Things We Do for No Reason™: Prescribing Thiamine, Folate and Multivitamins on Discharge for Patients With Alcohol Use Disorder

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" (TWDFNR) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent clear-cut conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CLINICAL SCENARIO

A 56-year-old man with alcohol use disorder (AUD) is admitted with decompensated heart failure and experiences alcohol withdrawal during the hospitalization. He improves with guideline-directed heart failure therapy and benzodiazepines for alcohol withdrawal. Discharge medications are metoprolol succinate, lisinopril, furosemide, aspirin, atorvastatin, thiamine, folic acid, and a multivitamin. No medications were offered for AUD treatment. At follow-up a week later, he presents with dyspnea and reports poor medication adherence and a return to heavy drinking.

WHY YOU MIGHT THINK IT IS HELPFUL TO PRESCRIBE VITAMIN SUPPLEMENTATION TO PATIENTS WITH AUD AT HOSPITAL DISCHARGE

AUD is common among hospitalized patients.¹ AUD increases the risk of vitamin deficiencies due to the toxic effects of alcohol on the gastrointestinal tract and liver, causing impaired digestion, reduced absorption, and increased degradation of key micronutrients.².³ Other risk factors for AUD-associated vitamin deficiencies include food insecurity and the replacement of nutrient-rich food with alcohol. Since the body does not readily store water-soluble vitamins, including thiamine (vitamin B_1) and folate (vitamin B_9), people require regular dietary replenishment of these nutrients. Thus, if individuals with AUD eat less fortified food, they risk developing thiamine, folate, niacin, and other vitamin deficiencies. Since AUD puts

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patients at risk for vitamin deficiencies, hospitalized patients typically receive vitamin supplementation, including thiamine, folic acid, and a multivitamin (most formulations contain water-soluble vitamins B and C and micronutrients). Hospitalists often continue these medications at discharge.

Thiamine deficiency may manifest as Wernicke's encephalopathy (WE), peripheral neuropathy, or a high-output heart failure state. Untreated, acute WE can progress to irreversible Korsakoff's psychosis. Given the serious morbidity and mortality of unrecognized and untreated WE, hospitalists often start high-dose intravenous (IV) thiamine of 200 to 500 mg every 8 hours for at least 72 hours for patients with WE risk factors (including AUD) or those with suspected WE based on clinical presentation.^{4,5}

Hospitalists empirically treat with thiamine, folate, and other vitamins upon hospital admission with the intent of reducing morbidity associated with nutritional deficiencies. Repletion poses few risks to patients since the kidneys eliminate water-soluble vitamins. Multivitamins also have a low potential for direct harm and a low cost. Given the consequences of missing a deficiency, alcohol withdrawal-management order sets commonly embed vitamin repletion orders.

WHY ROUTINELY PRESCRIBING VITAMIN SUPPLEMENTATION AT HOSPITAL DISCHARGE IN PATIENTS WITH AUD IS A TWDFNR

Hospitalists often reflexively continue vitamin supplementation on discharge. Unfortunately, there is no evidence that prescribing vitamin supplementation leads to clinically significant improvements for people with AUD, and patients can experience harms.

Literature and specialty guidelines lack consensus on rational vitamin supplementation in patients with AUD. $^{2.7,8}$ Due to inaccuracies, do not test for folate levels. 9 In fact, clinical data, such as body mass index, more accurately predict alcohol-related cognitive impairment than blood levels of vitamins. 10 In one small study of vitamin deficiencies among patients with acute alcohol intoxication, none had low B_{12} or folate levels. 11 A systematic review among people experiencing homelessness with unhealthy alcohol use showed no clear pattern of vitamin deficiencies across studies, although vitamin C and thiamine deficiencies predominated. 12

In the absence of reliable thiamine and folate testing to confirm deficiencies, clinicians must use their clinical assessment

TABLE. Assessment for Vitamin Deficiency Risk Factors in Patients With AUD With Heavy, Regular Alcohol Intake

Dietary history revealing limited food intake, "tea and toast" diet Food insecurity

Malnutrition evidenced by weight loss, loss of muscle mass, cachexia

Confirmed vitamin deficiencies

Gastrointestinal conditions such as gastritis, chronic pancreatitis, gastric bypass

skills. Clinicians rarely evaluate patients with AUD for vitamin deficiency risk factors and instead reflexively prescribe vitamin supplementation. An AUD diagnosis may serve as a sensitive, but not specific, risk factor for those in need of vitamin supplementation. Once the diagnosis of AUD is made, further investigation can help discern which AUD patients will benefit from vitamins after discharge.

Other limitations make prescribing oral vitamins reflexively at discharge a low-value practice. Thiamine, often prescribed orally in the hospital and on discharge, has poor oral bioavailability. Unfortunately, people with AUD have decreased and variable thiamine absorption. To prevent WE, thiamine must cross the blood-brain barrier, and the literature provides insufficient evidence to guide clinicians on an appropriate oral thiamine dose, frequency, or duration of treatment. While early high-dose IV thiamine may treat or prevent WE during hospitalization, low-dose oral thiamine may not provide benefit to patients with AUD.

