High-dose thiamine and Parkinson's disease

A. COSTANTINI[1], E. GROSSI[2], R. FANCELLU[3], S. MONDONICO[4], C. JENNER[1], S. PROIETTI[1] AND M.I. PALA[1]

[1]*Department of neurological rehabilitation "Villa Immacolata", Viterbo, Italy*
[2]*Bracco Foundation, Milano, Italy*
[3]*Unit of Neurology, ASL3 Villa Scassi Hospital, Genova, Italy*
[4]*Centro Diagnostico Italiano, Milano, Italy*

ABSTRACT

Parkinson's disease (PD) is a progressive neurodegenerative disorder clinically characterized by both motor (bradykinesia, tremor, rigidity, flexed posture, postural instability) and non-motor symptoms. Pathological feature is the degeneration of pigmented dopaminergic neurons in *substantia nigra* and of other cerebral circuits. Currently, PD is the only chronic neurodegenerative disease with effective symptomatic therapies; however, no treatment has yet been identified that could significantly modify its natural progression.

Thiamine deficiency causes disorder in peripheral and central nervous system; its role has been described in dominant and recessive cerebellar ataxia, such as spinocerebellar ataxia type 2 (SCA2) and Friedreich ataxia, and also in PD pathology; parenteral high-dose thiamine administration might have a role in dopaminergic and non-dopaminergic neuron activity.

In a previous paper, we described a 47 year-old man affected by SCA2, treated for three months with intramuscular injection of thiamine; in this patient fatigue as well as motor symptoms improved. Thus, we hypothesized that the pathogenesis of symptoms in some inherited and degenerative diseases of the nervous system could be linked to a thiamine deficiency due to dysfunction of intracellular thiamine transport or to structural enzymatic abnormalities.

The aim of our study was to analyze the potential symptomatic effect of thiamine in PD. We recruited 26 PD patients; two subjects were newly diagnosed and drug-naïve patients, while the others 24 patients were in treatment with dopaminergic drugs. All the patients were assessed at baseline with the Unified Parkinson's Disease Rating Scale (UPDRS) and started to be treated with 100 mg of thiamine i.m. two days a week, without any change to personal therapy. Sixteen patients (12 men, 4 women; age 71.1±10.1 years) were re-evaluated after one month and three months of thiamine treatment; the re-assessment of the remaining 10 patients is scheduled in the next months. In all the patients basal levels of plasma thiamine were in normal reference range. Thiamine treatment led to significant improvement of motor symptoms of the 16 re-assessed patients: mean total UPDRS scores improved from 36.25±14.28 to 10.00±8.82 ($p<0.0001$, t-test for paired data).

Our results showed that administration of high doses of thiamine was effective in improving motor symptomatology in PD patients. This clinical improvement was stable over time in all the patients; the two patients with milder phenotype had complete clinical recovery, without necessity of dopaminergic therapy. We speculate that high doses of thiamine improve the energetic metabolism of surviving cells in *substantia nigra*, leading to an increased synthesis of the endogenous dopamine and a better utilization of the exogenous levodopa. The abnormalities in thiamine-dependent processes could be overcome by diffusion-mediated transport at supranormal thiamine concentrations. Moreover, we hypothesize that a focal, severe thiamine deficiency due to a dysfunction of thiamine metabolism could cause a selective neuronal damage in the cerebral areas involved in PD.

Further studies are necessary to investigate the role of thiamine in basal ganglia, in particular whether the dysfunction of thiamine-dependent processes might be a primary pathogenic pathway leading to the failure of dopaminergic and non-dopaminergic neurons in PD.