



## Alcohol Withdrawal Syndrome: The Importance of Glutamatergic System

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Alcohol withdrawal syndrome (AWS) is a complex phenomenon that involves several neurotransmission systems. Its signs and symptoms are related to the adrenergic autonomic hyperstimulation and to the hypofunction of the gabaergic system. Moreover, alcohol is an antagonist of the NMDA (N-Methyl-D-Aspartate) receptors, which are excitatory, in the central nervous system [1].

The glutamatergic hyperactivity resulting from AWS via NMDA receptors would cause a large calcium influx, and increase the activity of the nitric oxide synthase enzyme. This action would increase the excitotoxic activity, accelerate the production of oxygen free radicals and cause neuronal death [2].

It is known that the glutamatergic hyperactivity results in great damage to the cortical function; concentration and impulse control [3-6]. Impulsivity and damage to frontal functions are considered risk factors for the development of alcohol dependence [7,8], and AWS would aggravate such damage, thus contributing to the perpetuation of this dependence [9,10].

Several studies have shown the association between the number of previous AWS episodes and cognitive deficits [11,12] caused by neurodegeneration of pre-frontal areas [13], in turn caused by glutamatergic hyperfunction [14]. Czapla et al. (2015) [15] have concluded that the number of AWS episodes is a significant predictor of relapse and decreased impulse control by individuals with alcohol dependence.

These phenomena are perfect examples of the vicious cycle the addicted brain may enter when in abstinence of any psychotropic substance. Even though permanent use of alcohol may damage neurons, sudden lack of this substance in the brain is toxic in much the same way, stimulating oxidative processes in the central nervous system, leading to neuron death and neuron lesions, which, in turn, may result in aggravating symptoms in the long run.

In order to prevent this perpetuating cycle, one of the main measures clinicians should implement is the adequate treatment of AWS as a clinical condition of great significance that should be treated with pharmacological, behavioral and social approaches.

Even though there are many pharmacological studies concerning the treatment of AWS, there is still the need to find new substances that modulate the glutamatergic system [16]. We have recently proposed the use of microelements such as zinc and magnesium as such substances, as they are natural modulators of this system.

In fact, in a study we developed, we observed a direct association between lower plasmatic levels of zinc and magnesium and greater intensity of AWS symptoms [17].

Therefore, it stresses the importance of early identification and implementation of effective measures to treat and attenuate the AWS as well as focus on relapse prevention [18,19].

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