Wernicke-Korsakoff Syndrome: Pathophysiology in Alcoholics

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Introduction

Wernicke-Korsakoff Syndrome (WKS) (Figure 1) is a neuropathic disorder caused by deficiency of thiamine (or vitamin B1), which is predominantly observed in individuals with a higher intake of alcohol.

Two hypotheses non-exclusive explain the damage in the central nervous system (CNS) in alcoholics developing WKS (Figure 2).

Thiamine Deficiency

- Unbalanced nutrition

- Interference with active transport carriers: THTR

- Low or insufficient doses of thiamine (oral or parenteral)

- Magnesium deficiency (cofactor for alcoholics): damage

- Neurotoxicity caused either by alcohol exposure and thiamine deficiency results in an increase of damage potential when both are combined

Thiamine Deficiency in Alcoholic Brain

In alcoholics with WKS, the combination of thiamine deficiency and alcohol consume leads to a synergic effect for damage in CNS (Figure 8).

Studies from autopsies revealed that the disorder is still greatly underdiagnosed. Then, clinical considerations for proper diagnosis and treatment are also going to be discussed.

Pathophysiology of Chronic Alcohol Exposure in CNS

Ethanol enhances GABA<sub>A</sub> receptors and inhibits NMDA receptors (Figure 6).

Figure 6. Alcohol interacts with the GABA and N-methyl-D-aspartic acid (NMDA) systems. The structure of receptors involved are also represented.

Chronic alcohol consumption leads to neuroadaptative compensatory mechanisms:

- GABA<sub>A</sub> receptor expression
- NMDA receptor expression
- Chronic alcohol exposure

Repeated episodes of drinking and withdrawal results in glutamate-induced excitotoxicity and lasting neuronal damage (Figure 7). Moreover, the potential for neurotoxicity increases during withdrawal periods.

Clinical Considerations for Diagnosis and Treatment of WKS

Post-mortem findings indicate that prevalence of WKS in alcoholics is higher than appreciated. Non-recognition of patients with WKS is probably due to the fact that most of them only exhibit only one or two classic symptoms of the triad (Figure 10).

Those alcoholics individuals suspected of suffering WKS should be treated with parenteral thiamine since treatment with oral thiamine is ineffective (Figure 11). Nevertheless, the optimal treatment strategies for WKS still remain in dispute.

Conclusions

- WKS lesions in CNS result more severe in alcoholic patients, due to the synergic effect when thiamine deficiency and alcohol exposure are combined.
- Alcohol consume contributes to thiamine deficiency through different mechanisms, which increases the risk of developing WKS.
- Most alcoholics with WKS prior to death are underdiagnosed, then clinical considerations are needed for the proper diagnosis.
- Further work is needed to optimize the treatment of WE and to prevent the progression to KS.

Bibliography