High-Dose Thiamine as Possible Medical Treatment for Spinocerebellar Ataxias

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ABSTRACT

Spinocerebellar ataxias are a heterogeneous group of neurodegenerative disorders, characterized by incoordination of voluntary movements, mainly involving stance, gait, eye, limb, and speech. Two main etiological categories are distinguished: hereditary and sporadic ataxias; sporadic ataxias may be symptomatic or idiopathic. No effective cure is currently available for several forms of ataxia.

Thiamine deficiency causes disorder in peripheral and central nervous system. Its role has been described in spinocerebellar ataxia: some studies reported normal blood thiamine values but low cerebrospinal fluid levels, as well as a significant decrease in thiamine and thiamine monophosphate in cerebrospinal fluid in ataxic patients compared to controls. In addition, several authors observed a dysfunction of pyruvate dehydrogenase complex in Friedreich ataxia (FRDA). In a previous paper, we described a 47 year-old man affected by spinocerebellar ataxia type 2 (SCA2), treated for three months with intramuscular injection of thiamine; in this patient fatigue as well as motor symptoms improved and stabilized for more than a year. The same positive results we described in two patients affected by FRDA treated for two years. Thus, we hypothesized that the pathogenesis of symptoms in some neurodegenerative diseases 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 some forms of spinocerebellar ataxias.

We recruited in June 2011 two SCA2 patients and from July 2013 twenty FRDA patients and two patients with sporadic idiopathic ataxia. All the patients were assessed at baseline with the Scale for the Assessment and Rating of Ataxia (SARA) and started to be treated with i.m. 100 mg of thiamine 1 or 2 times a week, without any change to personal therapy. In all the patients basal levels of plasma thiamine were in normal reference range. The patients were re-evaluated after one month and then every three months. Thiamine treatment led to significant improvement of motor symptoms. In FRDA group, total SARA scores improved from 26.40±8.66 to 22.95±8.52 ($p<0.0001$, t-test for paired data). Moreover, 13 out of 17 patients with absence of deep tendon reflexes at baseline, showed normal deep tendon reflexes after one month of treatment. At SARA scale both the two patients with SCA2 improved of 50%, while the two patients with sporadic ataxia improved of 25% and 50%.

Our results showed that administration of high doses of thiamine was effective in improving motor symptomatology in ataxic patients; this clinical improvement was stable over time in all the patients. 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 centers typically involved in this pathology. Further studies are necessary to investigate the pathogenetic and neuroprotective role of thiamine in spinocerebellar ataxias.