Recognition, Prevention and Treatment of Wernicke-Korsakoff Syndrome (WKS): An Infrequent yet Preventable Cause of Cognititive Dysfuction and Neurological Damage

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Key Highlights:

- Wernicke-Korsakoff syndrome (WKS) is a neurological disorder caused by thiamine (vitamin B1) deficiency due to malnutrition in chronic alcohol consumption but also in other less recognised conditions that include vomiting, massive weight loss and thiamine deficiency nutrition such as cancer, chronic inflammatory disease, prologed fasting, hyperemesis gracvidarum and anorexia nervosa.
- The acute (Wernicke) form is defined by the classic triad of symptoms: altered mental status, ocular signs, and ataxia while the chronic irreversible syndroem is called Korsakoff's characterized by amnestic and behavioral disorders
- Alcohlic and non alcoholic pathogenesis may be different, with mechanism of neurotoxocity not fully understood but responsive to high dose thiamine treatment
- Thiamine requirements can differ among different patients, however replacement must early and adequate with high dosage of parenteral thiamine in order to prevent progression of brain damage and reverse symptoms.

Introduction: Wernicke-Korsakoff syndrome (WKS) is a neurological disorder caused by thiamine (vitamin B1) deficiency. Its acute form Wernicke's syndrome is characterized by the classic triad of symtoms: confusion, ataxia, and eye-movement disorders, while the chronic, irreversible form results in the amnestic and behavioral syndrome, known as Korsakoff's syndrome. When presenting together, the patient can be defined to suffer from Wernicke-Korsakoff's syndrome. The pathogensis of WKS is attributed to alcohol abuse or other less known causes of nutritional deficits, such as hyperemesis gravidarum, cancer, bariatric surgery, hunger strike, soft drink consumption in the pediatric population, anorexia nervosa, or inflammatory bowel diseases. While the incidence of WKS is better known in alcoholic patients, the occurance related to other conditions is often underestimated. Also, the risks of suboptimal thiamine replacement in WKS either in relation to dose or duration are not fully known.

Description: Vitamin B1 is required in the Krebs cycle for production of adenosine triphosphate (ATP). It is also a cofactor in the production of acetylcholine and certain neurotransmitters. Thiamine deficiency is common in chronic alcohol abuse because of the poor nutritional content of alcohol as the main msource of calories. Moreover, thiamine as a vitamin is not stored in the body, and without repletion reserves are consumed in 10-14 days. Although the exact pathogenesis of neurotoxicitiy cahracteristic of certain brain regions in WKS is not fully understood, it is known that administration of thiamine can prevent neurological damage.

The acute phase of WKS was characterized by Carl Wernicke in 1881, as the triad: altered mental status, ocular signs, and ataxia. The chronic phase of WKS, called Korsakoff's syndrome (KS), was described by Sergei Korsakoff in 1887, as an amnesic disorder with confabulations. However, alcohol consumption is not the only etiology of WKS: conditions like prolonged fasting, anorexia nervosa, or a diet of polished rice are also associated with thiamine deficincy. Additional less known causes are parenteral nutrition without thiamine in malnourished individuals and formulas without thiamine in little children. Other conditions increasing risk are vomiting or

chronic diarrhea, hyperemesis gravidarum in pregnant women, obese patients after bariatric surgery, inflammatory bowel diseases, or malnourishment in oncologic patients. WKS unrealted to alcohol use is more common in realtively younger populations, and WKS appears to be more frequent in females compared to males. Early indicators of nonalcoholic WKS are vomiting and significant weight loss. Imaging findings assocaited with WKS include atrophy of the thalamus, mammillary bodies and/or periaqueductal gray matter.

Treatment and Outcome: If undetected or untreated, WKS is progressive and irreversible. Also, negative outcomes are assocaited with undertreatment of WKS with too low of thaiamine dose. Oral administration of the usual 300 mg of thiamine is not sufficient in preventing WKS for those with vomiting and weight loss including pregnant women and infants and children. Some authors suggests parenteral thiamine treatment of 300-500mg, three times a day before glucose load during the acute phase and until the nutritional deficit has been corrected. Studies suggest that the pathology of WKS is different between nonalcoholic and alcoholic patients, with the latter requiring higher doses of thiamine repletion. Also, responses are variable with some patients requiring relatively higher doses (over 1g of parenteral thiamine) and others responding to lower doses. Sometimes other coexisting nutritional deficiencies, such as magnesium, folate, or other B complex vitamins, must be corrected in order to allow thiamine to function. Intramuscular administration of Vitamin B1 seems to have a lower incidence of anaphylactic reactions compared to IV, and oral administration has the lowest risk.

Conclusion: Unlike many other forms of cognitive dysfucntion and neurological damage, thiamine deficiency is preventable and treatable. Increased awareness of WKS and greater recognition of early warning signs in nonalcohol-related cases, like vomiting and weight loss, should be prioritized. Prophylactic treatment with parenteral thiamine should be initiated in those at risk for nutritional deficiency even when WKS is only suspected. Treatment dose and duration should be adequate, in order to prevent irrversible brain damage.

REFERENCES:

1. *Oudman E, Wijnia JW, Oey MJ, van Dam M, Postma A. Wernicke-Korsakoff syndrome despite no alcohol abuse: A summary of systematic reports. J Neurol Sci. 2021 Jul 15;426:117482. doi: 10.1016/j.jns.2021.117482. Epub 2021 May 7. PMID: 34000679.*
2. *Popa I, Rădulescu I, Drăgoi AM, Trifu S, Cristea MB. Korsakoff syndrome: An overlook (Review). Exp Ther Med. 2021 Oct;22(4):1132. doi: 10.3892/etm.2021.10566. Epub 2021 Aug 5. PMID: 34466144; PMCID: PMC8383329.*

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