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Malnutrition-Induced Wernicke's Encephalopathy Following a Water-Only Fasting Diet

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Abstract

Background: Wernicke's encephalopathy is a critical condition of neurological dysfunction resulting from a deficiency in thiamine. Chronic alcoholism is recognized as the most common cause of Wernicke's encephalopathy, but other causes, including fasting/starvation and malnutrition, have been documented within the scientific literature. These causes may not be readily recognized by healthcare professionals and may lead to Wernicke's encephalopathy being overlooked as a diagnosis when a nonalcoholic patient presents with classic signs and symptoms of the disorder. *Materials and Methods*: A narrative review of thiamine and its relationship to the development, diagnosis, and treatment of Wernicke's encephalopathy is presented based on a review of evidence-based guidelines and published research. To heighten awareness of the development of Wernicke's encephalopathy in fasted/starved and malnourished patients and to contribute to the scientific body of knowledge for the identification and management of Wernicke's encephalopathy in these patients, the clinical course and treatment of an adult woman who developed Wernicke's encephalopathy following a 40-day water-only fasting diet is outlined. *Results*: Clinical suspicion was required to identify the patient's condition and initiate immediate intervention through parenteral thiamine administration. Oral thiamine supplementation of 100 to 800 mg per day for 6 months was required to aid recovery. *Outcomes*: The patient's clinical course and response to treatment illustrate the necessity for clinical awareness and suspicion of Wernicke's encephalopathy among healthcare professionals, timely and adequate parenteral thiamine administration, and oral thiamine supplementation at therapeutic doses to correct the nutrient deficiency, halt the progression of Wernicke's encephalopathy, and promote recovery. (*Nutr Clin Pract*. 2015;30:92-99)

Keywords

fasting; malnutrition; thiamine; Wernicke encephalopathy; thiamine deficiency; avitaminosis

Initially identified by Carl Wernicke in 1881, Wernicke's encephalopathy (WE) is a critical condition of neurological dysfunction resulting from a deficiency in thiamine.[1] This deficiency leads to the inadequate supply of thiamine to the brain and the subsequent development of brain lesions.[2,3] These brain lesions impede normal neural-motor signaling, causing mental impairment and the related traditional clinical signs and symptoms of WE. If WE is not diagnosed and treated in a timely manner, the brain lesions will become permanent, and Korsakoff syndrome will arise.[2-4] Korsakoff syndrome is a chronic, permanent, and potentially deadly condition evidenced by short-term memory loss and psychosis.[4]

In the early to mid-1900s, Alexander and Jolliffee recognized the relationship between WE and thiamine deficiency.[1] This realization led to the ability to prevent and treat WE through thiamine supplementation. Because a known therapeutic intervention exists for this high-risk and potentially fatal condition, randomized controlled trials investigating strong evidence-based interventions for the prevention and treatment of WE are lacking and are unlikely to emerge.[5] As a result, the existing knowledge about the causes and contributing factors, pathophysiology, and management of WE is based primarily on case reports and case series. Through these reports, chronic alcoholism has been identified as the most common cause of WE,[2,3,5] and existing treatment guidelines focus on the management of WE in alcoholics.[2,5]

Within the scientific literature, other more acute and nutritionally relevant causes of WE have been documented (Table 1), including fasting/starvation and malnutrition.[2,5,10,11] These clinical states rank as the fourth (10.2% of cases) and seventh (4.2% of cases), respectively, most frequent non-alcohol-related causes of WE.[5] These causes may not always be readily recognized by healthcare professionals and may lead to WE being overlooked as a diagnosis when a nonalcoholic patient presents with classic signs and symptoms of WE. In addition, if WE is

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Table 1. Identified Nutrition-Related Nonalcoholic Causes of Wernicke's Encephalopathy.

