HYPEREMESIS GRAVIDARUM (HG) AND WERNICKE'S ENCEPHALOPATHY

1 MOM is 2 Many

amplify, educate, advocate

DIAGNOSIS

Wernicke encephalopathy (WE) is a potentially life-threatening neurological condition primarily caused by severe thiamin deficiency. WE is characterized by confusion, change in level of consciousness, aphasia, oculomotor changes, ataxia, dysarthria, and hyperreflexia. Fetal loss rates and maternal morbidity are high without early and adequate intervention. (Vasan, 2020) (MacGibbon, 2015)

HG AND WE

» 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).

» Due to poor diet leading to malnutrition, vomiting and resulting gastrointestinal damage, 45% increase in demand for thiamin during pregnancy (Oudman 2019), and use of common medications, patients with HG are at very high risk for WE, especially if symptoms are prolonged or severe.

» Supplementation of vitamin B1 in all HG patients regardless of body mass index should be universally implemented before/at the onset of nausea and vomiting, and all women with nausea and/or vomiting should be screened at every visit.

- Women with HG rarely tolerate prenatal vitamins throughout their pregnancy. Further, not all prenatal vitamins have thiamin, and none have adequate doses (≥ 50 mg minimum) for patients experiencing HG.
- Obese patients and those with poor nutrition prior to HG may have preexisting thiamin deficiency and develop WE symptoms rapidly.
- Due to intermittent IV hydration with vitamins, occasional prenatal vitamin intake, and extreme irregularity in diet often with a high carbohydrate intake, symptoms of thiamin deficiency may persist at varying levels chronically until a healthy diet is tolerated.
- Because thiamin deficiency mimics and exacerbates HG, all women with HG should be prescribed oral thiamin, as well as IV thiamin when symptomatic and with every bag of IV fluid.

INITIAL SIGNS/SYMPTOMS

The classic triad of signs includes ocular signs, cerebellar dysfunction and confusion but these are not always present, esp in those with HG where vision changes, apathy, muscle weakness and extreme weight loss are common. (Lonsdale and Marrs, 2017) (Oudman, 2019) (Nhari, 2018)

» Ocular signs (double vision, palsies)
» Altered mental status (dizziness, drowsiness, apathy, confusion)
» Pain sensitivity
» Cerebellar dysfunction (ataxia)
» Anorexia or inadequate diet
» Weight loss
» Pain (head, abdomen, muscles)
» Nausea/vomiting
» Peripheral neuropathy
» Muscle weakness
» Mood changes (depression, irritability)
» Cognitive changes

» The incidence of WE due to HG is unknown but reports of WE secondary to HG have increased with 177 total cases to date published. (Oudman et al., 2019)
  - HG as a major risk factor for WE, with one study finding 86.2% of multigravida women with WE had hyperemesis in at least one previous pregnancy. (Chiossi, 2006) (Di Gangi, 2012) (Ashraf, 2016)
» Although there have been recent advances in the diagnosis and management of WE (Sutaamnartpong, 2013) (Sechi, 2007),
  - 53.1% of HG patients lack Wernicke's classic triad (confusion, ocular abnormalities, and ataxia), especially with gradual or episodic WE symptoms. (Di Gangi, 2012) (Garla, 2017) (Nhari, 2018)
  - 18.6% of non-alcoholic WE cases were undiagnosed until postmortem evaluation. (Scalzo, 2015)
  - Complete remission of WE occurs in only 21-31.7% of cases, with symptom resolution requiring months to years and permanent impairments were common. (Chiossi, 2006) (Di Gangi, 2012) (Scalzo, 2015)
  - Korsakoff Syndrome develops in those with inadequate or delayed thiamin replenishment, and results in permanent amnesia, memory loss, impaired ability to acquire new information, behavioral dysfunction, apathy, affective disorders, and changes in emotions and social cognition. (Pacei et al., 2020) (Thomson, 2002)
  - Approximately 20% of the patients with WE do not survive, and 68% develop severe cognitive problems. Neurological damage or death may occur in the children as well. (Oudman et al., 2019)
  - MR imaging is highly predictive, however, location of lesions for HG patients may differ from typical alcoholic patients. (Galvin et al., 2010)

Health professionals play a crucial role in the prevention, recognition, and early treatment of WE in women with HG so women and their children have a chance at surviving and having a healthy future.

