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Neuroprotective impact of a vitamin trace element composition – a randomized, double blind, placebo controlled clinical trial with healthy volunteers

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Abstract

OBJECTIVES: Neurotoxic metabolites and oxidative and nitrosative stress reactions play a crucial role in the pathways leading to neuronal cell death and neurodegeneration. The bioavailability of the many antioxidant ingredients a vitamin and trace element composition was investigated, to reveal the neuroprotective (preventive) potential of the composition.

METHODS: We recruited 159 healthy volunteers, assigned them randomly and double blind to a placebo and verum group. Physicians excluded volunteers with severe chronic diseases or interfeering medications. 142 participants finished the six month trial. Laboratory parameters were determined 1) before participation, and 2) after three and 3) six months. We confirmed the bioavailability of ingredients, and determined metabolic parameters associated with the integrity of the blood brain barrier, mitochondrial deficiency (Q 10), neurodegeneration (homocystein), and antioxidative capacity (e.g. lipidperoxidation), and superoxid-dismutase activity.

RESULTS: Starting from baseleine, after three months neuroprotective ingredients increased within their physiological borders, folic acid ($p<0.003$), pyridoxin ($p<0.001$), cobalamin ($p=0.001$), and the fat soluble vitamin tocopherol ($p<0.001$). In parallel, homocytein decreased after 3 and 6 months ($p<0.001$, and $p<0.025$, respectively). Other paramters like zinc reacted slower, significant changes were observed only after 6 months.

CONCLUSION: The observed metabolic changes and alteration of the oxidative status after 3 and six month of regular intake underlines the compositions' potential to ameliorate neurodegenerative processes. We conclude that the subsitution of vitamins and traceelements with natural source in a proper manner may be effective for neuroprotection in healthy population.

ORIGINAL ARTICLE

INTRODUCTION

The increase of life expectance in industrial countries is paralleled by increasing prevalence of various neurodegenerative diseases. To date, no causal therapy is known. Several pathomechanisms are debated.

Mitochondrial dysfunction in nerve cells is a commonly discussed aetiologic factor for many forms of neurodegeneration. Mitochondria play a pivotal role in cellular bioenergetics and cell-survival. Prolonged oxidative stress and the resultant hypoperfusion in the brain tissues stimulate the expression of nitric oxide synthase (NOS) enzymes. This further drives the formation of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which collectively contributes to the dysfunction of the blood-brain barrier (Aliev *et al.* 2014).

In animal studies the activity of the mitochondrial enzyme activity of Mn-superoxide dismutase (SOD) plays an important role regulating oxidative stress in the mitochondria, resulting in high levels of lipid peroxidation, and low levels of ATPase and cytochrome C oxidase activity in the infected cerebral mitochondria (Choi *et al.* 1998). A positive impact of oxidative and nitrosative stress reduction and morphological findings in the cortex indicated that particularly at the onset of progressive neurodegeneration, compounds with antioxidative properties may be effective in slowing down brain injury (Gasparova *et al.* 2012; Gasparova *et al.* 2014).

In a rat model of paraquat-induced neurodegeneration, coenzym Q10 supplementation halted the progression of neurodegeneration (Muthukumaran *et al.* 2014). A neuroprotective effect was also observed after kainate injection when coenzym Q10 pretreatment significantly attenuated severity and incidence rate of the higher seizure severity during status epilepticus and spontaneous seizure phases (Baluchnejadmojarad & Roghani 2013). Again in a rat model the combination of resveratrol, omega-3 fatty acids, and coenzym Q10 ameliorated a cisplatin-induced peripheral neuropathy (Bhadri *et al.* 2013).

The role of cholesterol homeostasis in the neurodegenerative process has been debated (Anchisi *et al.* 2012). The levels of high-density lipoprotein (HDL) cholesterol were positively correlated with cognitive impairment of subjects and increased triglycerides associated with bilateral grey matter loss (Gonzalez-Escamilla *et al.* 2014).

Homocystein markedly increased the vulnerability of hippocampal neurons to excitotoxic and oxidative injury in cell culture and in vivo, suggesting a mechanism by which HCY may contribute to the pathogenesis of neurodegeneration (Maler *et al.* 2003): Under in vitro conditions D,L-HCY caused a time and dose-dependent gliotoxic effect (Kruman *et al.* 2000).

There is a still ongoing controversy about adaequate supply of antioxidants in the population by normal diet (Guallar *et al.* 2013; Bjelakovic *et al.* 2014; Caldwell *et al.* 2014). Antioxidant treatment has been suggested as remedy for Alzheimers disease (Gilgun-Sherki *et al.* 2003). Oxidative stress may deteriorate the blood brain barrier (Enciu *et al.* 2013). Some evidence suggests that dietary supplementation with folate and other homocystein lowering vitamins reduce the risk for neurodegeneration (Mattson *et al.* 2002). Folic acid deficiency and HCY weaken the DNA repair in neurons, sensitizing them to oxidative damage induced by neurotoxic proteins (Kruman *et al.* 2002). Accordingly, epidemiological studies show a positive, dose-dependent relationship between mild-to-moderate increases in plasma total HCY concentrations and the risk of neurodegenerative diseases (Herrmann & Obeid 2011).

The test substance LaVita® is a vitamin-trace-element-composition (ViteC). In view of the ingredients and the oxygenradical absorbance capacity we hypothesized whether or not the regular intake generates a neuroprotective potential to justify regular intake as preventive strategy.

MATERIAL AND METHODS

The trial was announced in regional newspapers. 159 healthy volunteers were recruited according to predefined inclusion and exclusion criteria by a medical physician.

We aimed to recruit healthy vounteers in a steady state life condition. The exclusion criteria eliminated participants with known risk factors for study bias. Volunteers acute disease and/or medical treatments which could interfere with our endpoints were not admitted. More specifically, we excluded persons with:

- age below 18 and over 90 years
- acute disease; hospitalization in the last 4 weeks
- recovering from surgery (surgery in the last 12 weeks)
- holiday or other larger travel (availability, change of living environment)
- diabetes or severe metabolic disease, fructose intolerance, to reduce interference with metabolic conditions
- drug or alcohol abuse to reduce risk of low compliance
- oncologic treatment in the last 3 months
- inflammatory bowel disease (e.g. Colits), signs of malabsorption
- disease with remissions and relapses (Arthritis, Multiple sclerosis, etc.) to exclude endpoint variance related to disease associated conditions
- dementia, diagnosed and medically treated neurodegeneration?
- receiving cortison treatment or any orther acute medical intervention (antibiotics) to exclude interefference and study bias due to medical condition treatment
- participation at another trial, to exclude interference with other trials.