Condition[5]	Rationale for Deficiency
Acquired immune deficiency syndrome	Inadequate nutrient intake; heightened metabolic use secondary to hypermetabolism characterized by wasting syndrome[6]
Bariatric surgery	Procedure-related restricted nutrient intake; procedure-related maldigestion and malabsorption; impaired nutrient intake secondary to postsurgical vomiting[7]
Cancer	Impaired nutrient intake, digestion, and absorption
Hyperemesis gravidarum	Impaired nutrient intake secondary to vomiting
Inflammatory bowel disease	Impaired nutrient digestion and absorption secondary to altered gastrointestinal mucosa
Parenteral nutrition administration	Inadequate nutrient provision; heightened metabolic use secondary to the provision of a high-dextrose solution
Renal disease with dialysis	Inadequate nutrient intake secondary to anorexia and fatigue; loss during dialysis treatment,[8] particularly in peritoneal dialysis[9]
Starvation/fasting	Inadequate nutrient intake

diagnosed in a nonalcoholic, malnourished patient, the literature lacks evidence-based guidelines for its management in these patients. To heighten awareness of the development of WE in fasted/starved and malnourished patients and to contribute to the scientific body of knowledge for the identification and management of WE in these patients, this clinical observation provides a brief discussion of thiamine and its relationship to the development, diagnosis, and treatment of WE before outlining the clinical course and treatment of an adult woman who developed WE following a 40-day water-only fasting diet.

Thiamine and Its Relationship to the Development of WE

Thiamine, or vitamin B_1, is an essential water-soluble vitamin found in both animals and plants. Good dietary sources of thiamine include pork, salmon, organ meat, wheat germ, whole cereal grains, and legumes.[12,13] Foods enriched with thiamine include refined grain products such as bread, pasta, cereal,[12,13] and rice.[13] Raw fish (sushi),[14] coffee, tea,[15] blueberries, black currants, Brussels sprouts, and red cabbage[12] contain anti-thiamine factors, or thiaminases, that degrade the thiamine in these foods[11,14] and inhibit thiamine absorption within the gastrointestinal tract.[15] Thiamine may also be destroyed by alkaline conditions (pH > 8) and by heat.[12] Vitamin C and citric acid may be used as reducing agents to prevent the destruction of thiamine.[12]

The recommended dietary allowance for thiamine is 1.1 mg per day for adult (≥19 years old) women and 1.2 mg per day for adult men.[16] These amounts equate to 0.5 mg per every 1,000 kcal consumed.[10] Because of a lack of evidence to support toxicity-related adverse events, no tolerable upper intake level has been established.[16]

Being an essential water-soluble nutrient, thiamine must be obtained through regular consumption. Thiamine is present in food as either free thiamine or a phosphorylated form. Since thiamine is absorbed in the free form, the phosphorylated forms must be digested prior to absorption.[12] Thiamine is absorbed throughout the small intestine by both active and passive transport carriers.[17] The rate and amount of thiamine absorbed depend on the concentration of thiamine present.[18]

The body is capable of storing 30 to 50 mg of thiamine,[3] which quickly becomes depleted in the absence of adequate thiamine intake. Depending on the amount stored and the level of intake, these thiamine stores can be depleted in an average of 3 to 4 weeks.[3,10] At this time, the function of thiamine-dependent enzyme systems becomes impaired as the concentration of thiamine circulating in the bloodstream is reduced.[10] Cells throughout the body, particularly brain and other neurological cells, depend on thiamine as a coenzyme for various metabolic processes. These neural cells rely on thiamine for the metabolism of carbohydrate for cellular energy, the metabolism of lipids for the integrity of the myelin sheath, and the metabolism of amino acids for the synthesis and functionality of neurotransmitters.[2,10] Alterations in these metabolic processes result in cell impairment and damage.[2,10] This damage begins as early as 4 days after thiamine deficiency and steadily progresses in severity, eventually leading to programmed cell death. After 14 days of deficiency,[10] lesions develop on the brain.[2,10] These lesions and the neurological impairment that they cause are considered the classic signs and symptoms of WE.