The literature also provides sparse evidence for folate supplementation and its optimal dose. Since 1998, when the United States mandated fortifying grain products with folic acid, people rarely have low serum folate levels. Though patients with AUD have lower folate levels relative to the general population, 15 this difference does not seem clinically significant. While limited data show an association between oral multivitamin supplementation and improved serum nutrient levels among people with AUD, we lack evidence on clinical outcomes. 16

Most importantly, for a practice lacking strong evidence, prescribing multiple vitamins at discharge may result in harm from polypharmacy and unnecessary costs for the recently hospitalized patient. Alcohol use is associated with decreased adherence to medications for chronic conditions,¹⁷ including HIV, hypertension, hyperlipidemia, and psychiatric diseases. In addition, research shows an association between an increased number of discharge medications and higher risk for hospital readmission. The harm may actually correlate with the number of medications and complexity of the regimen rather than the risk profile of the medications themselves.¹⁸ Providers underestimate the impact of adding multiple vitamins at discharge, especially for patients who have several co-occurring medical conditions that require other medications. Furthermore, insurance rarely covers vitamins, leading hospitals or patients to incur the costs at discharge.

WHEN TO CONSIDER VITAMIN SUPPLEMENTATION AT DISCHARGE FOR PATIENTS WITH AUD

When treating patients with AUD, consider the potential benefit of vitamin supplementation for the individual. If a patient with regular, heavy alcohol use is at high risk of vitamin deficiencies due to ongoing risk factors (Table), hospitalists should discuss vitamin therapy via a patient-centered risk-benefit process.

When considering discharge vitamins, make concurrent efforts to enhance patient nutrition via decreased alcohol consumption and improved healthy food intake. While some patients do not have a goal of abstaining from alcohol, providing resources to food access may help decrease the harms of drinking. Education may help patients learn that vitamin deficiencies can result from heavy alcohol use.

Multivitamin formulations have variable doses of vitamins but can contain 100% or more of the daily value of thiamine and folic acid. For patients with AUD at lower risk of vitamin deficiencies (ie, mild alcohol use disorder with a healthy diet), discuss risks and benefits of supplementation. If they desire supplementation, a single thiamine-containing vitamin alone may be highest yield since it is the most morbid vitamin deficiency. Conversely, a patient with heavy alcohol intake and other risk factors for malnutrition may benefit from a higher dose of supplementation, achieved by prescribing a multivitamin alongside additional doses of thiamine and folate. However, the literature lacks evidence to guide clinicians on optimal vitamin dosing and formulations.

WHAT WE SHOULD DO INSTEAD

Assess patients for AUD, provide motivational interviewing, and offer AUD treatment. Hospitalists should initiate and prescribe evidence-based medications for AUD for patients interested in reducing or stopping their alcohol intake. We can choose from Food and Drug Administration FDA-approved AUD medications, including naltrexone and acamprosate. Unfortunately, less than 3% of patients with AUD receive medication therapy.²⁰ Our healthcare systems can also refer individuals to community psychosocial treatment.

For patients with risk factors, prescribe empiric IV thiamine during hospitalization. Clinicians should then perform a risk-benefit assessment rather than reflexively prescribe vitamins to patients with AUD at discharge. We should also counsel patients to eat food when drinking to decrease alcohol-related harms. ¹⁹ Patients experiencing food insecurity should be linked to food resources through inpatient nutritional and social work consultations.

Elicit patient preference around vitamin supplementation after discharge. For patients with AUD who desire supplementation without risk factors for malnutrition (Table), consider prescribing a single thiamine-containing vitamin for prevention of thiamine deficiency, which, unlike other vitamin deficiencies, has the potential to be irreversible and life-threatening. Though no evidence currently supports this practice, it stands to reason that prescribing a single tablet could decrease the number of pills for patients who struggle with pill burden.

RECOMMENDATIONS

- Offer evidence-based medication treatment for AUD.
- Connect patients experiencing food insecurity with appropriate resources.
- For patients initiated on a multivitamin, folate, and highdose IV thiamine at admission, perform vitamin de-escalation during hospitalization.
- Risk stratify hospitalized patients with AUD for additional risk factors for vitamin deficiencies (Table). In those with additional risk factors, offer supplementation if consistent with patient preference. Balance the benefits of vitamin supplementation with the risks of polypharmacy, particularly if the patient has conditions requiring multiple medications.

CONCLUSION

Returning to our case, the hospitalist initiates IV thiamine, folate, and a multivitamin at admission and assesses the patient's nutritional status and food insecurity. The hospitalist deems the patient—who eats regular, balanced meals—to be at low risk for vitamin deficiencies. The medical team discontinues folate and multivitamins before discharge but continues IV thiamine throughout the 3-day hospitalization. The patient and clinician agree that unaddressed AUD played a key role in the patient's heart failure exacerbation. The clinician elicits the patient's goals around their alcohol use, discusses AUD treatment, and initiates naltrexone for AUD.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No ReasonTM"? Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No ReasonTM" topics by emailing TWDFNR@hospitalmedicine.org.

