Wernicke-Korsakoff Syndrome in a Hunger Striker Despite Oral Thiamine Supplementation

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Case: We present the case of a 49-year-old woman who underwent a 237-day hunger strike on the streets of Pittsburgh, Pennsylvania. Despite medical supervision and appropriate micronutrient supplementation, including higher-than-recommended dosing of oral thiamine, the patient developed Wernicke’s Encephalopathy and subsequent Korsakoff Syndrome. She is now permanently impaired.

Introduction: Hunger strikers are subject to numerous sequelae of micronutrient deficiency. Among these are the paired conditions of Wernicke’s Encephalopathy and Korsakoff Syndrome, conditions secondary to prolonged thiamine deficiency. Unfortunately, few published guidelines exist regarding the medical management of hunger strikers. Preventative dosing guidance is borrowed from what is recommended for prolonged malnourishment from eating disorders or chronic alcohol use. Available guidelines are rarely academic. Rather, they were created by governmental agencies for the management of hunger strikers in prison or similar states of detention or incarceration. There is an indirect body of evidence that oral thiamine supplementation is rarely protective against the sequelae of thiamine deficiency in hunger strikers. We discuss supplementation recommendations and the evidence for their failure in practice. We briefly explore the historical evidence for the anatomic and physiologic changes of prolonged starvation that potentially explain this treatment failure, and offer alternatives to standard supplementation.

Conclusion: The current recommendations of the management of hunger strikers regarding the prevention of thiamine deficiency are inadequate, and rarely prevent the clinical sequelae. Alternate management strategies need to be both researched and empirically used, while that research is being carried out. Novel lipid-soluble thiamine derivatives have promise, but prophylactic intravenous/intramuscular thiamine should be explored as the current standard of care.

Keywords: Wernicke’s Encephalopathy, Korsakoff Syndrome, thiamine deficiency, hunger strike, hunger striker

Case Description
A 49-year-old woman began a hunger strike. Her son died under unclear circumstances while away at college, and she began a public protest in order to ascertain the details surrounding his death, and to affect systemic changes within the campus police force regarding body camera use and de-escalation training.

Other than an elevated BMI, the patient had no other past medical or surgical history, including no history of mental health concerns. She took no medications and did not smoke or drink. She worked as a government analyst and functioned with a high degree of personal and professional responsibility. Nearly 1 year after her son’s death, she began her public protest while living on the street in a tent.

She was routinely monitored by volunteer emergency medical technicians, student nurses, medical students, and a group of medical residents from the local free clinic. She was given hydration guidelines and a supply of micronutrient supplements, including thiamine (150 mg twice daily as isolated liquid thiamine hydrochloride, and 150 mg of thiamine in her liquid multivitamin once per day for a total of 450 mg per day). Supplement specifics include Supplement 1: Adult Liquid Multivitamin taken once daily. Amounts listed as % of Daily Value. Vitamin A: 100%. Vitamin C: 100%. Vitamin D: 100%. Vitamin E: 100%. Vitamin B 1,2,3,5,6,7,9,12: 100%. Iron: 19%. 1.12 mg of proprietary blend trace colloidal minerals. Supplement 2: Powder mineral supplement taken twice daily. Calcium: 37%. Magnesium: 29%. Supplement 3:
1000 mcg subcutaneous Vitamin B12 given every 3 months. Supplement 4: Thiamine Hydrochloride, 150 mg, liquid, taken twice daily. She received frequent exams by a team of medical providers, verification of appropriate medication use and storage, and regular vitamin B12 injections. Compliance was monitored by proxy, by checking that she was asking for refills at appropriate times. Oral micronutrient supplementation began on day 14 of her strike and continued until day 237 when she was hospitalized. In addition to water, the patient occasionally consumed iced tea, coffee, and lemonade with calories totaling 200–400 per day, and was instructed not to consume her coffee or tea within an hour of taking her supplements.

Symptoms progressed and accumulated throughout her strike. Starting within weeks of beginning her fast, she developed abdominal discomfort, orthostasis, and diarrhea. Generalized muscle spasms happened intermittently. By the last week of the first month, she was experiencing episodic vertigo without reproducible nystagmus, and was having regular episodes of syncope and emotional lability. She soon developed severe insomnia, fatigue, heart palpitations, and had to walk slowly and deliberately due to feelings of instability. By month 3, her exam was notable for trace peripheral edema, ambulatory instability and ataxia, profound orthostasis, lateral rectus palsy as well as intermittent nystagmus, bradycardia, bradykinesia, word-finding difficulties, difficulty with attention, and anterograde amnesia. In the days leading up to her hospitalization, she had been rendered immobile by headaches, ataxia, repeated syncope, and persistent vertigo.