Identification of WE

The global prevalence of WE is estimated to range from 0.4%–2.8% of adults.[5] In the United States, it appears to affect up to 2.2% of adults.[10] Only 5%–14% of patients with WE are diagnosed during their lifetime, leaving 85%–95% of patients undiagnosed.[2] A variety of factors affect the underdiagnosis of WE, including its progressive nature ending in untimely death, its presentation in chronic alcoholics who often fail to seek treatment, and the lack of disease-specific diagnostic criteria. As a result, a diagnosis of WE may be overlooked or excluded in

Table 2. Categorization of Frequent Signs and Symptoms of Wernicke's Encephalopathy.[21]

Mild Wernicke's Encephalopathy	Moderate Wernicke's Encephalopathy	Severe/Terminal Wernicke's Encephalopathy
Anorexia	Short-term memory loss	Disorientation
Nausea/vomiting	Apathy/anxiety	Confabulation
Visual alterations	Apprehension	Onset of coma
	Emotional changes	

patients who present with nonclassic cases.[2,5] Awareness of WE is crucial for identifying patients with WE and treating them quickly.

WE is diagnosed primarily by the classic triad of signs, which include confusion, lack of muscle coordination, and involuntary eye movement or eye paralysis.[2,5] Because these classic signs occur in only 10%–20% of cases,[19] Caine et al[20] developed what is known as operational criteria for the diagnosis of WE. Based on these criteria, WE should be diagnosed when 2 of the following 4 signs are present: dietary deficiency, oculomotor abnormalities, impairment in voluntary motor function, and either altered mental state or mild memory impairment. Apart from the classic signs and operational criteria, Thomson et al[21] have identified and classified other clinical signs and symptoms of thiamine deficiency based on 15 studies published over a 125-year period. For nonalcoholic malnourished patients, these signs and symptoms depend on the magnitude of the WE, whether it is mild, moderate, or severe (Table 2). In the guidelines for the management of WE published by the European Federation of Neurological Societies, Galvin et al[5] note that signs of vomiting and dietary deficiency are more common in nonalcoholics, and impaired eye movements and motor function are more common in alcoholics. In addition, alcoholics present with the classic triad of symptoms more frequently than nonalcoholics.[5] This variation demonstrates the need for clinicians to assess signs and symptoms of WE beyond the classic triad and operational criteria, particularly in nonalcoholic patients (Table 3).

Laboratory and radiographic testing may be used to support and confirm the clinical diagnosis of WE, but they are not recognized as methods for diagnosing WE.[2,10] To assess the concentration of available thiamine in the bloodstream, a direct measurement of thiamine and its phosphorylated forms may be performed by high-performance liquid chromatography.[5] For accuracy, blood should be drawn prior to the administration of thiamine. It should be noted that this test suffers from a number of limitations. While the normal range of thiamine is 60–200 nm, no minimum level has been established for diagnosing WE.[5] Thomson et al[3] advise that an abnormal value be used to confirm WE in the presence of signs and symptoms but that a normal value not be used as the sole basis for excluding WE if classic and/or operational signs and symptoms are present. The results of this laboratory test may take days to obtain, time that a patient with WE does not have because of the fast progression and deleterious nature of WE. Thus, it is strongly recommended that treatment occur immediately upon even the suspicion of WE.[3,10]

"MRI [magnetic resonance imaging] is currently considered the most valuable method to confirm a diagnosis of Wernicke's encephalopathy."[10(p450)] This statement is supported by the European Federation of Neurological Societies guidelines.[5] MRI is used to detect the presence of lesions on the brain, a sign of thiamine deficiency–induced neurologic damage. These lesions are typically found in the thalamus and mammillary bodies in alcoholics with WE and throughout other regions of the brain in nonalcoholics with WE.[5] Like laboratory testing, MRI suffers from inadequacies. Because of its low sensitivity (53%) but high specificity (93%) and positive predictive value (89%),[22] it should be used to help clinicians rule out but not solely diagnose the disorder.[10]

Management of WE

Since WE is a progressive condition with both potentially permanent and lethal consequences, it is considered a medical emergency. Early identification and immediate intervention, as outlined in Figure 1, are crucial to producing positive patient outcomes.[3,10] Even in the absence of a confirmed diagnosis, it is advised that clinicians initiate interventions in suspected cases.[3,10]

The treatment of WE focuses on the administration of thiamine at therapeutic doses. The lack of randomized controlled trials precludes the establishment of strong evidence-based guidelines for thiamine administration. The current published guidelines are based primarily on case reports. While no consensus exists as to the ideal thiamine dose and form or duration of treatment, both the Royal College of Physicians[2] and the European Federation of Neurological Societies[5] have published guidelines for the treatment of WE in alcoholics. These guidelines must also serve as the basis for the management of WE in nonalcoholics since no published guidelines specific to this population exist.