RED FLAGS FOR ADVANCED WE

Any of these signs necessitate immediate and aggressive thiamin administration with methodical correction of electrolytes and other B vitamins to avoid death or serious long-term injury. (Sechi and Serra, 2007)

» Weakness
» Dysarthria
» Confabulation
» Hallucinations
» Akinetic mutism
» Hearing loss
» Spastic paresis
» Amnesia
» Aphasia
» Hypo/hyperthermia
» Epileptic seizures
» Mental status changes (memory loss, cognitive impairment)
» Gait abnormalities
» Respiratory difficulty
» Aphonia
» Myoclonus with nuchal rigidity
» Absent reflexes
» Comatose state
» Cardiac Symptoms
  - Pulmonary and peripheral edema
  - Heart failure
  - Orthopnea
  - Cardiomyopathy
  - Hypotension
  - Tachycardia
  - Arrythmias

RICK FACTORS FOR WE

(Galvin, 2010) (Sechi and Serra, 2007) (Oudman et al., 2019)

» Malnutrition/high carbohydrate diet
» Gastrointestinal symptoms (vomiting, diarrhea)
» Medication usage (antibiotics, antiacid, diuretics)
» Malabsorption syndromes
» Parenteral nutrition
» Refeeding syndrome
» Thyroid disease
» Weight loss
» Infection
» Peptic ulcers

RECOMMENDATIONS/ TREATMENT

In the absence of a universal standard of care for WE during HG, the HER Foundation proposes the following based on the scientific literature and medical society guidelines.

» Royal College of Physicians (Thomson, 2002):
  - WE: B1 500 mg IV 3 times per day for 3 days, then 250 mg daily until clinical improvement ceases.
  - Prevention: B1 250 mg IV daily for 3-5 days.
  - Parenteral B vitamins should be given in 100 ml normal saline over 30 min.
  - Give additional B2, B6, B3 & vitamin C.
» The European Federation of Neurological Societies (Galvin et al., 2010):
  - WE: B1 200 mg IV 3 times daily. (Note: This is for non-alcoholic patients.)
  - B1 500 mg IV daily for patients in a catabolic state with a normal diet.
  - B1 200 mg thiamine IV diluted with 100 ml of normal saline or 5% glucose over 30 min.
  - B1 200 mg IV before beginning carbohydrates in severely malnourished patients.
» There is no consensus on WE prevention and treatment. Given most recommendations are for non-pregnant patients without HG, higher doses for a longer time may be needed. Following are our recommendations based on the research.
  - Women with a history of HG should take a high-quality prenatal multivitamin and a B complex vitamin prior to conception, and as tolerated during pregnancy.
  - WE+HG: B1 500 mg 3 times per day IV for 1 week or until symptoms subside or no further benefit is seen. (** MUST BE IV THIAMIN **)
  - Methodical replacement of electrolytes, especially Mg & Phos, and other vitamins (B2, B6, Niacin, D, C, K) is important during treatment and recovery from HG and WE.
  - Before or simultaneous to beginning intravenous glucose and enteral or parenteral nutrition, IV thiamin of at least 200 mg is required in HG patients.
  - IV thiamine supplementation should continue daily in symptomatic patients and those unable to consistently tolerate daily oral supplementation.
  - After IV B1 replenishment, thiamin 100 mg orally 3 times per day is needed in pregnant women recovering from WE for at least 1-3 months, longer if breastfeeding, inadequate nutrition, and/or ongoing or severe HG.
  - See HER Foundation treatment algorithms for HG and thiamin deficiency. hyperemesis.org/tools

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