

## Short Communication

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## Nausea and Vomiting in Pregnancy-The Bump in the road of Motherhood

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### INTRODUCTION

Early pregnancy is commonly associated with nausea and/or vomiting, known by the lay term morning sickness and this can impact the Quality of Life (QoL) of the pregnant woman despite being considered a part of the first trimester of pregnancy's physiology.

Hyperemesis gravidarum refers to severe vomiting associated with systemic effects and the diagnosis criteria includes pregnancy related vomiting that occurs greater than three times per day in conjunction with a weight loss greater than 3 kg or 5% of body weight and ketonuria unrelated to other causes.<sup>1</sup>

### INCIDENCE

Nausea with/without vomiting tends to be more common in the younger primigravid of western nations but generally occurs in 50-90% of all pregnancies while hyperemesis gravidarum has been reported in 0.3 to 3% of pregnancies.<sup>2</sup>

### RISK FACTORS

There is an increased association with multiple gestation,<sup>3</sup> hydatidiform mole,<sup>4</sup> acid-reflux disease<sup>5</sup> and a similar pregnancy history.

An increased incidence has also been noted in those who experience nausea and vomiting related to estrogen based medications while alcohol use, cigarette smoking<sup>6</sup> and anosmia do appear to be protective.<sup>7</sup>

### Pathogenesis

Unknown but theories propagated include:

- **Hormonal changes:** Although not firmly established, higher levels of serum HCG has been observed in women with hyperemesis including those with multiple gestations and hydatidiform mole. Serum concentrations of HCG also peak in the first trimester, which corresponds to the time hyperemesis gravidarum is typically seen.
- **Psychological factors:** Individual response to stress and the pregnancy has been proposed as contributing factors.<sup>8</sup>
- **Abnormal gastrointestinal motility:** Dysrhythmic gastric motility has been suggested as well as gastroesophageal reflux but this does not account for why symptoms get better as pregnancy progresses.<sup>2</sup>
- **Helicobacter pylori:** Case reports have shown improvement in symptoms with treatment of

infection but this is in need of confirmatory evidence.<sup>9</sup>

### DIAGNOSIS AND CLINICAL COURSE

The onset of symptoms is usually between 5 and 6 weeks with peak around 9 weeks of gestation. It usually abates at 16-20 weeks but in 15-20% of pregnancies, it does continue till the third trimester and till delivery in 5% of cases.<sup>10,11</sup>

It can occur at any time of the day and in most instances, normal vital signs, physical and laboratory examinations are the norm.

In contrast, women with hyperemesis have orthostatic hypotension, physical signs of dehydration as well as laboratory abnormalities and often need hospitalization for stabilization.

The Motherisk-PUQE scoring index and the Rhodes index have been used in research with higher scores indicating a need for serum electrolyte check and evaluation for dehydration.

### Evaluation

Standard evaluation includes:

- Measurement of weight
- Orthostatic blood pressures
- Heart rate check
- Serum Electrolytes/urea and creatinine
- Urine Ketones and specific gravity
- Obstetrical Ultrasound for gestational age, no. of gestations and to rule out hydratiditiform mole.
- Others include a complete blood count, liver function tests, thyroid function tests, amylase/lipase and calcium level.
- If liver disease is suspected, an ultrasound examination of the liver is indicated.

### Associated findings include

Electrolyte derangements- hypokalemia, hypochloremic metabolic alkalosis and ketosis.

Hematocrit increase due to hemoconcentration.

Abnormal liver enzymes, especially an elevation of alanine aminotransferase.

Serum amylase and lipase may increase by 5 fold.<sup>10</sup>

Mild hyperthyroidism may occur due to an elevated serum level of HCG and this tends to resolve without any need for intervention.

### Treatment

Management should generally be aimed at reducing symptoms, minimizing the effects on the fetus and reversing consequences.

#### i. Non-Pharmacologic Interventions include:

Dietary measures through the ingestion of small, frequent carbohydrate meals, eliminating coffee and spicy, odorous, fatty and sweet foods while cold carbonated drinks can also be helpful.

Triggers such as Iron supplements, heat, humidity and odors should be avoided until symptoms resolve while hypnosis, psychotherapy and acupuncture might be of help.

#### ii. Pharmacologic Interventions include:

Ginger in the form of ginger supplements or ginger containing food such as ginger tea is used based on the mild improvement seen in randomized controlled studies.<sup>12</sup>

Pyridoxine or vitamin B6 is a water-soluble vitamin that can be used alone or in conjunction with doxylamine succinate.<sup>13</sup> Pyridoxine has a good safety profile with minimal side effects and is usually given as 25 mg orally every six to eight hours.

