

THEME

Nausea and vomiting



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Hyperemesis gravidarum

Assessment and management

BACKGROUND

Nausea and vomiting are common symptoms in early pregnancy. In most women the condition is mild and self limiting. A small percentage of women experience severe nausea and vomiting. This is known as hyperemesis gravidarum. Outcomes have improved with intravenous rehydration therapy. Consequences include decreased quality of life, time off work and secondary depression.

OBJECTIVE

This article outlines the aetiology, outcomes, history and examination of women with hyperemesis gravidarum. Treatment modalities are discussed together with evidence regarding use.

DISCUSSION

It is important to exclude other causes of nausea and vomiting such as urinary tract infection and thyrotoxicosis. Assessment of severity by checking for ketones is important as severity determines management. Management will include rehydration (intravenous or oral). Evidence is lacking regarding dietary and lifestyle recommendations but some women find them useful. Pyridoxine and metoclopramide (category A) are first line in treatment of hyperemesis gravidarum followed by prochlorperazine (category C), prednisolone (category A), promethazine (category C) and ondansetron (category B1). Benefit has been reported with the use of ginger. Evidence is mixed regarding acupressure and acupuncture.

Nausea and vomiting affects up to 85% of pregnant women.¹ Although popularly known as 'morning sickness' one study demonstrated that less than 2% of women experienced nausea only in the morning and 80% reported nausea throughout the day.² The condition is usually mild and self limiting, peaking at around 9 weeks gestation and usually resolving, frequently quite abruptly, before 14 weeks gestation. In the same study however, 13% of women reported nausea lasting beyond 20 weeks gestation.

Hyperemesis gravidarum

A small percentage of women experience a severe form of nausea and vomiting known as hyperemesis gravidarum. Estimates of the incidence of hyperemesis vary from 0.3–1.5% of all live births.³ Diagnosis is subjective, but the condition is usually described as intractable vomiting leading to fluid, electrolyte and acid base imbalance, nutritional deficiency and weight loss.

Outcome and complications

Before the introduction of intravenous (IV) rehydration, the mortality from hyperemesis was considerable, the

most well known case probably being that of Charlotte Bronte who died in 1855 from severe nausea and vomiting 4 months into her pregnancy.⁴ Cases have been reported in the literature with advanced vitamin and metabolite disturbances such as Wernicke encephalopathy, coagulopathy and peripheral neuropathy.

Although vomiting is the most obvious concerning symptom, persistent, debilitating nausea can severely adversely affect the woman's quality of life. In studies, 35% of women with paid employment lost time from work through nausea and 26% lost time from housework.¹

Nausea and vomiting in early pregnancy are consistently associated with lower rates of miscarriage.⁵ There are no other associations with pregnancy outcomes. Psychosocial morbidity for the mother is common enough however, as up to 60% of women with hyperemesis gravidarum develop secondary depression.⁶

Aetiology

The aetiology is unknown. The endocrine factor most commonly invoked is human chorionic gonadotropin hormone (HCG) on the basis of the observed temporal

association, that incidence of hyperemesis is highest at the time that HCG production reaches its peak. In addition, hyperemesis is said to have a higher incidence in those conditions associated with elevated HCG concentrations such as twin and molar pregnancies. This is not uniformly supported by experimental evidence. Of the 15 studies published since 1990, only 11 showed significantly higher HCG concentrations in patients compared to controls.³ It has been proposed that HCG stimulates thyroid function because of its structural similarity to thyroid stimulating hormone (TSH). There is evidence to support a relationship between HCG and transient thyrotoxicosis in pregnancy but the causative role in hyperemesis is still obscure.

Many other aetiological factors have been proposed including oestrogen, placental serum markers, adrenocorticotrophic hormone (ACTH) and cortisol, growth hormone and prolactin. Severe nausea and vomiting is consistently associated with the presence of a female fetus, one study finding that women hospitalised for hyperemesis had a 50% increased chance of having a female fetus compared to controls.⁷ The usual explanation for this is higher oestrogen concentrations.

Historically there was thought to be an association between hyperemesis and psychological conflict regarding the pregnancy. Studies of hyperemesis patients have found no difference in marital status, whether the infant was planned, or positive feelings about the pregnancy.⁸ More recent studies have suggested that psychological symptoms are the result of the stress and the burden of hyperemesis rather than the cause.³

History and examination

Identification of other causes

Other, more unusual causes of nausea and vomiting such as hepatitis, pancreatitis, gastrointestinal obstruction, peptic ulcer disease, thyroid disease, and adrenocortical insufficiency should be excluded. Investigations may include midstream urine (MSU) to exclude urinary tract infections, electrolytes and liver function tests, an ultrasound to exclude trophoblastic disease or multiple pregnancy and TSH if there is suspicion of thyrotoxicosis.

Assessment of severity

Initial management depends on the assessment of severity/degree of dehydration (on examination and evidence of ketonuria).

Initial management

An obviously dehydrated woman, with ketonuria

Table 1. Common dietary advice

- Drink small amounts often
- Sometimes other fluids are managed better than water – flat lemonade, sports drinks, diluted fruit juice, cordial, weak tea, clear soup
- Small amounts of food more often, rather than large meals
- Avoid having an empty stomach – nibble on light snacks between meals
- Early morning nausea may be helped by eating a dry biscuit before getting out of bed
- Salty foods may help – try potato crisps or salty biscuits
- Try sucking on barley sugar or boiled sweets
- Avoid fatty, rich or spicy foods

Table 2. Common lifestyle advice

- Make the most of your best time of day – eat well when you feel best or whenever you feel hungry
- If the smell of hot food makes you feel ill – try having cold food instead. If possible avoid cooking and ask for help from friends and family
- Lie down when nauseated
- Avoid stress – living with the constant threat of nausea and/or vomiting is a stressor in itself

greater than 2++ on urinalysis unquestionably requires admission to hospital for IV rehydration and antiemetic therapy. Lesser degrees of severity may benefit from other management options. For severe, prolonged hyperemesis, consideration should be given to IV thiamine supplementation (100 mg/day) to prevent Wernicke encephalopathy. Extreme cases may require nasogastric or parenteral nutrition.