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References

- Makdissi R, Stewart SH. Care for hospitalized patients with unhealthy alcohol use: a narrative review. Addict Sci Clin Pract. 2013;8(1):11. https://doi. org/10.1186/1940-0640-8-11
- Lewis MJ. Alcoholism and nutrition: a review of vitamin supplementation and treatment. Curr Opin Clin Nutr Metab Care. 2020;23(2):138-144. https://doi. org/10.1097/mco.000000000000622
- Bergmans RS, Coughlin L, Wilson T, Malecki K. Cross-sectional associations
 of food insecurity with smoking cigarettes and heavy alcohol use in a population-based sample of adults. *Drug Alcohol Depend*. 2019;205:107646.
 https://doi.org/10.1016/j.drugalcdep.2019.107646

- Latt N, Dore G. Thiamine in the treatment of Wernicke encephalopathy in patients with alcohol use disorders. *Intern Med J.* 2014;44(9):911-915. https://doi.org/10.1111/imj.12522
- Flannery AH, Adkins DA, Cook AM. Unpeeling the evidence for the banana bag: evidence-based recommendations for the management of alcohol-associated vitamin and electrolyte deficiencies in the ICU. Crit Care Med. 2016;44(8):1545-1552. https://doi.org/10.1097/ccm.000000000001659
- Wai JM, Aloezos C, Mowrey WB, Baron SW, Cregin R, Forman HL. Using clinical decision support through the electronic medical record to increase prescribing of high-dose parenteral thiamine in hospitalized patients with alcohol use disorder. J Subst Abuse Treat. 2019;99:117-123. https://doi. org/10.1016/j.jsat.2019.01.017
- American Society of Addiction Medicine. The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management. January 2020. https://www.asam. org/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf?sfvrsn=ba255c2_2
- O'Shea RS, Dasarathy S, McCullough AJ. Alcoholic liver disease. Hepatology. 2010;51(1):307-328. https://doi.org/10.1002/hep.23258
- Breu AC, Theisen-Toupal J, Feldman LS. Serum and red blood cell folate testing on hospitalized patients. J Hosp Med. 2015;10(11):753-755. https://doi.org/10.1002/jhm.2385
- Gautron M-A, Questel F, Lejoyeux M, Bellivier F, Vorspan F. Nutritional status during inpatient alcohol detoxification. *Alcohol Alcohol*. 2018;53(1):64-70. https://doi.org/10.1093/alcalc/agx086
- Li SF, Jacob J, Feng J, Kulkarni M. Vitamin deficiencies in acutely intoxicated patients in the ED. Am J Emerg Med. 2008;26(7):792-795. https://doi.org/10.1016/j.ajem.2007.10.003
- 12. Ijaz S, Jackson J, Thorley H, et al. Nutritional deficiencies in homeless persons with problematic drinking: a systematic review. *Int J Equity Health*. 2017;16(1):71. https://doi.org/10.1186/s12939-017-0564-4
- Day GS, Ladak S, Curley K, et al. Thiamine prescribing practices within university-affiliated hospitals: a multicenter retrospective review. J Hosp Med. 2015;10(4):246-253. https://doi.org/10.1002/jhm.2324
- Day E, Bentham PW, Callaghan R, Kuruvilla T, George S. Thiamine for prevention and treatment of Wernicke-Korsakoff syndrome in people who abuse alcohol. Cochrane Database Syst Rev. 2013;2013(7):CD004033. https://doi.org/10.1002/14651858.CD004033.pub3
- Medici V, Halsted CH. Folate, alcohol, and liver disease. Mol Nutr Food Res. 2013;57(4):596-606. https://doi.org/10.1002/mnfr.201200077
- Ijaz S, Thorley H, Porter K, et al. Interventions for preventing or treating malnutrition in homeless problem-drinkers: a systematic review. Int J Equity Health. 2018;17(1):8. https://doi.org/10.1186/s12939-018-0722-3
- Bryson CL, Au DH, Sun H, Williams EC, Kivlahan DR, Bradley KA. Alcohol screening scores and medication nonadherence. *Ann Intern Med*. 2008;149(11):795-803. https://doi.org/10.7326/0003-4819-149-11-200812020-00004
- Picker D, Heard K, Bailey TC, Martin NR, LaRossa GN, Kollef MH. The number of discharge medications predicts thirty-day hospital readmission: a cohort study. BMC Health Serv Res. 2015;15:282. https://doi.org/10.1186/s12913-015-0950-9
- Collins SE, Duncan MH, Saxon AJ, et al. Combining behavioral harm-reduction treatment and extended-release naltrexone for people experiencing homelessness and alcohol use disorder in the USA: a randomised clinical trial. *Lancet Psychiatry*. 2021;8(4):287-300. https://doi.org/10.1016/S2215-0366(20)30489-2
- Han B, Jones CM, Einstein EB, Powell PA, Compton WM. Use of medications for alcohol use disorder in the US: results From the 2019 National Survey on Drug Use and Health. JAMA Psychiatry. 2021;78(8):922–4. https://doi. org/10.1001/jamapsychiatry.2021.1271