

Can Wernicke's Encephalopathy Be Precipitated by Administering Glucose before Thiamine in Severely Malnourished or Alcoholic Patients?

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Abstract

We discuss the safety and controversy regarding the administration of glucose before thiamine with regards to precipitation of Wernicke's Encephalopathy in the severely malnourished and alcoholic patient population. Herein we review clinical features, pathophysiology and the relevant literature to provide an evidenced-based recommendation that thiamine replacement should not delay glucose administration acutely in the malnourished patient population.

Keywords

Wernicke's Encephalopathy, Thiamine, Glucose

1. Introduction

Can Wernicke's Encephalopathy be precipitated by administering glucose before thiamine in severely malnourished or alcoholic patients? The answer is not obvious and the bottom line is that physiologically, this can happen but most patients already have the manifestations of encephalopathy before they present to the emergency department. Moreover, the process does not happen immediately but rather evolves throughout a hospital course as documented in case reports and literature reviews. Current established guidelines are straightforward with the recommendation to not delay glucose administration while waiting for thiamine. In this article we review the current literature and case reports behind the controversy that still exists and make a case for why administration of glucose should not be delayed while waiting for thiamine in the emergency department

or other acute care settings.

2. Discussion

Thiamine deficiency manifests itself as a disease of the central and peripheral nervous system, cardiovascular system, and the gastrointestinal tract. Wernicke's Encephalopathy is a well known, serious complication of thiamine (Vitamin B1) deficiency characterized by a syndrome of altered mental status, ophthalmoplegia, and gait ataxia. Some other thiamine deficiency diseases are listed in **Table 1**.

The pathophysiology behind the disease relates to thiamine's key role in glucose metabolism. Thiamine is a cofactor for several enzymes in the TCA cycle including α -ketoglutarate dehydrogenase, pyruvate dehydrogenase, and transketolase. Thiamine is utilized after phosphorylation to thiamine pyrophosphate. In particular, a decrease in enzymatic activity leads to utilization of non-oxidative pathways for energy production and thus lactate accumulation in the brain, muscle and serum since pyruvate is not able to be shuttled into the TCA cycle. Severe lactic acidosis has been associated with thiamine deficiency [1] and worsened in these cases by glucose administrations. Although this may explain why thiamine deficiency is harmful, the association with causing Wernicke's Encephalopathy after glucose treatment remains unclear. But it seems some association likely exists.

In chronic alcoholics, thiamine absorption in the gut is inhibited for reasons that are not entirely clear. Subramanya and coworkers [2] recently described a mechanism of significant inhibition in carrier-mediated thiamine transport across the jejunal brush-border membrane associated with a significant reduction in levels of expression of thiamine transporter-1 in rats that were chronically fed alcohol. This work is based on the previous discovery that thiamine absorption in human small intestinal brush-border membranes proceeds via a pH-dependent, electroneutral, carrier-mediated mechanism [3].

There are two reports [4] [5] citing acute encephalopathy in 5 profoundly malnourished patients after receiving IV glucose solutions. However, none of these patients developed symptoms after a single dose of glucose. Additionally these patients developed their symptoms over a course of days. Nevertheless, proponents of "thiamine before glucose" feel otherwise and conclude that if a blood glucose test reveals no hypoglycemia, thiamine should be administered

Table 1. Syndrome—hallmarks of disease.

Wernicke's Encephalopathy	Mental status changes, ocular abnormalities, gait ataxia
Wet Beriberi	High-output cardiac failure with edema
Dry Beriberi	High-output cardiac failure without edema
Neuritic Beriberi	Polyneuropathy
Gastrointestinal Beriberi	Abdominal pain, lactic acidosis, vomiting

before glucose if possible as part of therapy [6]. Patients in starvation states can still exhibit normal serum glucose levels however because degraded proteins are not replenished and serve as carbon sources for glucose synthesis.