In patients who are identified as at risk for developing WE, who display WE-like symptoms, or who are diagnosed with WE, immediate high-dose thiamine administration either intravenously (IV) or intramuscularly (IM) is recommended to raise the blood concentration and cellular uptake in a timely manner.[2,5] Time is of the essence in reversing and preventing neurologic damage. For at-risk patients, free thiamine of 250 mg plus additional B-complex vitamins (250 mg thiamine, 4 mg riboflavin, 160 mg niacin, 50 mg vitamin B_6) and 500 mg of vitamin C should be infused IV daily for 3 to 5 days.[2] An alternative approach is an IM injection of 250 mg thiamine daily for 3 to 5 days.[3]

In patients with either a confirmed or a suspected diagnosis of WE, free thiamine of 500 mg plus additional B-complex

Table 3. Identification of Frequent Signs and Symptoms of Wernicke's Encephalopathy Through Clinical Assessment.

Clinical Assessment	Description	Sign or Symptom[5,21]
Food/nutrition-related history	Conduct interview to gather information	Anorexia Inadequate dietary intake Nutrient deficiency
Anthropometric measurements	Measure weight and obtain weight history	Weight loss
Patient affect	Conduct interview to gather information	Apathy, fatigue, weakness Mental status changes Confusion, confabulation Apprehension, fear, anxiety
General physical examination	Visually inspect body posture, gait, musculature	Uncoordinated muscle movements
Cranial nerve examination	Optic nerve (CN II): Use a pen light to assess pupillary reaction	Loss of vision Double vision Poor reactivity to light
	Oculomotor (CN III), trochlear (CN IV), abducens (CN VI): Use a pen light to assess eye movements using the H or Box Test	Uncoordinated eye movement
	Spinal accessory (CN XI): Test range of motion and muscle strength by having the patient move his or her head from left to right and shrug his or her shoulders with and without resistance applied	Uncoordinated muscle movements
Client history	Conduct interview to gather information	Nausea and vomiting Seizures

CN, cranial nerve.

vitamins and vitamin C, the same amount as those listed above for at-risk patients, should be infused IV 3 times daily for 3 days. Some patients may require up to 1 g of thiamine within the first 12 hours.[2] These high doses are necessary since the pathophysiological alterations of WE temporarily diminish the body's ability to store thiamine and slow the thiamine-induced metabolic pathways.[5] Thus, more thiamine is required to stimulate cellular uptake and use. Depending on the severity of nutrient deficiencies, these patients may also require daily supplementation with magnesium (10–30 mEq), potassium (60–180 mEq), and phosphate (10–40 mmol). If improvement is observed after the 3 days, either IV infusion or IM injection should continue with 250 mg of thiamine plus B-complex and vitamin C once daily for 5 additional days or until no further improvement is experienced by the patient. At this point, the patient may be transitioned to oral administration of 100 mg thiamine 3 times daily.[2] No specified time frame for oral supplementation has been defined.

The oral administration of thiamine is ineffective in correcting the moderate to severe thiamine deficiency seen in patients with WE.[5] This ineffectiveness results from 2 causes. First, the intestinal absorption of thiamine is a saturable process, meaning that a threshold exists at which a maximum amount is able to be absorbed at a single time.[2,3] Second, the malnourished state that patients with WE exhibit can reduce the degree of nutrient absorption, including thiamine absorption.[2] In a healthy individual with adequate thiamine status, the body is able to absorb only 4.5–5.6 mg from a single oral dose of 30 mg of thiamine.[3,23] In patients with malabsorption, the amount of thiamine absorbed decreases to only 1.5 mg per single 30-mg oral dose.[2,3] Until recently, it has been assumed that the 30-mg dosage is the threshold point at which the body absorbs the maximum level of thiamine and that higher oral doses do not lead to increased absorption. However, Smithline et al[18] demonstrated enhanced thiamine absorption with the oral administration of single doses of 1,500 mg versus 100 mg and 500 mg. The doses of 100 mg and 500 mg led to a gradual increase in whole blood and plasma thiamine concentration 3 hours after administration and then stabilized. In contrast, the dose of 1,500 mg led to a steep increase, significantly more than the other doses, 4 hours after administration and then gradually declined thereafter but still remained higher than the 100-mg and 500-mg doses. While this study did not assess thiamine saturation of body tissues nor the efficacy of these doses in treating thiamine deficiency, this study does demonstrate that higher thiamine doses may be more bioavailable to the body.[18] This area warrants further investigation, particularly as it pertains to the use of oral thiamine in the management of WE.

