

Nausea and Vomiting in Pregnancy

Over 75 per cent of pregnant women experience some degree of nausea and vomiting during pregnancy. Up to 1 per cent of pregnancies are complicated by the severe syndrome referred to as hyperemesis gravidarum, which frequently prompts hospital admission for control of symptoms and the accompanying biochemical abnormalities.

A treatment algorithm for this spectrum of symptoms, based on the available evidence, is suggested in Figure 1.

Appendix 1 offers insight into interventions considered **not** helpful for the treatment of hyperemesis, plus a discussion on areas of controversy.

1. Mild Nausea and Vomiting of Pregnancy

Try the following in a stepwise or cumulative fashion:

- a. Advise the patient to temporarily discontinue her prenatal vitamins with iron if she feels they are upsetting her stomach.
- b. Make dietary adjustments (small, frequent, low fat meals, etc.).
- c. Add ginger 975-1500mg/d (250 PO QID)
- d. Try alternative therapies such as chamomile, peppermint teas, or acupressure / acupuncture. (see Appendix 1: Controversies)
- e. Prescribe pyridoxine (vitamin B6) 50 mg po BID - TID.
- f. Add the H1-receptor blocker doxylamine 12.5 mg po tid if needed.
- g. Consider combining B6 and doxylamine at the same time tid
- h. Prescribe a phenothiazine (e.g. promethazine 12.5-25 mg po/pr), or an antihistamine (e.g. hydroxyzine 12.5-25 mg po), anti-emetic for p.r.n. use for periodic more severe symptoms.

2. Moderate Nausea and Vomiting of Pregnancy

If symptoms persists despite the above methods, consider adding:

- a. Metoclopramide 5-10 mg po tid
- b. If relief is not obtained, consider the 5-HT-3 receptor inhibitor, ondansetron 4 - 8 mg po tid, or dolasetron 25-100 mg po tid.

3. Severe Nausea and Vomiting of Pregnancy (Hyperemesis gravidarum)

Defined as intractable vomiting, not responsive to the above outpatient treatments, and associated with weight loss >5%, dehydration, 4+ ketonuria, and/or electrolyte derangements (usually hypokalemia), such that hospitalization for intravenous hydration is required.

1. Admit.
2. NPO; advance to sips and chips as tolerated.
3. IV hydration, with electrolyte replacement as indicated.
(Potassium replacement not greater than 10 meq/hr)
4. Rule out other causes (cholecystitis/pancreatitis, pyelonephritis, hepatitis, etc.)

5. Treatment with anti-thyroid medications is usually not indicated, does not relieve nausea and vomiting, and may cause the patient, and the fetus, to become hypothyroid if continued beyond 18 weeks gestation.
6. IV multivitamin replacement, especially thiamine 100 mg per liter
7. Any of the following parenteral anti-emetics:
 - a. dimenhydrinate 50 mg in 50 mL NS q4-6h IV over 20 minutes
 - b. metoclopramide 5-10 mg q8h IV
 - c. promethazine 12.5-25 mg q4h IV
 - d. dolasetron 4-8 mg over 15 minutes q12h IV

When the patient tolerates adequate oral intake, she may be considered for outpatient management. She may be sent home on the pharmacologic interventions recommended above for "Moderate Nausea and Vomiting of Pregnancy".

Figure 1. Management algorithm for prevention and treatment of nausea and vomiting of pregnancy (NVP)

* If one is considering stress doses of methylprednisolone, please consult MFM

* GERD: Gastroesophageal reflux disease, which can be treated with H2 receptor antagonists and proton pump inhibitors.

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Table 1 Common pharmacologic interventions