Koguchi and colleagues [7] describe a case in which a 61 year-old man with a significant history of alcoholism presented with altered mental status and after starting IV glucose, the patient fell into a coma. No time frame is given in the report, but the patient already had radiographic evidence of Wernicke's Encephalopathy as evidenced on MRI imaging of the head during his hospitalization. As shown in **Figure 1**, MRI revealed hyperintense lesions of the mammillary bodies and horns of the fourth ventricles consistent with Wernicke's Encephalopathy. Although the patient did not receive thiamine until Day 5 of his admission and died 3 months later from pneumonia, the authors concluded that an infusion of glucose to patients with a known thiamine deficiency is potentially fatal.

There also exists several cases of Wernicke's Encephalopathy occurring in patients with hyperemesis gravidarum [8] [9], some indolently via IV glucose administration. For the most part, neurologic symptoms were already present before therapy. In these patients, body stores of thiamine can be depleted in weeks and chronically ill patients may already have critically low thiamine levels; RBC transketolase activity requires thiamine as a cofactor and an assay of enzymatic activity will reflect the robustness of thiamine stores. However in animal models, glucose loading had no significant clinical consequence when administered to rats fed a thiamine-deficient diet for 21 days. Advanced neurologic dysfunction with glucose administration was only seen in rats fed thiamine-deficient diets for 28 - 35 days and that ataxia and other neurologic sequela were clinically noted prior to glucose challenge [10] [Table 2].

3. Conclusions and Summary of Recommendations

Much controversy still exists regarding acute precipitation of Wernicke's Encephalopathy by administering glucose before thiamine in severely malnourished and alcoholic patients. The bottom line is that physiologically, this can happen but in most documented case reports, patients already had the manifestations of encephalopathy before they presented to the emergency department or other

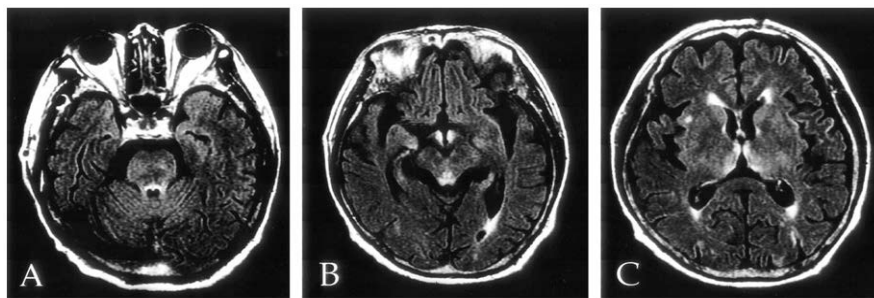


Figure 1. MRI image showing hyperintense lesions of the mammillary bodies and horns of the fourth ventricles consistent with Wernicke's Encephalopathy [7].

Table 2. Some causes of Wernicke's Encephalopathy.

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- Alcohol Abuse
 - AIDS
 - Malignancy
 - Hyperemesis gravidarum
 - Prolonged total parenteral nutrition
 - Post surgical patients
 - Iatrogenic glucose loading in any predisposed patient
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acute care setting.

Moreover, the process has been shown to actually evolve throughout a hospital course, rather than the acute care and initial treatment in the emergency department. Even in one case example where acute decompensation is described, no actual time course is given, and thiamine administration was delayed until 5 days after glucose. The established recommendations are straightforward: do not delay glucose administration while waiting for thiamine. Furthermore, thiamine is best administered parentally, preferably IV versus IM, since GI absorption in malnourished patients is very low. The recommended dose is 250 - 500 mg although there is little to no evidence-based studies supporting any dose (even doses as low as 2 mg have been effective).

In summary, Wernicke's Encephalopathy can be hastened by glucose administration but not in the time frame of a typical single emergent care visit. Moreover, glucose administration should not be delayed while waiting for thiamine administration. We did not uproot any studies reporting immediate findings of Wernicke's Encephalopathy, coma or death from appropriately treating a malnourished patient. In these patients, glucose and thiamine, amongst other nutrients, should be replaced via IV administration as soon as possible, but treatment with glucose should not be delayed if awaiting thiamine.

Conflicts of Interest

The authors have no conflicts of interest to report.

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