While presently not recommended for the active treatment of WE, oral thiamine supplementation is recommended for the prevention and maintenance stages of WE. Otherwise healthy patients with mild thiamine deficiency should consume 30 mg

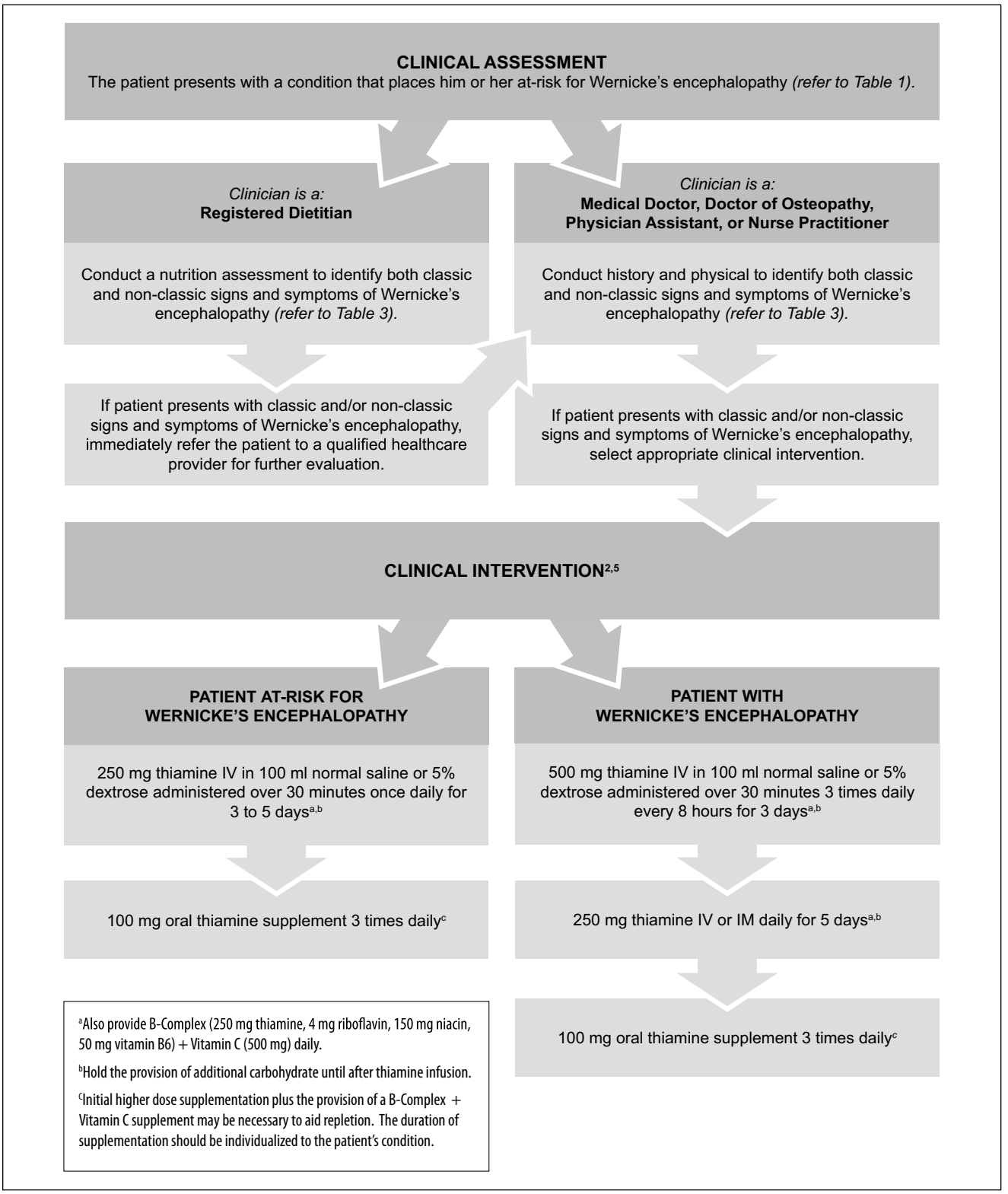

Figure 1. Pathway for the clinical assessment and intervention of Wernicke's encephalopathy.

