HYPEREMESIS GRAVIDARUM (HG) AND THIAMIN

1 MOM is 2 Many

amplify, educate, advocate

WHAT IS THIAMIN?

Thiamin (or thiamine) is a water-soluble B vitamin, also known as vitamin B1. Thiamin has many contributing roles including being an antioxidant, maintaining the myelin sheath, ATP production, branched-chain amino acid production, carbohydrate and lipid metabolism, and glucose-derived neurotransmitter synthesis (Pacei, 2020; Sechi, 2007; Thompson, 2002).

Sources: Thiamin naturally comes from food and supplements since the body cannot make significant amounts on its own. Magnesium and other electrolytes are important in proper absorption of B1 which occurs mainly in the upper jejunum, then it's transported for liver storage. The body has four forms of thiamin: free thiamine and three phosphorylated forms, including mono-(ThMP), di-(ThDP) and triphosphate (ThTP), with 80% of the body's thiamin being ThDP, which is metabolically the active form (Pacei, 2020).

Usage: Multiple enzyme complexes require the essential cofactor, ThDP, also known as thiamine pyrophosphate (TPP). Thiamin is delivered by erythrocytes to high use organs including the brain, heart, muscles, liver and pancreas. With thiamin, rapid reductions in ATP will occur with oxidative stress and eventually cell death (Pacei, 2020).

HG AND THIAMIN

Hyperemesis Gravidarum (HG) is defined as a potentially life-threatening pregnancy disease that may cause weight loss, malnutrition, dehydration, and debility due to severe nausea and/or vomiting and may cause long-term health issues for mother and baby(ies).

- **Storage:** The body's 25-30 mg of thiamine storage is depleted after about 2-3 weeks of restricted intake regardless of BMI, and more is needed during pregnancy (Chiossi, 2006; Manto, 2014; Veeprapaneni, 2014). So once a pregnant patient has been experiencing significant nausea and/or vomiting for 2 weeks or weight loss, they are at high risk of thiamin deficiency (TD).
- **Intake:** The recommended thiamin intake of 1.4-1.5 mg during pregnancy is inadequate for pregnancies with multiple gestations or HG (MacGibbon, 2015).
- **Absorption:** Studies report absorption by normal patients with oral dosing of thiamin at 300 mg/day will actually be reduced to 1/3rd or less of the dose (Thompson, 2002), suggesting those with HG and thus impaired absorption will need substantially higher doses. Further, malnutrition may reduce absorption of thiamin by up to 70% (Thompson, 2002).
- **Requirements:** HG patients also require high-dose B1 due to their high carbohydrate diet, coexisting deficiencies, limited food variety, impaired absorption, and reduced muscle mass for storage (Bellad, 2015; Ortega, 2004; Tanasescu, 2012; Xiong, 2015).
- The half-life of thiamin is short, just 1-12 hours (Pacei, 2020), necessitating more frequent administration in those with symptomatic thiamin deficiency.
- **Deficiency & HG:** TD may make nausea and vomiting refractory to treatment.
- **Complications:** Severe TD may trigger Wernicke's encephalopathy, while less severe or prolonged deficiency may lead to tachycardia, mental status changes, weight loss, peripheral neuropathy, and fetal loss or neurological damage in the child (Lonsdale, 2017; Sechi, 2007).

Oral Thiamin Derivatives:
(Lonsdale, 2017 p203-204)
Thiamin hydrochloride is readily available but not as absorbable as derivatives such as TTFD which provides a higher blood concentration of B1.

1. Thiamine tetrahydrofurfuryl disulfide (TTFD), a synthetic derivative, is preferred because it penetrates into cells without a thiamine transporter and crosses the blood-brain barrier. (Fursultiamine, Lipothiamine)
2. S-Benzoylthiamine monophosphate (Benfotiamine) does not cross the blood-brain barrier.

» Women with HG report to the HER Foundation that they have varying degrees of memory and cognitive impairment after HG and symptoms of TD, however, they were not diagnosed with or treated for TD or Wernicke's encephalopathy (WE). This suggests chronic TD during HG may pose risks of long-term neurological deficits even if WE does not fully develop.
» TD increases the risk of fetal loss, Sudden Infant Death Syndrome, and neurological disorders in children of mothers with HG. (Lonsdale, 2017)

THIAMIN DIFICIENCY (TD) SYMPTOMS

Thiamin deficiency (TD) can manifest after just 1 week as tachycardia at rest, peripheral neuropathy, weakness, and decreased reflexes. (Pancei, 2020) Continued deficiency develops into dry beriberi (neurological symptoms) or wet beriberi (cardiac symptoms), Wernicke's encephalopathy, or Central Pontine Myelinolysis (Manzo, 2014) that require immediate and aggressive intervention to prevent serious morbidity and mortality.

Early signs of TD mimic and exacerbate HG. Distinguishing symptoms from HG and the side-effects of some antiemetics that cause sleepiness, movement disorders, depression, dizziness and instability is problematic.

Assume all patients with HG have TD and prescribe IV and/or oral thiamin. Symptomatic patients require close assessment and IV infusion of thiamin.

