HOW DOES SUPEROXIDE DISMUTASE 1 CAUSE FAMILIAL AMYOTROPHIC LATERAL SCLEROSIS AND TREATMENT OPTIONS?

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ABSTRACT

The purpose of this study was to evaluate how superoxide dismutase 1 (SOD1) mutation causes familial amyotrophic lateral sclerosis (ALS). This study also evaluates the mechanism of action of approved treatments for ALS and evaluates the action of plants that can also be used in treatment.

INTRODUCTION

Amyotrophic Lateral Sclerosis (ALS) is a disease of the upper motor neurons (UMN) which eventually affects the lower motor neurons, therefore, many doctors in other countries use the alternative name motor neuron disease (MND). The disease progresses to muscle weakness and atrophy, and this eventually leads to respiratory failure which is fatal unless mechanical ventilation is used.

The incidence of ALS in the United States is approximately 5000 individuals being diagnosed per year (1). The majority of cases are sporadic meaning there is no family connection or prior known cases linked. The exact percentage of sporadic cases is currently being researched as there is a finding more cases, however, as of now it is estimated as 85% of the cases.

The first discovered mutation linked to familial ALS (fALS) is a mutation to the gene coding for the enzyme superoxide dismutase (Cu/Zn). The enzyme is located within the cytosol of human cells. This enzyme is involved in counteracting oxidative stress of the cell.

- Individuals with familial patterns of ALS begin to have symptoms in their late 40s and early 50s.

METHODOLOGY

Search using the following terms: SOD1 in familial amyotrophic lateral sclerosis (ALS) or ALS reversal 1 of 44 hits in PubMed Database used.

A few mutations to SOD1 gene have decreased enzymatic activity. However, most mutations in SOD1 have a toxic gain of function. Key to proper function of the SOD1 enzyme is correct maturation. SOD1 containing copper without zinc has been shown to create more toxic species of ROS. Furthermore, without zinc the enzyme collapses slowly since zinc strengthens the enzyme structure. Rough endoplasmic reticulum stress needs to be eliminated for proper protein synthesis. The ubiquitin/proteasome pathway needs to work properly, as well as autophagy to eliminate misfolded SOD1 mutations.

Neuroinflammation contributes to the pathology and increases the speed of mortality in ALS patients. Riluzole addresses the glutamine excitotoxicity. Moderate decreases oxidative stress and modulates the production of inflammatory cytokines. The adaptogens: Withania somnifera and Withaferin A as well as, Coriaria buxifolia decrease neuroinflammation. Vitamin D3 is important to increase SOD and lower neuroinflammation. Vitamin E acts to prevent lipid peroxidation which is important to protect the neurons from respiratory burst of microglia.

RESULTS

Physicians need to monitor proper zinc and CuZn cholecalciferol levels in SOD1/ALS starting in their teen years.

Withania somnifera acts as an adaptogen and lower neuroinflammation. It is prescribed in two SOD1 mg capsules two times per day.

ADAL patients and their children should be encouraged to use turmeric freely in all foods. As a standardized extract (containing 95% curcuminoid) dose is 500 mg twice per day. These herbal remedies are just a few that could benefit individuals with ALS. Furthermore, lifestyle factors such as exercise, avoidance and detoxification of environmental toxins, getting enough sleep, managing emotional stress, and eating a healthy nutritive diet are all factors that any doctor should work towards with ALS patients and any family members caring the genetic mutation which predispose them to ALS.