Nausea and Vomiting in Pregnancy - including Hyperemesis Gravidarum

Nausea and vomiting are both common in early pregnancy. There is no evidence of fetal damage as a result of the nausea and vomiting. Nausea and vomiting can occur at any time of the day and may be constant.

The causes of nausea and vomiting in early pregnancy are unknown. Nausea in later pregnancy may be due to reflux oesophagitis and it responds to antacids.

Nausea and vomiting are very common in pregnancy but are usually mild and only require reassurance and advice. However, persistent vomiting and severe nausea can progress to hyperemesis gravidarum. Hyperemesis gravidarum refers to persistent and severe vomiting leading to fluid and electrolyte disturbance, marked ketonuria, nutritional deficiency and weight loss. Without treatment, hyperemesis gravidarum may lead to central nervous system complications, liver failure and acute kidney injury but these complications are now rare in the developed world. See the section ‘Hyperemesis gravidarum’ at the end of this article.

Epidemiology[1]

- Nausea and vomiting are common in pregnancy, affecting up to 90% of pregnant women. 35% of affected women are thought to have clinically significant symptoms.
- Nausea and vomiting in pregnancy are more common in:
  - Primigravidae.
  - Multiple pregnancy.
  - History of previous hyperemesis gravidarum or motion sickness.
  - Molar pregnancy.
  - Pregnancy where the fetus is female.
  - Younger women.
  - Obese women.
  - Women who are sero-positive for Helicobacter pylori.
- It tends to be a disease of Western society and is less common in developing countries, especially in rural communities.

Presentation[1]

- Symptoms usually start between 4 and 7 weeks of gestation and resolve by 16 weeks in about 90% of women.
- Check for signs of dehydration and any possible underlying cause.
- If symptoms begin after 12 weeks of pregnancy, there is usually another cause.

Differential diagnosis

Other causes of nausea and vomiting should be considered.[2]

- Gastrointestinal - eg, gastroenteritis, gastritis, cholecystitis, peptic ulceration, hepatitis, appendicitis, pancreatitis, gastrointestinal obstruction.
- Neurological - eg, migraine, raised intracranial pressure.
- Urinary tract infection.
- Ear, nose, and throat disease - eg, labyrinthitis, Ménière's disease, vestibular dysfunction.
- Drugs - eg, opioids, iron.
- Metabolic and endocrine disorders - eg, hypercalcaemia, diabetes, Addison's disease, uraemia (acute kidney injury, chronic kidney disease) and thyrotoxicosis.
- Psychological disorders - eg, bulimia.
- Pregnancy-associated conditions - eg, pre-eclampsia, gestational trophoblastic disease, twisted ovarian cyst, fatty liver of pregnancy.

Investigations

- These are only required if there is a possible alternative diagnosis or in the assessment of the well-being of mother and fetus.
- In primary care investigations are usually not required, unless there is concern that the mother is not maintaining adequate fluid intake. Check urine for ketones if this is a concern. If there are signs of dehydration, further investigation is usually undertaken in secondary care.
- In cases of hyperemesis gravidarum: renal function and electrolytes, LFTs, midstream urine (for infection and ketones) and ultrasound (exclude multiple or molar pregnancy).
Management\textsuperscript{[1, 3]}

Most cases are mild and do not require treatment. Nausea and vomiting in pregnancy usually resolve spontaneously within 16 to 20 weeks and are not associated with a poor pregnancy outcome. However, persistent vomiting and severe nausea can progress to hyperemesis gravidarum if the woman is unable to maintain adequate hydration and fluid and electrolyte balance. Nutritional status may be jeopardised.\textsuperscript{[4]}

Repeated Cochrane reviews have found no strong evidence for benefit of any one intervention, whether dietary, complementary medicine or traditional medication. They point out this does not mean the interventions studied are ineffective and that the available evidence is limited.

General advice

Dietary suggestions which may help some women include:

- Advise the patient to rest; eat small, frequent meals that are high in carbohydrate and low in fat.
- Avoid any foods or smells that trigger symptoms.
- The use of ginger products may be helpful. Evidence is limited and lacks consistency but there is some evidence of benefit over placebo.
- Try eating a dry biscuit first thing on waking in the morning before getting up.

Cochrane reviews have found no evidence for the benefit of acupuncture in this situation. P6 (wrist) acupressure is recommended as a potential option by 2008 National Institute for Health and Care Excellence (NICE) guidelines, although subsequent Cochrane reviews have found there to be limited evidence of benefit.\textsuperscript{[4]} Vitamin B6 supplements have also been recommended in the past but again the reviews have found limited evidence of benefit.