» Weight Loss
» Confusion
» Memory loss
» Muscle weakness
» Cardiovascular symptoms (tachycardia, enlarged heart)
» GI Symptoms (vomiting, diarrhea, colitis)
» Peripheral neuropathy
» Fatigue
» Lack of appetite
» Vision, speaking, or thinking changes
» Irritability
» Pain in abdomen or head
» Mental changes, such as apathy or depression

MATERNAL COMPLICATIONS

(Said, 2010)

» Peripheral nerve damage
» Degeneration of thalamus and cerebellum
» Reduction of blood flow
» Vascular resistance
» Cardiac/respiratory failure
» Wernicke-Korsakoff Syndrome

CHILD COMPLICATIONS

85.2% of babies born to TD mothers are also deficient. (Xiong, 2015) If maternal TD while breastfeeding, infants develop TD within 3-4 weeks and have greater incidence of (Butterworth 2001; Lonsdale, 2017; Ortega, 2004):

» SIDS
» Behavioral changes
» Autism
» Delayed language development, and
» Decreased visual alertness.

RECOMMENDATIONS/ TREATMENT

- **Administer** B1 proactively and routinely during pregnancy, especially in malnourished HG patients, to prevent morbidity and mortality.
- Slower IV administration results in higher absorption and less renal elimination. (Drewe, 2003)
- **Dilute** B1 in 100 cc of IV fluid and infuse over 30+ minutes.
- **Monitor electrolytes** (esp. Mg, Phos, Na) and methodically correct along with B vitamin cofactors (Niacin/B3, B6).

Safety

High intake of thiamin has not been associated with any adverse effects and anaphylaxis from IV thiamin is extremely rare. (Juel, 2013)

TD Prevention

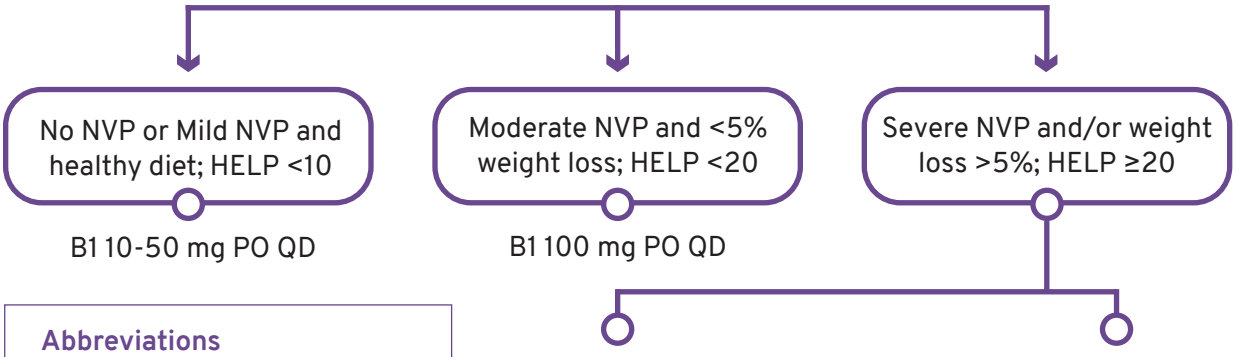
- Give B1 100-500 mg IV in every IV bag.
- Proactively add 200mg of IV thiamin to every IV bag with glucose.
- Give B1 100 mg sublingual or orally 1-3 times per day.
- Dietary consult to encourage foods high in B1.
- Monitor diet for excessive carbohydrate intake and B1 rich foods using the HG Care app food diary (hyperemesis.org/HGapp).

TD Treatment

- B1 100-500 mg IV 1-3 times per day for a minimum of 3 days or until symptoms resolve. Continue with B1 100 mg TID orally for 4+ weeks on a healthy diet.

For more info: HER website (hyperemesis.org/neuro), Thiamin (B1) Fact Sheet, Wernicke's Encephalopathy Fact Sheet, and NVP algorithm and protocol (hyperemesis.org/tools) for more clinical guidance.

THIAMIN (B1) DEFICIENCY PREVENTION & TREATMENT



Abbreviations

B1 = Thiamin
TID = Three times a day
QD = Every day
PO = Per oral
PRN = As needed
Vit = Vitamin
IV = Intravenous
IM = Intramuscular injection
NVP = Nausea & vomiting in pregnancy
MVI = Multivitamin Infusion
HELP = HyperEmesis Level Prediction Score (hyperemesis.org/tools)

Asymptomatic:

- B1 100 mg IV/PO TID until adequate intake for 4+ weeks.
- MVI + B2, B3, B6, B9 with IV hydration.
- Electrolytes prn.

Symptomatic:

- **Daily** IV: MVI + Vit C + B2, B3, B6, B9
- **TID:** B1 250-500 mg IV TID for 3+ days.
- **PRN:** Electrolytes (esp Mg, Phos!)

MEDICATIONS THAT IMPACT THIAMIN LEVELS

- Antacids
- Anticonvulsants
- Diruetics
- Hormonal therapy
- Parenteral nutrition
- Antibiotics
- IV dextrose

FOOD SOURCES WITH THIAMIN

Heat and processing reduce thiamin levels in foods.

- Pork
- Poultry
- Eggs
- Fish (trout)
- Legumes (navy beans, lentils)
- Nuts (macadamia)
- Whole grains & cereals
- Seeds

CLINICAL KEYS

- MVI has only 6 mg B1.
- Always give 200 mg B1 IV with dextrose and 100 mg TID IV/PO with a high carbohydrate diet.
- Methodically correct electrolytes.
- B1 Lab testing is unreliable.
- Avoid IM B1 (atrophy, pain).
- High doses of B1 TID increase absorption.
- Oral absorption decreased by vomiting and malnutrition (up to 70%) (Thomson, 2002).

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