thiamine 3 times per day.[2] Prophylactically, alcoholics should consume 200 mg thiamine plus additional B-complex vitamins daily.[2] Patients recovering from WE should consume 100 mg thiamine 3 times per day.[2] Consideration should be given to the

half-life and T_{max} of oral thiamine doses when determining timing of supplementation. Tallaksen et al[24] found the half-life of 50 mg of oral thiamine to be about 150 minutes. Smithline et al[18] found the T_{max} of 100 mg, 500 mg, and 1,500 mg to be approximately 3 to 4 hours. Thus, oral doses should be spaced 3 to 5 hours apart to maintain a consistent thiamine concentration in the blood.

Thiamine administered orally, IV, or IM at the recommended therapeutic doses is deemed safe. Documented side effects with high-dose (at least 100 mg) IV and IM administration include localized (at the injection site) and generalized skin irritation[25] and anaphylaxis.[26,27] Those with a history of asthma and allergies are assumed to be at the greatest risk for developing these adverse reactions.[3] The risk of skin irritation may be reduced by administering IV thiamine diluted in either 100 mL normal saline or 5% dextrose over a time period of at least 30 minutes.[3,5] The risk of anaphylaxis may be further reduced by administering thiamine as a time-infused dose (i.e., over the course of 30 minutes)[2] through a small number of divided doses.[2,3] As a precautionary measure, high nonoral doses of thiamine should be administered under medical supervision in the event that resuscitation is required.[2,3,5] Pertaining to oral doses, in patients with Alzheimer disease, divided doses slowly titrated up to 7,000 mg and provided daily for 12 months demonstrated overall safety.[28] Only minor side effects of nausea and indigestion were noted. Therefore, as previously mentioned, no tolerable upper intake level has been established, and the recommended therapeutic doses of thiamine administered either orally, IV, or IM for the prevention and treatment of WE are considered safe.

A Case for Consideration: Patient Profile—Background, History, and Clinical Course

Having discussed the identification, management, and serious nature of WE, primarily as it applies to the classic cause of alcoholism, it is imperative for clinicians to consider how WE develops, may be identified, and may be treated in patients with nonclassic causes, such as malnutrition/starvation. The following case illustrates the clinical course of a patient with fasting-induced WE and her response to both standard and nonstandard interventions.

The patient was a 54-year-old Caucasian woman who presented to the emergency department of a local hospital 2 weeks after completing a 40-day water-only fasting diet for religious purposes. After completing the fast, she began to slowly consume food, starting with vegetable broth and coconut milk and advancing to bland solid foods. One week later, she began to experience apathy, confusion, and disorientation. At this time, her family took her to a local hospital, where she underwent a computed tomography scan, laboratory testing, and IV administration of normal saline. When the tests came back negative for any clinically relevant diagnosis, the physician recommended that she undergo a lumbar puncture and be admitted for observation. She refused and was discharged. Upon discharge, a family member who is a registered dietitian advised the family of potential nutrient deficiencies (including thiamine) and refeeding syndrome. The family purchased over-the-counter thiamine and B-complex supplements and began to more aggressively reintroduce a nutrient-dense diet to the patient. Upon initial administration of 100 mg oral thiamine caplets every 4 hours, the patient's condition improved slightly for 2 days, but after 2 days, her condition deteriorated, to the point of short-term memory loss, disorientation/confusion, confabulation, and visual impairment, leading her family to again seek medical attention at a local hospital. Upon presentation to a different hospital, she was alert and responsive with confusion and altered mental status.