The most important step is for the patient to drink enough fluids to avoid dehydration, which exacerbates nausea. If the woman is unable to tolerate oral fluids admission to hospital is mandatory.

Dietary and lifestyle advice

There are no clinical trials of these recommendations, however they do have a considerable tradition. In one survey, most women found them at least somewhat useful.⁹ The usual instruction is frequent nibbling of plain dry cracker biscuits before rising and throughout the day, and careful attention to adequate hydration. A summary of some of the most common dietary advice is given in *Table 1*. Common lifestyle advice is given in *Table 2*.

Antiemetics

Women and families tend to overestimate the teratogenic risk of medications for nausea vomiting and as a consequence these therapies are probably underutilised. In the wake of the thalidomide tragedy of the 1960s

Table 3. Outpatient antiemetic treatment of hyperemesis gravidarum

Medication	Suggested dose	Administration
Pyridoxine (vitamin B6)	25 mg three times per day	Oral
Metoclopramide	10 mg 3–4 times per day	Oral
Prochlorperazine	25 mg/day or twice per day	Rectal
Prednisolone	40–60 mg/day reducing by half every 3 days (lower dose eg. 5 mg/day may be effective but slower to act)	Oral
Ondansetron	4–8 mg 2–3 times per day	Oral
Doxylamine	25 mg at night and 12.5 mg in the morning accompanied by 10 mg of pyridoxine*	Oral
Ginger	1–4 g/day in divided doses	Oral (biscuits, confectionary, crystals, powder, tablets, capsules, fresh ginger)

* Equivalent to debendox which has been withdrawn from the market because of suspected teratogenic effects. Meta-analyses conclude no evidence of teratogenicity²

and the increasingly litigious nature of our society, limiting pharmacologic treatments in early pregnancy is understandable, but the judicious use of well used medications may alleviate considerable morbidity (*Table 3*).

Pyridoxine (vitamin B6) has been demonstrated to be effective in trials using doses of 30–75 mg/day. Up to 100 mg/day can be given in divided doses, however the most common regimen is 25 mg three times per day which is well tolerated with least side effects. The most commonly prescribed drug is metoclopramide (category A) usually a dose of 10 mg 3–4 times per day as necessary. A sedating antihistamine such as promethazine may be of benefit as an additional therapy, although in view of resulting drowsiness it may be most appropriate for use at night.

For women experiencing continued vomiting despite the above, further medical therapy options include prochlorperazine (category C), available as a 25 mg suppository. Oral prednisolone (category A) has also been shown to be of benefit, starting with a dose of 40–60 mg and reducing by half every 3 days. An alternative low dose regimen of 5 mg/day has been demonstrated to be as effective as promethazine (although slower to act) with fewer side effects in at least one randomised trial.¹⁰ Ondansetron (category

B1) 4–8 mg is also effective, although usually as a last resort in view of the increased costs compared to other medications.

Debendox was widely prescribed to women before its voluntary withdrawal in 1983 following concerns over possible teratogenic effects. This drug has been the focus of at least 25 epidemiological studies and two meta-analyses making it the world's most studied drug in pregnancy.² The meta-analyses conclude that there is no evidence of teratogenicity from treatment with this medication (data on 17 427 women taking the medication and 141 237 controls). Although the medication is no longer available, it is possible to recreate the original formulation using doxylamine 25 mg at night and 12.5 mg in the morning accompanied by 10 mg pyridoxine.

Alternative therapies

One trial of 66 women compared ginger (1 g) in capsule form with placebo, reporting benefit both for vomiting and for nausea with no adverse effects.¹¹ Ginger is available in a number of forms such as tea, biscuits, confectionary, and crystals or sugared ginger, and although none has been subject to randomised controlled trials, there is some evidence that these forms of ginger may be beneficial and without adverse effects.¹²

Acupuncture and acupressure have been the subject of a number of trials in hyperemesis. Acupuncture requires a trained practitioner and acupressure may be a cheaper and more readily available option. Acupressure involves the stimulation of the P6 Neiguan point either manually or with elasticised bands. The P6 point is on the inside of the wrist, about 2–3 finger breadths proximal to the wrist crease between the tendons about 1 cm deep. Manual pressure is applied to this point for 5 minutes every 4 hours. Alternatively pressure can be applied by wearing an elasticised band with a 1 cm round plastic protruding button centred over the acupressure point.⁸ Unfortunately, the evidence is mixed. It has not been shown to be clearly more effective than 'sham' or 'dummy' acupressure, or than standard dietary and lifestyle advice.² However, in the absence of any evidence, the manual application of acupressure is harmless and without cost.

Summary of important points

- Women unable to tolerate oral fluids require admission to hospital.
- Women should be provided with dietary and lifestyle advice to prevent dehydration.
- Maintaining hydration is more important than nutrition in the short term.

- Severe or prolonged cases may require supplementation with thiamine, nasogastric or parenteral nutrition.
- Medications are probably underutilised. Of the various medications shown to be effective, pyridoxine has the least side effects. The most commonly prescribed drug is metochlopramide.

Conflict of interest: none declared.

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