Wernicke's Encephalopathy

Author: Richard Moleno, DO // Editor: Larissa Velez, MD

Thiamine, also known as vitamin B1, is required in areas of the **brain with high metabolic turnover**. Thiamine enters the circulation after being absorbed in the duodenum. Once into the circulation it must cross the blood-brain barrier, where it is converted to thiamine pyrophosphate. This is a key cofactor for many enzymes such as α-ketoglutarate dehydrogenase complex and the pyruvate-dehydrogenase complex in the tricarboxylic acid cycle, and transketolase in the pentose-phosphate pathway. When these enzymes are starved of essential cofactors, changes at the cellular level can begin to be seen within 4 days .[1] Brain lesions can begin to **develop within 2-3 weeks, as this is the time necessary to deplete body stores of thiamine**.

Thiamine deficiency can manifest as several different syndromes. Although this paper focuses on Wernicke's encephalopathy (WE), thiamine deficiency can also manifest as Wet Beriberi (high cardiac output heart failure with edema), Dry Beriberi (without edema), Neuritic Beriberi (polyneuropathy), and Gastrointestinal Beriberi (abdominal pain, lactic acidosis, vomiting).[2] First described in 1881 by Carl Wernicke, Wernicke's encephalopathy has classically been described as **the triad of mental status changes, ophthalmoplegia, and gait ataxia.** The possibility of all three symptoms being present however has been reported to be **as low as 10%**, with most cases of Wernicke's encephalopathy being diagnosed at autopsy and **in people who are not alcoholics**. To be able to better diagnosis WE, Caine et al developed operation criteria that included needing two of the following: **risk factors for thiamine depletion, oculomotor abnormalities, cerebellar dysfunction, and mental status changes/mild memory impairment**. When using this criteria detection of antemortem WE can be achieved with a high degree of specificity.[3]

Wernicke-Korsakoff syndrome is an often-used term that describes two different syndromes, one acute and one chronic. Wernicke's encephalopathy, as described above, is an acute syndrome that requires immediate treatment to prevent death and neurologic morbidity. It is a medical emergency that can carry **up to 20% mortality**. Korsakoff's psychosis is a chronic condition that has the symptoms of **anterograde amnesia, retrograde amnesia, confabulation, and personality changes**. It represents neurologic changes that are **irreversible** in nature.

Wernicke's encephalopathy syndrome is classically described in alcoholics, however **anyone who is malnourished is at risk**. There have been many case reports of patients with **hyperemesis gravidarum** which resulted in WE and, subsequently Korsakoff's syndrome.4 **Post bariatric surgery** patients are also at risk. The condition is most often observed after gastric bypass surgery, especially in patients that experienced frequent vomiting.5 A small study out of MD Anderson Cancer Center in Houston revealed 5 patients who developed MRI-confirmed WE while being treated for **rapidly growing cancers**. They all experienced difficulty with oral intake due to nausea from their chemotherapy regimens. Confusion was the most common presenting symptom in these patients.[6]

Many different conditions can put a patient at risk for WE. Emergency physicians must have a high clinical suspicion and a low threshold to treat patients who start developing symptoms who are at risk. Patients at risk include anyone with **hyper-metabolic states, those with poor diets or deficient food intake, and those with intestinal malabsorption**.

The mainstay of treatment for WE is replacing the vitamin deficiency that caused the problem in the first place. Traditionally, this has been achieved by a parenteral dose of **100 mg**

thiamine per day. However, there have been **no randomized controlled trials to date that have tested this regimen**. **Many British authors advocate for even higher doses of thiamine, up to 500 mg per day, although there is little evidence to support** their recommendations. The hypothesis is that these very high doses are needed to help facilitate the passive transport of thiamine across the blood-brain barrier. Clinicians have also contested the 1 dose per day frequency of administration. This regimen was originally used before methods were available to measure the half-life of thiamine. In healthy individuals, which are not always the patients receiving supplementation, the average half-life was 96 minutes. This short half-life would support the need for more frequent dosing regimens. The safety profile of low- and high-dose thiamine is excellent, with only **3 case reports of anaphylaxis** reported in the last 40 years. A commonly recommended regimen is 500 mg of thiamine IV, diluted in 50-100 ml of saline and infused over 30 minutes.[7] For people leaving the hospital that will continue supplementation, they can be discharged on 100 mg thiamine PO once per day. There have been **no studies to date on the optimal length of treatment** for these patients.[2]

In closing, it is clear that not only is WE most likely under-diagnosed, it is also likely under-treated. In those patients with suspected or confirmed WE, higher doses of intravenous thiamine and more frequent dosing regimens seem both safe and clinically rational.

References

1. Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol. 2007;6(5):442-55.
2. Donnino MW, Vega J, Miller J, Walsh M. Myths and misconceptions of Wernicke's encephalopathy: what every emergency physician should know. Ann Emerg Med. 2007;50(6):715-21.
3. Caine D, Halliday GM, Kril JJ, Harper CG. Operational criteria for the classification of chronic alcoholics: identification of Wernicke's encephalopathy. J Neurol Neurosurg Psychiatr. 1997;62(1):51-60.
4. Di gangi S, Gizzo S, Patrelli TS, Saccardi C, D'antona D, Nardelli GB. Wernicke's encephalopathy complicating hyperemesis gravidarum: from the background to the present. J Matern Fetal Neonatal Med. 2012;25(8):1499-504.
5. Aasheim ET. Wernicke encephalopathy after bariatric surgery: a systematic review. Ann Surg. 2008;248(5):714-20.
6. Kuo SH, Debnam JM, Fuller GN, De groot J. Wernicke's encephalopathy: an underrecognized and reversible cause of confusional state in cancer patients. Oncology. 2009;76(1):10-8.
7. Thomson AD, Cook CC, Touquet R, Henry JA. The Royal College of Physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident and Emergency Department. Alcohol Alcohol. 2002;37(6):513-21.