On examining the patient on day 236, her medical providers found her to be encephalopathic. She presented to the emergency department and was admitted to the hospital on a medicine service for assessment. Her strike lasted 237 days. Her weight and BMI loss was over 40%. Her Glasgow Coma Score (GCS) was 13. Her admission labs were notable for multiple but relatively mild abnormalities. Labs obtained included a complete blood count, a comprehensive metabolic panel, electrolytes (including calcium, magnesium, and phosphorous), a thyroid stimulating hormone level, fat-soluble vitamin levels, trace minerals (copper and zinc), folic acid and B12, an HIV test, and an iron panel. All labs were within normal limits except for folic acid (3.9 ng/mL: normal is >5.0), percentage iron saturation (20%; normal is 25–50%), lymphocyte percentage on differentiation (50%; normal is 13–44%), reticulocyte count (0.016/L × 10^{12}; normal is 0.018–0.158/L × 10^{12}), vitamin D 25-OH (16 ng/mL: normal is 25–100). Her admission diagnosis was Wernicke’s Encephalopathy based on her clinical findings of ataxia, encephalopathy, nystagmus, memory difficulties, and her recent span of prolonged malnutrition. She was started on maintenance fluids and IV thiamine, 500 mg three times daily. She responded immediately, showing dramatic and rapid improvement in alertness, vertigo, ataxia, nystagmus, encephalopathy and headache within 36 hours. She received no other therapeutic intervention during the first 36 hours. This regimen was continued for 5 days. When her encephalopathy had resolved, she ended her strike at the request of her medical providers. She began a supervised refeeding program and was monitored for refeeding syndrome. She was discharged with close follow-up.

Her cognitive recovery was incomplete due to sustained damage from thiamine deficiency. After returning to her job, she still suffered from insomnia, emotional lability, deficits in concentration, and severe anterograde amnesia that made her unable to perform the duties of her job. She has regularly followed up with her primary care physician and has established care with a neurologist and an occupational therapist. Despite the longitudinal efforts of her medical team, appropriate work accommodations and assistive techniques, she filed for, and has since been approved for, long-term disability due to Korsakoff Syndrome.

**Patient Approval**

Institutional Review Board (IRB) approval was not required for this case study. The patient has approved the use of her medical information in a case study and has approved the final text of this manuscript. She has signed a consent form indicating her approval.

**Introduction**

Wernicke-Korsakoff Syndrome is a constellation of acute and chronic sequelae of thiamine deficiency. Immediate manifestations can include encephalopathy, nystagmus, and ataxia, while long-term patients can suffer from anterograde amnesia among other pathologic manifestations.\(^1\) While traditionally seen in patients with heavy alcohol use and those
experiencing refeeding syndrome after a period of starvation, prolonged malnourishment from other causes has been recognized as well.\textsuperscript{2} In prolonged hunger strikes, the disease is common.\textsuperscript{3}

Few published guidelines exist regarding the medical management of hunger strikers. Those that mention thiamine recommend supplementing just before and during the refeeding period, or at maintenance dosing during the strike. Preventative dosing guidance is understandably sparse, and seems to be borrowed from what is recommended for prolonged malnourishment from eating disorders or chronic alcohol use. Available guidelines are rarely academic. Rather, they were created by governmental agencies for the management of hunger strikers in prison or similar states of detention or incarceration. The standard and unvaried recommendation, among those guidelines that specify, is to offer preventative oral supplementation in the isolated form of thiamine hydrochloride 100 mg PO daily, in conjunction with other B vitamins in a complex, or in multivitamins.\textsuperscript{4,5}

**Discussion**

As the patient was reluctant to take pills, micronutrient supplementation was provided via liquid, powder, and injectable formulations at doses consistent with daily requirements. Prophylactic thiamine was given as liquid thiamine hydrochloride at a dose of 300 mg per day in two divided doses, as well as 150 mg once daily with her multivitamin. Despite reported compliance with her oral thiamine regimen and appropriate guideline-informed dosing, the patient went on to develop signs and symptoms consistent with Wernicke’s Encephalopathy as determined by the Caine Criteria, eventually developing the associated Korsakoff Syndrome and significant permanent disability.\textsuperscript{6}

Non-compliance with her oral prophylactic regimen was a possibility. However, a review of the literature shows that this is not an isolated incident. A prospective case series by Basoglu et al, 2006 that followed 41 active incarcerated hunger strikers over a prolonged period of fasting, found that despite following dosing regimens several times higher than the recommended preventative thiamine supplementation (200–600 mg daily), all patients developed sequelae of Wernicke’s Encephalopathy, and most went on to develop permanent difficulties with amnesia and executive functioning. In this study, thiamine supplementation, and therefore compliance, was observed and documented by prison nursing staff, given with water containing both dissolved sucrose and salt. In this trial, supplementation began between day 9–20 of the strike.\textsuperscript{7}

Mechanisms for this prophylactic failure are speculative. Prolonged starvation and its effect on intestinal function, particularly on absorption, are understandably not studied in humans under controlled experimental conditions. Data that exists is extrapolated from a series of experiments on various animal models, or from case studies and series on humans. The latter knowledge is observational, gleaned from malnutrition due to disparate conditions, such as famine, voluntary fasts, substance abuse, and eating disorders.