Agent	Drug Class	Dosage	Rx
Pyridoxine (Vitamin B6)	Vitamin B6	25 mg po	Oral: 10-25 mg po tid Most prenatal vitamins contain 2-10 mg Vit B6
Doxylamine	Antihistamine (H-1 Blocker)	12.5 mg po	Oral: 12.5 mg po tid (½ of 25 mg) 3-4 x / day NB: Some OTC preps contain diphenhydramine
Fructose, dextrose, and orthophosphoric acid *	Antiemetic	15-30 mL	Oral: 15-30 mL on arising; repeat every 3 hours or when nausea threatens
Doxylamine / pyridoxine* Available in Canada, not available in U.S.*	Antihistamine (H-1 Blocker) Vitamin B6	Doxylamine succinate 10 mg po / pyridoxine hydrochloride 10 mg po	Oral: Two delayed release tablets (a total of doxylamine 20 mg and pyridoxine 20 mg) at bedtime. In severe cases or in cases with nausea/vomiting during the day, dosage may be increased by 1 tablet in the morning and/or afternoon.
Promethazine	Antihistamine Phenothiazine Derivative Sedative	12.5-25 mg po	Oral, I.M., I.V., rectal: 12.5-25 mg every 4-6 hours as needed
Hydroxyzine*	Antihistamine	12.5-25 mg po	Oral: 12.5-100 mg/dose every 4-6 hours as needed
Dimenhydrinate*	Antihistamine	50-100 mg 50 mg IV	Oral: 50-100 mg every 4-6 hours, (not to exceed 400 mg/day or 200 mg/day if on doxylamine) I.V. 50 mg in 50 mL NS q4-6h IV over 20 minutes
Metoclopramide	Cholinomimetic	5-10 mg po	Oral: 10-15 mg/dose up to 4 times/day 30 minutes before meals or food and at bedtime. Single doses of 20 mg are

			occasionally needed for provoking situations I.V.: 5-10 mg q8h IV (5-10 mg/kg)
Dolasetron	Selective 5-HT3 Receptor Antagonist	25-100 mg po 4-8 mg IV	Oral: 25-200 mg single dose I.V.: 4-8 mg over 15 minutes q12h IV (0.6-5 mg/kg as a single dose 50 mg 1-2 minute bolus 2.4-3 mg/kg 20-minute infusion)

*Over the counter names available on request

Appendix 1

Interventions considered not helpful for the treatment of hyperemesis and areas of controversy

1. Long term total parenteral nutrition

Long term total parenteral nutrition is not recommended because of life-threatening complications secondary to central intravenous access complications. This form of therapy may have more hazards to the patient than the underlying disorder, Short-term peripheral parenteral nutrition (through a "PICC-Line") may be appropriate for selected cases.

2. Parenteral steroids

Parenteral steroids (e.g., methylprednisolone) have not been consistently shown to be helpful in the aggregate meta-analysis data, and are no longer recommended for inpatient treatment of hyperemesis. They have been associated with a 3-4 x increased risk of cleft lip and palate if taken before 10 weeks gestation.

3. Psychotherapy

There is little evidence that psychotherapy is helpful for hyperemesis, but the social situation of some patients may make short-term counseling a helpful adjunctive treatment modality.

4. Areas of Controversy

Does acupuncture work?

Acupressure at the wrist P6 locus has not been shown to be superior to placebo in the available aggregate data.

On the other hand, P6 acupuncture or acupressure wristbands do not require a prescription and have become a popular self-administered intervention. P6 acupuncture or acupressure has not been associated with any adverse effects on pregnancy outcome.

A Cochrane review of randomized trials did not find P6 acupuncture or acupressure wristbands significantly more effective than sham therapy, although some individual trials showed a benefit. One reason may be that a strong placebo effect has been

observed in patients who receive sham therapy. Self-administered nerve stimulation therapy over the volar aspect of the wrist at the P6 acupressure point using a commercial device also showed some promise in a randomized, controlled trial.

Do these medications cause birth defects?

There is no clear increase in the risk of birth defects among offspring of gravida with hyperemesis gravidarum, whether or not they take antiemetic medications. Although there is good evidence that women with nausea and vomiting in early pregnancy have a lower rate of miscarriage than women without these symptoms, these studies have not correlated outcome with respect to the severity of the disorder. Most of the women in these studies had mild symptoms, rather than hyperemesis. Although long-term follow-up data are limited, one small observational cohort study found no evidence of neurodevelopmental delay in 3 to 7 year old children of mothers with hyperemesis gravidarum who were treated with pyridoxine and doxylamine succinate or untreated.

Thyroid function testing

Many patients with hyperemesis will demonstrate biochemical evidence of a hyperthyroid state, but this is usually secondary to their high HCG levels. There is not support for routine thyroid testing in hyperemesis.

Treatment with anti-thyroid medications is usually not indicated, does not relieve nausea and vomiting, and may cause the patient, and the fetus, to become hypothyroid if continued beyond 18 weeks gestation. If one is concerned about hyperthyroidism, please consult the Thyroid Disease in Pregnancy guideline.

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