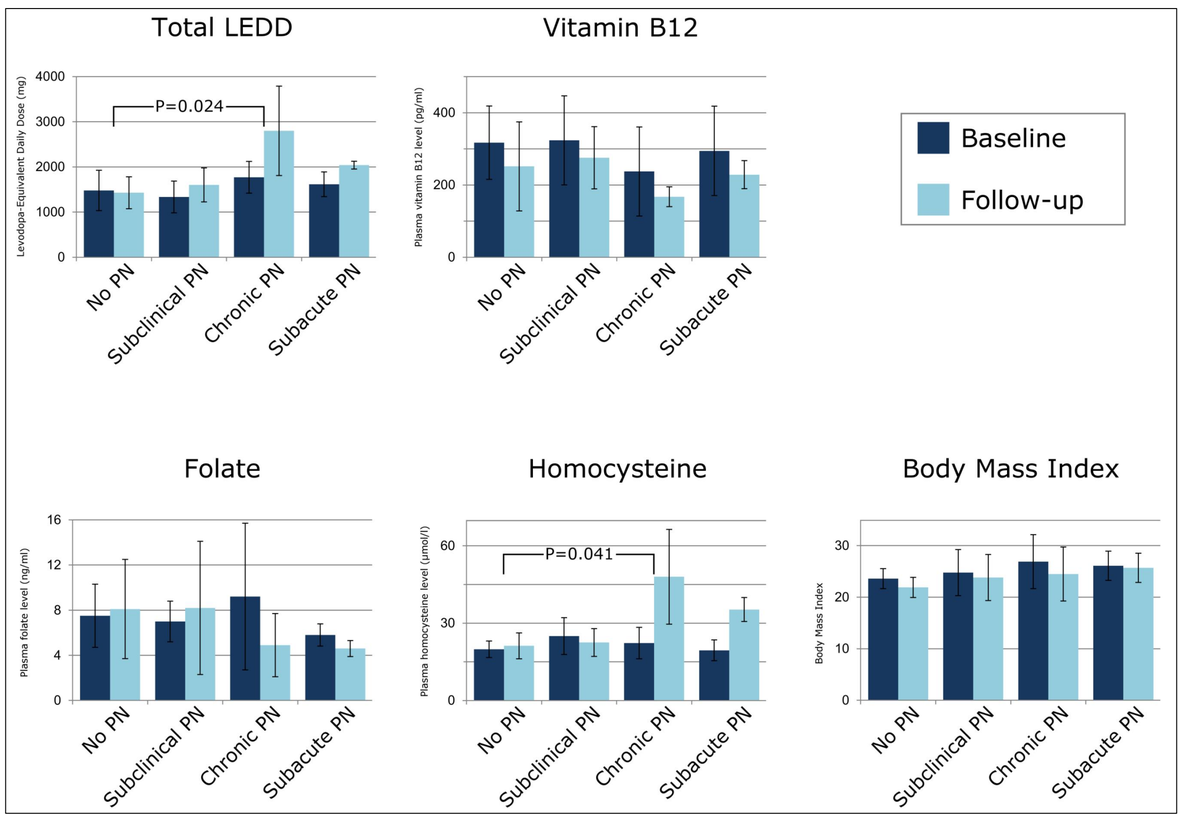

Figure 1: levodopa-equivalent daily dose (LEDD),vitamin B12, folate, homocysteine and body mass index at baseline and follow-up. Chronic PN patients showed a more marked increase in LEDD and plasma homocysteine compared to patients without clinical-EP alterations. ⌜⌝: significantly different trend over time (*p<0.05*).

References:

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