Anti-emetic medication

Medication should be avoided in pregnancy unless the benefit outweighs the potential risk, particularly in the first trimester. Anti-emetics should only be used if dietary measures have failed and symptoms are persistent, severe and preventing daily activities. There is no evidence that any one anti-emetic is better than another. If medication is required, NICE Clinical Knowledge Summaries (CKS) advice is to use:

- Promethazine or cyclizine first-line.
- Metoclopramide, prochlorperazine or ondansetron second-line:
  - Metoclopramide should not be used under the age of 20 due to the increased risk of extra-pyramidal side effects, or for more than five days in line with the Medicines and Healthcare products Regulatory Agency (MHRA) recommendations.\textsuperscript{[5]}
  - Ondansetron is more expensive. Evidence suggests there is no significant risk of adverse fetal outcome when used in pregnancy.\textsuperscript{[6]}

Proton pump inhibitors and histamine H2-receptor antagonists may be used in women who also have dyspepsia, and may be a useful adjunctive treatment.\textsuperscript{[2]}

Admission

- Women with severe symptoms should be referred for fluid, electrolyte and vitamin replacement (usually intravenously). Nutritional support (enteral or parenteral) is needed in women who have intractable symptoms and weight loss, despite appropriate therapy.
- Indications for referral to secondary care include:\textsuperscript{[2]}
  - Continued nausea and vomiting associated with ketonuria or weight loss (>5% body weight), despite oral anti-emetics.
  - Continued nausea and vomiting and inability to keep down oral anti-emetics.
  -Confirmed or suspected comorbidity (such as confirmed urinary tract infection and inability to tolerate oral antibiotics, or diabetes).

Prognosis\textsuperscript{[1]}

Most cases are self-limiting and settle without complication as pregnancy progresses. However, nausea and vomiting may cause significant psychosocial difficulties, time off work and a restriction of domestic and leisure activities. Mid-to-moderate nausea and vomiting do not affect pregnancy outcome adversely; indeed there is some evidence that these symptoms are associated with a lower rate of miscarriage.

Potential medical complications of hyperemesis gravidarum are discussed below.

Hyperemesis gravidarum\textsuperscript{[2, 7]}

Different definitions of hyperemesis gravidarum exist but the important features are intractable vomiting associated with weight loss of more than 5% of pre-pregnancy weight, dehydration, electrolyte imbalances, ketosis and the need for admission to hospital.

Epidemiology
Hyperemesis gravidarum occurs in less than 1% of pregnancies. One study found that a moderate intake of water and adherence to a healthy diet that includes vegetables and fish before pregnancy are associated with a lower risk of developing hyperemesis gravidarum. A Canadian study found that hyperemesis gravidarum is more common when the fetus is female. There is evidence that hyperemesis gravidarum is more common when the fetus is female.

Presentation
Vomiting that begins after 12 weeks of gestation is unlikely to be caused by hyperemesis gravidarum, and other pathological causes should always be considered before attributing nausea and vomiting in pregnancy to hyperemesis gravidarum. See 'Differential diagnosis', above.

Management
- Advice, including dietary advice, and support.
- Fluid and electrolyte replacement:
  - Women who are severely dehydrated and ketotic need to be assessed in secondary care, with intravenous fluid and electrolyte replacement (with normal saline or Hartmann's solution).
  - Fluid and electrolyte balance must be reassessed frequently.
  - Potassium must be replaced appropriately.
- Nutritional support (enteral or parenteral) may be required.
- Vitamin supplements:
  - Thiamine supplements should be given routinely - orally if tolerated, or intravenously - to all pregnant women admitted to hospital as a result of prolonged vomiting.
- Thromboprophylaxis:
  - Risk of venous thrombosis is increased due to dehydration and immobility, and consideration of prophylactic low molecular weight heparin is required.
- Anti-emetic medication: see 'Management', above.
- Corticosteroids: may be used for intractable cases of severe hyperemesis gravidarum in secondary care.

Complications
In severe cases, dehydration, weight loss, electrolyte disturbance (e.g., ketosis) and nutritional deficiency can occur. Hyperemesis gravidarum is rarely associated with death but may lead to serious complications, including Wernicke's encephalopathy, central pontine myelinolysis and spontaneous oesophageal rupture.

Maternal
- Weight loss (10-20% of body weight).
- Dehydration.
- Acidosis.
- Hyponatraemia, from persistent vomiting (which may cause lethargy, headache, confusion, nausea, vomiting, seizures or respiratory arrest). Excessive correction of hyponatraemia can lead to central pontine myelinolysis.
- Hypokalaemia (which may cause muscle weakness or cardiac arrhythmias).
- Vitamin deficiencies:
  - Vitamin B1 (thiamine) deficiency (causing Wernicke's encephalopathy, which may also be precipitated by high concentrations of dextrose).
  - Vitamin B12 and vitamin B6 deficiencies may cause anaemia and peripheral neuropathies.
- Mallory-Weiss tears of the oesophagus due to repeated vomiting.
- Retinal haemorrhages.
- Splenic avulsion.
- Pneumothorax.
- Postpartum complications: persistence of symptoms and food aversions, postpartum gallbladder dysfunction and symptoms of post-traumatic stress disorder.

Fetal complications
There is evidence that hyperemesis gravidarum is associated with a higher incidence of low birth weight (small-for-gestational-age and premature babies). Little is known about the long-term health effects of babies born to mothers whose pregnancies were complicated by hyperemesis gravidarum.

Further reading & references
- The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum - Green-top Guideline No.69; Royal College of Obstetricians and Gynaecologists (2016)

"I could not survive another day": Improving treatment and tackling stigma: lessons from women's experience of abortion for severe pregnancy sickness; Pregnancy Sickness Support and British Pregnancy Advisory Service (BPAS). April 2015

1. Nausea/vomiting in pregnancy; NICE CKS, June 2013 (UK access only)
5. British National Formulary (BNF); NICE Evidence Services (UK access only)

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