Hyperemesis Gravidarum: Current Approaches for the Diagnosis and Treatment

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Abstract

Hyperemesis gravidarum is defined as presence of nausea and vomiting in pregnancy that affect 50-90% of all pregnant women, seen in the first trimester. Hyperemesis gravidarum often presents with maternal weight loss, electrolyte imbalance, and nutritional abnormalities. It is the most common reason for hospitalization during the first trimester of pregnancy. The risk factors for the disease are nulliparity, younger age, pre-existing diabetes, psychiatric disorders, hepatic or hyperthyroid diseases. The diagnosis is supported with ketonuria, abnormal electrolytes, elevated liver function tests, and elevated hematocrit levels. The treatment options are depend on patient's clinical state. Non-pharmacological treatment may be offered as the first-line treatment. Patients with electrolyte imbalance and ketonuria may require medical treatment or hospitalization.

Keywords: Dehydration; Hyperemesis gravidarum; Pregnancy; Vomiting

Introduction

Hyperemesis gravidarum presents with minimal to severe nausea, vomiting, dehydration, ketosis, electrolyte and acid-base imbalance which lead to weight lost (at least 5% of body weight) and rarely with renal and hepatic failure. It usually starts at 4-8 weeks of pregnancy and ends before the 20 weeks of gestation.

Incidence and Risk Factors

The reported incidence is about 0.5-1 percent [1-5]. However, there is few studies have reported prevalence rates among ethnic groups, considering their food consumption and lifestyle, or environmental factors. There is a higher incidence in non-white populations (33% vs. 16%) in white populations [6].

The reported etiological factors are; increased levels of β-HCG, E2, progesterone presence of hyperthyroidism, upper gastrointestinal system dysmotility, immune system dysfunction, infection of Helicobacter pylori and psychological factors [7,8].

The definition can be supported with laboratory parameters such as; increased hematocrit values due to dehydration, elevated serum aspartate amino transferase, alanin amino transferase, amylase, lipase, elevated Τ4 and decreased TSH levels. Ketosis in urinalysis is an indication for hospitalization [9].

The differential diagnosis must be consider with other systemic disorders such as; gastroenteritis, biliary tract diseases, hepatitis, appendicitis, nephrolithiasis, pyelonephritis, diabetic ketoacidosis, pseudotumor cerebri, hyperthyroidism, migraines and the most importantly from hypertensive disorders of pregnancy [10].

Maternal and Fetal Effects

The complications may be present and can affect both for the mother and the fetus. As for the maternal complications; weight loss, dehydration, acidosis, alkalosis, hypokalemia, muscle weakness, tetani, Wernicke's encephalitis, central pontine myelinolysis (osmotic demyelination syndrome), Mallory-Weiss tears, esophageal rupture, pneumothorax, liver and kidney failure may be seen during the disease. Fetal complications may also be present and may be worsened when the mother's weight lost is more than 7%. It could be with preterm delivery and fetal low birth weight [11-13].

Non-Pharmacological Treatment for Hyperemesis Gravidarum

Treatment options depend on clinical status of the patients. Non-pharmacological treatment may be offered as the first-line treatment in the patients who presented with nausea and vomiting with stable vital signs. Some kind of diet regimen changes (less and slowly nutrition, patients should take their favorite foods), removal of the triggers (perfume, cigarette, moisture), acupuncture, hypnosis or even psychotherapy may be useful for the initial work up of these patient group [8,14,15].

Pharmacological Treatment for Hyperemesis gravidarum

The pharmacological treatment options for this patient group are; 1-1.5 g/day of cinnamon as tea or vitamin capsules, pyridoxine (vitamin B6) 25 mg three times/day peroral may reduce nausea, but has no effect on vomiting. H1 antagonists such as doxylamine, meclizine, dimenhydrinate and diphenhydramine can be safely used during pregnancy. 20 mg of doxylamine may be beneficial if taken peroral before bedtime [16-19].

If there are clinical signs of dehydration, the first steps of treatment are 4-6 times/day of diphenhydramine or dimenhydrinate 25-50 mg via peroral or intravenous route. The maximum daily dose for dimenhydrinate is 400 mg. The second step of treatment for the patients with dehydration, dopamine antagonists such as 5-10 mg of prochlorperazine 4 times/day via peroral, i.v. or i.m. route. However there is not enough evidence about the risk of fetal malformation for...
this agents. 10 mg use of metoclopramide 3 times/day via peroral, i.v., i.m. route can be considered 30 minutes before meals. It is reported as a safe agent considering fetal malformations. However it is reported that long term use of this agent may be with extrapyramidal symptoms. The pharmacological effect of this agent begins after 30-60 minutes of peroral, 1-3 minutes after i.v. administration and 10-15 minutes after i.m. injections and longs for 1-2 hours. A serotonin antagonist (5HT-3) ondansetron is safe considering fetal malformations. 4-8 mg 3 times/day peroral or i.v. administration may be beneficial. However, it is reported that prolongation of QT segment may be observed during ECG monitoring [20-23].

In some resistant cases additional treatments may be required. In case with complaints like gastritis or history of peptic ulcer antacids containing aluminum or calcium can be prescribed 3 to 4 times/day via peroral route before meals. H2 receptor antagonists such as, 150 mg of ranitidine or simetidine twice a day via peroral route can be used. A 40 mg of proton pump inhibitor lansoprazole via peroral use should be kept in mind as the another oral agent [24-26].

**Patient Selection for Hospitalization**

One of the major question for this population is about selecting the patients those will require hospitalization. The patients with severe vomiting, weight loss, ketonuria, dry mucous membranes, reduced skin turgor, dehydrated, hypotensive, alkalosis and hypokalemia should be hospitalized considering increased maternal fetal morbidity. After hospitalization a daily follow up for oral intake, weight and urinary output should be noted. A restricted oral intake may be required for a few days. Eating may be started with small portions after improvement in general vital signs. A psychological support and feel of confidence may be useful and psychological consultation should be offered.

If there is severe dehydration, electrolyte and acid-base irregularity A 2 lt solution of ringer lactate should be administered via i.v. route in 3-5 hours including B vitamins can be given. The vitamin B1 vitamin should be continued 100 mg/day following 2-3 days. The maintaining fluid can be 5% of Dextrose plus 0.45% of saline until urine output is more than 100 cc. It should be keep in mind that the first liquid should not be dextrose. After few days of oral intake restriction, if it is tolerable, oral feeding can be started with banana, rice, apple sauce and some toasts. For patients with resistant to treatment; 25-50 mg of chlorpromazine i.v./i.m. or 10-25 mg 4 times/day via peroral route can be used. A 16 mg of methylprednisolone i.v. three times/day may also be used after first trimester [23].

**Conclusion**

In conclusion, hyperemesis gravidarum is a common problem of pregnancy. The treatment should be focused on underlying cause of the disease and should be individualized.

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