The patient was a married homemaker with 2 adult children. Her history was negative for tobacco and alcohol use. Her family history was positive for Alzheimer disease (mother). Her medical history included asthma and seasonal affective disorder. Her surgical history was nonsignificant, and she was not taking any medications. Frequently, she used various over-the-counter herbal supplements and natural remedies for the management of her health. Prior to the fast, her diet was nutrient dense and varied. She consumed 24 fL oz of black tea and/or coffee daily. Because of food intolerances, she avoided chicken and pork products.

The patient's vital signs were within normal limits. Her physical examination revealed nothing physically abnormal. Neurologically, she demonstrated nystagmus, intermittent mental confusion, and uncooperative behaviors. She complained of blurred vision, stating that everything looked "white and warm and fuzzy," like an overexposed picture. Findings from a second computed tomography scan were normal. The patient refused an MRI and lumbar puncture.

Based on her nonexistent kilocalorie intake for ≥1 month, weight loss of almost 5% in >1 month, mild fat and muscle mass loss (as assessed through visual inspection), a lack of known inflammation, and a lack of fluid accumulation, the patient displayed starvation-related moderate malnutrition.[29] Her admission laboratory values demonstrated nutrient depletion and negative nitrogen balance related to her malnourished state. Although her albumin and prealbumin levels were within normal limits, these values can remain stable in malnourished and starved individuals[30] and must be interpreted with caution as they do not always identify malnutrition.

The family member who is a registered dietitian suggested to the attending physician that the patient may be experiencing thiamine deficiency leading to the development of WE. The physician agreed with this assessment. Parenteral thiamine 500 mg in 50 mL 5% dextrose piggyback 1,000 mL normal saline over 30 minutes was ordered and provided to the patient in the emergency department. The patient's condition improved immediately and dramatically, with her mental status reverting to normal.

The patient presented with WE secondary to acute fasting-induced thiamine deficiency. Although a direct whole-blood thiamine concentration was not drawn in the hospital to assess her thiamine status and confirm the medical diagnosis of WE,[3,5] her responsiveness to parenteral thiamine strongly suggests that she was thiamine deficient. This deficiency is not unreasonable to assume given her history of fasting for 40 days.

The patient received a total of 3 doses of parenteral thiamine 500 mg in 50 mL 5% dextrose piggyback 1,000 mL normal saline infused at 110 mL/h over 30 minutes every 12 hours while hospitalized overnight. Following discharge, she received 3 additional doses of parenteral thiamine 500 mg every 8–12 hours through outpatient treatment. She was advised by the discharging physician to consume 100 mg thiamine daily for at least 1 month and to follow a regular diet. The patient supplemented with 100 mg thiamine mononitrate (Solaray, Park City, UT) every 3 hours daily, a B-complex supplement providing an additional 5 mg thiamine daily (Garden of Life Vitamin Code Raw B Complex, West Palm Beach, FL), and a multivitamin providing an additional 4 mg thiamine daily (Garden of Life Vitamin Code 50 & Wiser Women) for the first 3 weeks postdischarge. During the first 2 days postdischarge, the patient consumed an over-the-counter thiamine supplement in caplet form; however, she did not feel that she was digesting and absorbing this well. She switched to a capsule form and broke the capsule prior to ingestion to ensure release of the thiamine into her gastrointestinal tract for faster and easier absorption. She also consumed the supplements with orange juice, which contains vitamin C to serve as a reducing agent, to enhance thiamine absorption.[12]

Two weeks postdischarge, blood was drawn at an outpatient clinic to assess her thiamine concentration, which was normal. After week 3, the outpatient physician advised her to reduce her daily oral dose of thiamine to 50 mg. After a couple of days of taking the 50-mg dose and noticing a decline in her condition, the patient increased her intake back to 100 mg daily. She continued this regimen sporadically for 6 months postdischarge, at which point she returned to her prefasting energy and mental acuity levels.

