

Three Common Micronutrient Deficiencies in Patients with Alcohol Use Disorder

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Nutrient deficiencies are common among patients with alcohol use disorder (AUD) and can greatly affect their health. Nutrient deficiencies are associated with cognitive impairment,¹ Wernicke's encephalopathy,² withdrawal seizures,^{3,4} and delirium tremens,³ all of which complicate clinical care.

Although there are many nutritional deficiencies associated with alcohol consumption (Vitamins A, B1, B2, B3, B6, B9, B12, C, D, E, selenium, and zinc), the three most common and impactful micronutrient deficiencies for patients with AUD include:

Vitamin B1 (Thiamine)

80% of patients with AUD are deficient in thiamine.⁵

Magnesium

44% and higher of patients with AUD are deficient in magnesium.⁶

Vitamin C (Ascorbic Acid)

70% and higher of patients with AUD are deficient in vitamin C.^{7,8}

Overview

Thiamine is related to the breakdown of glucose and the production of ATP (energy) at a cellular level.² Magnesium is a cofactor for thiamine-related enzymes and is involved in hundreds of different chemical reactions in the body. In fact, it is involved in 80% of the known human metabolic reactions.⁹ Without sufficient nutrients at the cellular levels in the body, the body behaves like an engine that has run out of gasoline (thiamine) and oil (magnesium).

Vitamin C deficiency impacts energy production (carnitine),¹⁰ neurotransmitter production,^{11,12} and destabilizes the C-amidated peptide hormone system which includes a group of over 70 hormones that regulate multiple body functions.¹³

Thiamine - Clinical Features and Management Considerations



Mechanism of Action

Thiamine breaks down glucose via the enzymes of transketolase, pyruvate dehydrogenase, and alpha-ketoglutarate dehydrogenase – these metabolic steps result in glucose breaking down into ATP molecules in the Krebs cycle.²



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Common clinical symptoms include mental status changes, balance changes, and ocular changes, but these are not always seen.²

Dysautonomia symptoms (like POTS, non-cardiac chest pain, and CRPS) are related to thiamine deficiencies.¹⁴ The more dysautonomia symptoms are present, the more likely thiamine deficiency is present.



Recommended Doses

Oral Thiamine Formulations (Outpatient or Maintenance/ Prevention):

- Thiamine tetrahydrofurfuryl disulfide (TTFD) 50–100 mg PO twice daily.¹⁵
- Benfotiamine 150–300 mg PO twice daily.¹⁶

Prevention of Wernicke's Encephalopathy (At-risk Patients Without Neurologic Symptoms):

- Thiamine hydrochloride 100–200 mg IV or IM once daily for 3–5 days, followed by thiamine 100 mg PO TID thereafter.¹⁷

Wernicke's Encephalopathy (Inpatient Settings):

- Thiamine hydrochloride 500 mg IV every 8 hours (TID) for 3–5 days followed by 100 mg PO TID for thereafter.^{14,17}
- Thiamine hydrochloride 200–500 mg IV daily may be continued for up to 7 days total based on clinical response, followed by transition to oral thiamine as above.



Common Side Effects of Supplementation

IV/IM: Anaphylaxis (1 case per 5 million doses; low risk)¹⁷

Oral: Headaches, nausea

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Contraindications & Precautions

Contraindications: Allergies to any component of the formulation of thiamine.

Formulation Precautions: There are no substantial differences in the oral absorption rates between thiamine tetrahydrofurfuryl disulfide and benfotiamine.¹⁸

Clear data demonstrate that oral thiamine hydrochloride¹⁵ or oral thiamine mononitrate¹⁸ are not well absorbed orally; therefore, IV or IM replacement in the inpatient setting is suggested. Thiamine hydrochloride in oral format does not work in patients with Wernicke's encephalopathy.¹⁹

Warnings and precautions: High-dose vitamin B1 therapy should not be used in pregnancy unless working with an obstetrician (OB) who is well-versed in this type of therapy. There are no known teratogenic harms, but due to a lack of research, vitamin B1 is category A in doses consistent with recommended dietary allowance (RDA) recommendations and category C in doses above RDA recommendations.



Additional Considerations

- **Functional lab findings:** For thiamine deficiency, lab findings may include anion gap metabolic acidosis, elevated glucose levels, and ketonuria (all signs of the glycolysis and the Krebs' cycle breaking down in their functions).
- **Direct serum levels** for thiamine deficiency may be obtained, but this may delay diagnosis and treatment.
- Most patients (80%+ of patients have this deficiency) should start supplementation, and the intensity of supplementation is setting specific (e.g., IV in acute care settings, oral / IM in outpatient settings).
- Thiamine needs magnesium as a cofactor to be utilized. If the thiamine treatment is not producing clinical improvement, then magnesium deficiency is often present.²⁰
- If thiamine and magnesium supplementation are not improving Wernicke's encephalopathy symptoms, then vitamin B3 deficiency (pellagra) is often the issue (around 50% of "Korsakoff" cases demonstrate signs of pellagra on autopsy).²¹
- The treatment for alcoholic pellagra is niacinamide 100 mg PO TID for 3-4 weeks.²²

Magnesium - Clinical Features and Management Considerations ▼



Mechanism of Action

Magnesium is a metal cofactor for hundreds of chemical reactions in the body and is involved in over 80% of known chemical reactions in the body.⁹



Manifestation

Common clinical symptoms of magnesium deficiency include muscle dysfunction (skeletal or smooth), muscle weakness, arrhythmia/palpitations, and osteopenia/osteoporosis.