Physician reports from famines in the early 20th century frequently refer to a “hunger diarrhea” that did not behave like standard infectious diarrhea and only affected the malnourished. Autopsies on those affected by famine show intestinal atrophy and flattening of anatomic folds. Just as in famine, post-mortem exams of hunger strikers showed intestines described as “transparent”.\textsuperscript{8} Intestinal biopsies of children suffering from acute malnutrition show a decrease in surface area predominantly caused by decreased height of intestinal villi.\textsuperscript{9,10} The microbiome may be affected as well, with studies suggesting the amount, location, and species of bacteria can be different in malnourished patients.\textsuperscript{11,12} Malnutrition from various causes has likewise been shown to alter intestinal permeability to nutrients.\textsuperscript{8,13} Thiamine deficiency can also be exacerbated by deficiencies in other nutrients, particularly magnesium, which is needed for optimal thiamine absorption and function.\textsuperscript{14} Intestinal changes in starvation have been observed more definitively in animal models, and often show findings consistent with what has been observed in humans.\textsuperscript{5}

Pharmacokinetics of absorbed substances, whether macronutrients, medicines, vitamins, or minerals, can be affected by many of these changing physiologic conditions.\textsuperscript{15,16} Thiamine absorption is a complicated process dependent on numerous factors, many of which are intraluminal or intracellular. It requires modification by secreted intestinal enzymes, and at standard concentrations is absorbed actively by a transporter protein given its poor lipid permeability. This transport process is also pH dependent. It is only at high concentrations that some amount of passive diffusion will occur.\textsuperscript{17} While the definitive cause of how hunger strikers receiving thiamine still develop deficiency and its sequelae remains unknown, it is worth considering if the limitations of atrophied intestinal mucosa, as well as the accompanying physiologic changes of starvation, cause a problem of bioavailability.
Given the complexity of thiamine absorption and the concerns about absorption in those undergoing hunger strikes, as well as numerous cases documenting the failure of current guideline-directed dosing, changing recommendations regarding management seems reasonable.

For those who are not incarcerated, supervising medical providers could consider higher and more frequent doses of oral thiamine, potentially relying on the less efficient passive diffusion that occurs at higher concentrations. The regimen may, however, be ineffective and require an overly restrictive dosing schedule. Intramuscular (IM) is likely to be more protective than oral dosing, but the supplies may be harder to obtain. While there are no published studies on a lack of availability of IM thiamine and delivery devices, the medical team for the patient who is the subject of this case study was not able to acquire this form from local pharmacies, either hospital or private. Many cities, at least in the US, have infusion centers that will administer thiamine with or without a physician prescription. While utilizing emergency departments has its limitations, it could be used as a safety net in this process. For those who are incarcerated, supervising providers should consider intravenous (IV) thiamine on a regular dosing schedule, although no tested regimen exists.

For those unwilling to have supplements repleted via an intravenous route, newer oral formulations of thiamine that are more lipid soluble, and thus able to be passively absorbed, could be more effective than standard formulations. Both Benfotiamine and thiamine propyl-disulfide are shown to produce higher thiamine levels in numerous body compartments. These formulations could be empirically considered in these patients if there is outright refusal or unavailability of IM or IV dosing. However, these options should be viewed as inferior as they have not been studied therapeutically to the same extent as parenteral thiamine, and they are completely untested in the hunger striker population. As absorption of other lipid-soluble vitamins is known to improve when ingested with lipids, there is reason for doubting absorption in someone undergoing a hunger strike. Despite some promising pharmacokinetic evidence from benfotiamine showing evidence for absorption without concurrent food administration in briefly fasted patients, extrapolating to a prolonged fasting population is currently premature.

There are several limitations in this case. The sample size of n = 1 limits generalizability and precludes statistical analysis, and the observational nature necessary in studying hunger strikers limits assessments of causality. While proxies of compliance were used in this study – appropriately timed refill requests by the patient, supervision and assistance by on-site volunteer medical staff, reported compliance by the patient – these metrics are not as robust as tracking compliance in an inpatient setting. However, the study by Basoglu et al shows that even when compliance is assured, the sequelae of thiamine deficiency are not prevented in hunger strikers.

This case study is unique because it calls into question the effectiveness of current guidelines for the prevention of Wernicke’s Encephalopathy in the hunger striker population. It provides evidence that extrapolating data and recommendations from other thiamine-deficient populations may not be externally valid for this population, and that these extrapolations have continued despite a growing body of evidence to the contrary. It is unfortunate that this case itself is not unique, and these possibly preventable outcomes continue. More studies are needed in this population regarding formulations and routes of preventative thiamine dosing.

**Conclusion**

The current recommendations on the management of hunger strikers regarding the prevention of thiamine deficiency and its clinical sequelae are inadequate. A growing body of evidence suggests that standard oral thiamine supplementation at doses used in refeeding syndrome or substance use is likely not protective, and alternate management strategies need to be both researched and empirically used, while that research is being carried out. Novel lipid-soluble thiamine derivatives may have promise but are lacking convincing evidence at this time. IV or IM thiamine should be explored as the current standard of care.

**IRB Approval**

This study did not require IRB approval, and the final manuscript was approved by the patient.

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Disclosure
The authors have no conflicts of interest to declare.

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