Discussion and Comparison to the Evidence

In this case, WE was caused by fasting leading to malnutrition.[2,5,10] If the body does not acquire adequate thiamine through oral ingestion, the body's thiamine stores will be depleted within 3 to 4 weeks,[3,10] initiating a metabolic cascade toward the development of WE. It is likely that she did not manifest symptoms of thiamine deficiency until after the fasting was completed and food was reintroduced for the following reasons. Within the first 72 hours of fasting, the rate of carbohydrate utilization for energy synthesis declined as glycogen stores were depleted. During this time, the rate of lipolysis and ketone body formation increased to provide the body's cells with needed energy.[31] Gluconeogenesis, or the production of glucose from noncarbohydrate sources, provided the necessary glucose for the body's cells, particularly the brain cells.[31] The patient's prefasting thiamine stores may have been adequate to sustain substrate oxidation during the fasted state. However, as dietary macronutrients were reintroduced and oxidation increased, the body's metabolic demands for thiamine greatly increased, yet the body's thiamine-deficient state could not meet these demands. At this point, the brain's demand for thiamine as a necessary coenzyme[2,10] exceeded supply, resulting in cellular damage and the manifestation of WE in the patient.

While the patient did not present with the classic cause (alcoholism) or all 3 of the classic symptoms of WE, she did present with 3 of the 4 operational criteria.[20] These included nutrient deficiency (fasting), ocolomotor abnormalities (nystagmus), and altered mental status and memory impairment. She also displayed symptoms of mild, moderate, and severe WE, including anorexia, visual alterations, short-term memory loss, apathy, apprehension, emotional changes, disorientation, and confabulation.[21] Ideally, to support and confirm the diagnosis of WE, the patient should have had blood work drawn to assess her whole-blood thiamine concentration and undergone an MRI to determine if brain lesions were present[2,10]; however, these 2 assessments were not performed. The physician did immediately order parenteral thiamine upon the suspicion of WE, which is encouraged within the management guidelines.[2,5]

The patient was treated with parenteral thiamine in accordance with the management guidelines for WE.[2,3,5] While she received up to 2 doses per day instead of the 3 that are recommended and transitioned to outpatient therapy earlier than advised, her treatment fulfilled the guidelines of providing infusions until no further improvement was observed. Although advised for patients to receive additional B vitamins, vitamin C, and electrolytes during initial repletion,[2] the physician did not feel that this was warranted.

Upon discharge, the patient followed a regimen of oral thiamine supplementation greater than advised in the literature. As opposed to 100 mg 3 times day[2] to provide a total of 300 mg per day, she consumed 100 mg up to 8 times per day to provide a total of 800 mg per day. This dosage is considered safe as it does not exceed the documented daily threshold of 7,000 mg per day.[28] However, she did develop a rash on her torso, which is a documented side effect of high-dose oral thiamine supplementation.[25] This reaction is more likely in individuals with asthma and allergies,[3] which the patient had in her medical history. She did consume additional B-complex vitamins through B-complex and multivitamin supplements and a nutrient-rich oral diet including foods high in protein, phosphorus, potassium, and magnesium. Initially, she eliminated foods and beverages high in thiaminases and slowly reincorporated them into her diet.

Application to Practice and Conclusion

As aptly stated by Sechi et al, "The best aid for a correct diagnosis [of WE] is clinical suspicion."[10(p450)] However, clinical suspicion, particularly with patients who fail to demonstrate nonclassic causes and symptoms, appears greatly lacking among healthcare professionals. This lack of suspicion results in underdiagnosis and may lead to the occurrence of preventable, permanent psychosis and death in such patients.[2,3,5,10] This case report provides awareness that WE can develop in fasted/starved and malnourished patients and that it may be effectively managed by following the same guidelines established for the management of WE in alcoholics. In contrast to these guidelines,[2,5] oral doses of 100 mg thiamine every 3 hours daily for up to 3 weeks post–parenteral therapy may be necessary to promote initial thiamine repletion. Apart from the development of a rash, this level of supplementation appears safe. After 3 weeks, daily supplementation with a minimum of 100 mg thiamine may be required for maintenance, leading to full recovery by 6 months.

In addition, this case highlights the deleterious consequences of fasting and starvation-type diets. Individuals following these diets should be advised about the potentially permanent and lethal consequences of WE and Korsakoff syndrome that may ensue when such a diet is followed long term and/or frequently. If an individual's nutrient intake is inadequate prior to following such a diet, the manifestation of a nutrient-deficient disease state may be hastened. It is imperative that clinicians advise against fasting diets but likewise be alert to disorders of nutrient deficiency when patients present under these circumstances.

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