Magnesium deficiency is commonly associated with metabolic diseases like hypertension, coronary artery disease, and diabetes.⁹



Recommended Doses

Magnesium sulfate 2 gm IV daily to BID for up to 7 days or around 350 – 400 mg PO daily with a highly bioavailable magnesium forms such as magnesium citrate and magnesium chelates like magnesium glycinate.²³

In the best study available, magnesium sulfate IV infusion of 3.6 grams per day for 7 days was equivalent to magnesium-lactate-citrate at 360 mg per day for 6 weeks with confirmed repletion status using a magnesium-loading test.²³



Common Side Effects of Supplementation

IV: Facial warmth, flushing²⁴

Oral: Nausea, diarrhea, GI cramping

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Contraindications & Precautions

Contraindications:

- Allergy to any component of the formulation.
- Severe renal disease.
- Severe gastrointestinal disease impairing absorption.
- Neuromuscular diseases like myasthenia gravis.²⁵

Warnings and precautions: High-dose therapy should not be used in pregnancy unless working with an OB who is well versed in this type of therapy. In oral doses up to the RDA, magnesium supplementation is category A. However, in high dose IV form for > 5 days (long term use) magnesium is category D.

The bioavailability of doses varies greatly between formulations. Salt formations are the least bioavailable (magnesium oxide is poorly absorbed and should not be used first line). The amino acid chelates are more bioavailable.²⁶ Consider the amino acid in the chelate as part of the therapy, as they have therapeutic effects themselves.



Additional Considerations

- **Functional lab findings:** For magnesium deficiency, lab findings may include hyponatremia, hypokalemia, hypocalcemia, hypophosphatemia, thrombocytopenia,²⁷ anion gap metabolic acidosis (thiamine cofactor), ketonuria (thiamine cofactor),² and AST/ALT/GGT elevations.²³
- **Direct serum magnesium levels** that are normal do not rule out significant whole-body magnesium deficiency. Abnormal functional labs (see above) are associated with magnesium deficiency (even with a normal serum magnesium level), and oral magnesium supplementation should be added until these other lab findings normalize.
- If the serum magnesium level is low, consider IV doses of magnesium sulfate until the serum level normalizes before converting to oral magnesium supplement therapy.

Vitamin C - Clinical Features and Management Considerations



Mechanism of Action

Vitamin C is an obligate cofactor of the PAM enzyme, which is responsible for activation of peptide hormones (including GLP-1, beta-endorphin, antidiuretic hormone, and around 70 others), neurotransmitter production, collagen production, and carnitine production.¹²



Manifestation

Common clinical symptoms of vitamin C deficiency include muscle weakness, easy bruising or bleeding, gingival changes, poor wound healing, and an association with upper GI bleeding.^{7,28}



Recommended Doses

Doses are individualized by GI toleration (high dose therapy can be limited by nausea, stomach cramping and diarrhea) but can be dosed up to 500 mg by mouth four times a day (2,000 mg per day) in oral ascorbic acid tablet form or 1,500 mg IV every 6 hours (6,000 mg per day) if the IV form is needed to correct the deficit.⁸

Individualization of dosage should consider other clinical factors (like history of renal stones or gastroesophageal reflux disease) and how well the patient tolerates the formulation (tablets, powders, liposomal). Some people will tolerate one form nicely but will have GI symptoms with another, and thus formulation should be determined on a case-by-case basis.

Liposomal forms, available in liquid, capsule, and sachet forms, are more bioavailable²⁹ and can be used if doses higher than 2,000 mg are needed in an oral format.

IV should be used when a person is unable to tolerate oral medications or supplements.

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Common Side Effects of Supplementation

IV: Oxalate nephropathy, hypernatremia, hemolysis in G6PD; overall, the adverse event rates are similar to placebo even in very high dose levels³⁰

Oral: Nausea, diarrhea, flatulence



Contraindications & Precautions

Contraindications:

- Frequent renal stone formation.
- Hemochromatosis.
- Glucose-6- phosphate deficiency (G6PD).
- Severe renal disease.

Warnings and precautions: High-dose vitamin C therapy should not be used in pregnancy unless working with an OB who is well-versed in this type of therapy. There are no known teratogenic harms, but due to a lack of research, vitamin C is category A in lower doses and category C in doses above 2,000 mg.

Doses higher than 2,000 mg may be needed in patients with severe vitamin C deficiency to improve their condition more rapidly.¹⁰



Additional Considerations

- **Functional lab findings:** For vitamin C deficiency, lab findings may include GGT elevation³¹ and other liver enzymes like AST and ALT.³²
- **Direct serum levels** for vitamin C may be obtained, but this may delay diagnosis and treatment.
- If the functional labs above are abnormal and there are clinical signs of deficiency, then vitamin C deficiency should be diagnosed empirically and treatment started.

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