Anti-Histamines including doxylamine, meclizine, dimenhydrinate, promethazine and diphenhydramine do significantly reduce pregnancy related nausea and vomiting as illustrated in controlled trials.<sup>14</sup> The mechanisms of action involve the inhibition of histamine at the H1 receptor and an indirect effect on the vestibular system by reducing the vomiting center stimulation. Lightheadedness, dry mouth, constipation and sedation are some of the associated side effects.

Dopamine antagonists mediate the inhibition of gastric motility through their action on dopamine receptors in the stomach and the three main classes are the butyrophenones (droperidol), phenothiazines (Promethazine) and benzamides (metoclopramide).

Serotonin antagonists are mainly selective antagonists at 5-HT<sub>3</sub> serotonin receptor such as ondansetron, given at 4 to 8 mg orally every eight hours, as needed or intravenously. Side effects include headache, constipation, drowsiness and fatigue. The use of this class of drugs for the treatment of nausea and vomiting of pregnancy has not been associated with congenital anomalies or other adverse effects.

Acid reducing agents are used as adjuncts to antiemetics and include antacids (aluminum or calcium containing), H<sub>2</sub> receptor antagonists (Ranitidine) or Proton pump inhibitors

(Omeprazole).

Hospitalization for hydration and medication is warranted in cases of failed outpatient therapy and emotional support is needed to deal with the stressful nature of the illness although a recent study demonstrates that individualizing care with the aid of the hyperemesis impact of symptoms questionnaire was not associated with any significant improvement in the quality of care.<sup>15</sup>

Dehydration may need correction with up to 2 liter of lactated Ringers solution over 3 to 6 hours while also giving appropriate electrolytes and vitamins. It is then changed to dextrose 5% in 0.45% saline and hydration is commonly continued for one to two days with urine output maintained at about 100 mls/hr.

Vitamins and minerals such as thiamine (Vitamin B1) is replaced by giving 100 mg intravenously with the initial rehydration fluids and 100 mg daily for the next two or three days to prevent the development of Wernicke encephalopathy. Multivitamin (MVI) 10 ml, folic acid 0.6 mg and vitamin B6 25 mg are given in every liter of fluid.

With hypocalcaemia, correct the low magnesium level by giving 2 g (16 meq) magnesium sulfate as a 10% solution over 10 to 20 minutes then 1 g (8 meq) in 100 ml of fluid per hour to raise the magnesium level to more than 0.8 meq/l. If the serum calcium is still low, 1-2 g calcium gluconate in 50 ml of 5% dextrose solution over 10 to 20 minutes is added.

Dietary measures including a period of bowel rest are followed by a BRAT diet (bananas, rice, apple sauce and toast) or full liquid diet and this is then advanced as tolerated.

Medications are usually given through non-oral routes until tolerated and for unresponsive patients, there is a role for the use of glucorticoids such as methylprednisolone (16 mg) intravenously every eight hours for 48 to 72 hours, converted to oral prednisone tapered over a two-week period with response, though the mechanism of action is still not well understood.

Enteral (tube feeding) or parenteral nutrition and intravenous fluids might be needed as long as necessary.

Generally, nausea and vomiting of pregnancy is associated with a lower rate of miscarriage than in women without these symptoms whereas with hyperemesis gravidarum, there is an increased risk of preterm delivery, low birth weight/small for gestational age infants and an association with placental dysfunction. Adverse effects of malnutrition such as Wernicke encephalopathy (Vitamin B1 deficiency), bleeding diathesis (Vitamin K deficiency), esophageal tears and rupture, pneumothoraxes, osmotic demyelination syndrome, hepatic insufficiency and acute tubular necrosis might occur with persistent severe

vomiting.

Prevention comprises of managing acid reflux disorders prior to pregnancy and the preconceptional intake of daily multivitamins with folic acid may help decrease the frequency and severity of nausea and vomiting during pregnancy.

#### DIFFERENTIAL DIAGNOSIS

Many conditions unrelated to pregnancy such as pancreatitis, cholecystitis, hepatitis and thyroid disease can result in nausea and vomiting of pregnancy while preeclampsia; HELLP syndrome and acute fatty liver of pregnancy are associated with emesis occurring in the latter half of pregnancy in combination with other clinical and laboratory findings.

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