

Treatment of nausea and vomiting in pregnancy

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SUMMARY

Most pregnant women will experience some degree of nausea or vomiting during pregnancy.

Dietary and lifestyle interventions, along with appropriate drug treatment, can enable women to continue their everyday life and work with minimal disruption.

Clinical guidelines for therapy are available, and early treatment has been shown to reduce the severity of symptoms.

Pregnant women should be reassured that nausea and vomiting do not usually harm the fetus. Also, medicines used to treat this condition are not associated with an increased risk of birth defects, miscarriage, prematurity or other adverse outcomes in pregnancy.

Severe nausea and vomiting (hyperemesis gravidarum) is associated with weight loss, dehydration and electrolyte abnormalities and may require hospitalisation.

Introduction

Nausea and vomiting during pregnancy affects up to 90% of women. The symptoms are usually worse in the morning (hence the name 'morning sickness') but can occur at any time of the day, and sometimes continue throughout the day. Nausea and vomiting typically commence around weeks 8 or 9 of pregnancy and subside after 12-14 weeks. However, in 10% of pregnancies symptoms may continue beyond 20 weeks and even until birth.

The cause of nausea and vomiting in pregnancy is unclear and probably has many contributing factors, although it is most likely related to hormonal changes. Before assuming a diagnosis, it is important to rule out other reasons for vomiting in a pregnant woman.

Women who have previously suffered from nausea and vomiting in pregnancy are more likely to have symptoms in a subsequent pregnancy. Symptoms can be more severe in women carrying twins.

Hyperemesis gravidarum is a more severe form of nausea and vomiting which occurs in less than 1% of pregnancies. It is characterised by maternal weight loss greater than 5% of the pre-pregnancy weight, dehydration and electrolyte imbalance, and often requires hospitalisation for intravenous rehydration.

Women can be reassured that mild to moderate nausea and vomiting will not affect their developing baby, and is actually associated with lower rates of miscarriage, stillbirth, premature birth, intrauterine growth restriction and birth defects.¹ However, unrelenting nausea and vomiting is debilitating and

affects a woman's capacity to carry out her normal daily tasks. Some women may choose to terminate an otherwise wanted pregnancy.²

Management

Research has shown that pre-emptive treatment early in pregnancy reduces the severity of symptoms³ and can have a profound effect on a pregnant woman's health and quality of life. However, studies have shown that many women do not receive appropriate information about lifestyle changes or timely drug treatment.⁴

When symptoms persist despite lifestyle, dietary and non-pharmacological interventions (see Box 1), drug treatment is indicated. Despite the prevalence of nausea and vomiting during pregnancy, there is a lack of high quality evidence to support current treatment guidelines.^{5,6} There are ethical issues regarding randomised controlled trials in pregnant women, as well as the difficulty in quantifying levels of nausea and vomiting.

Pharmacological therapies

In Australia, the Therapeutic Goods Administration determines a drug's pregnancy classification (tga.gov.au/hp/medicines-pregnancy-categorisation.htm) and updates are available on the Prescribing Medicines in Pregnancy Database.⁷ Additional information about a drug may be gained by clicking on the drug in the search field.

An evidence-based treatment algorithm developed by the Motherisk teratology information service in Canada⁸ has been adapted for use in Australia

(Box 2).⁹ Pregnant women can be reassured that there is extensive experience with the drugs included in the guidelines, and that none of them has been shown to increase the risk of adverse outcomes in pregnancy. It is worth emphasising that all women have a background risk of around 3% of giving birth to a baby with a major birth defect and that approximately 15% of known pregnancies end in miscarriage, regardless of any medicines taken by the mother.

Pyridoxine

Pyridoxine (vitamin B6, unclassified) is considered first-line therapy and can be taken in conjunction with other antiemetics.^{8,9}

Doxylamine with pyridoxine

A sustained-release tablet combining doxylamine 10 mg and pyridoxine 10 mg has been available for many years in Canada for nausea and vomiting in pregnancy. In 2013, it was also approved in the USA following a randomised, placebo-controlled trial which showed it was effective and well tolerated.¹⁰ A similar product (Debendox) was voluntarily withdrawn in Australia in 1983 after claims that it caused birth defects. Subsequent research has shown that this assertion was unfounded, yet for 30 years Australian women have been denied this safe and effective treatment.¹¹ However, the two separate medicines can be purchased over the counter in Australia.¹²

Box 1 Commonly practised interventions for nausea and vomiting in pregnancy

- identify and avoid known triggers
- avoid having an empty stomach
- eat small amounts of food often
- eat at times when less nauseous
- avoid spicy and fatty foods
- have food and fluids at separate times
- drink small amounts of fluid often, but try to have two litres daily
- cold or frozen drinks and foods are often better tolerated
- keep dry crackers and water by bedside, and eat before getting up in the morning
- get out of bed slowly, and avoid rushing
- herbal teas may help (peppermint, ginger)
- do not brush teeth straight after eating
- excess saliva can be relieved by spitting or using a mouthwash
- rest when possible as fatigue makes nausea worse
- acupuncture

Prochlorperazine

Prochlorperazine is a pregnancy category C drug. It carries the warning 'when given in high doses during late pregnancy, phenothiazines have caused prolonged neurological disturbances in the infant'. This is hardly relevant for mothers who take prochlorperazine in early pregnancy.

Metoclopramide

Metoclopramide is classified as pregnancy category A and is the most commonly prescribed antiemetic in pregnancy. Category A may appear reassuring in terms of safety, but does not give any indication of the drug's efficacy. In fact many pregnant women report that metoclopramide is ineffective for their nausea and vomiting.⁴

Ondansetron

Although ondansetron has limited safety data in pregnancy, it is often prescribed for women with hyperemesis gravidarum. It is not recommended as first-line therapy, especially in the first trimester of pregnancy.¹³ Ondansetron commonly causes constipation, which may already be a problem in pregnancy. Sparing use of ondansetron, and co-administration of laxatives (for example psyllium, docusate, lactulose, polyethylene glycol) is advisable.

Box 2 Drug treatments for nausea and vomiting in pregnancy – current guidelines ^{8,9} Added May 2014

- Pyridoxine 25–50 mg orally, up to 4 times daily (200 mg/day shown to be safe)
- If symptoms persist, continue pyridoxine and add one of the following antiemetics:
 - doxylamine (category A) 12.5–25 mg orally at night may be increased to 12.5 mg in the morning and early afternoon, and 25 mg at night if drowsiness is not a significant problem
 - promethazine (category C) 10–25 mg orally, 3–4 times a day
 - metoclopramide (category A) 10 mg orally, 3 times a day
 - prochlorperazine (category C) 5–10 mg orally, 3–4 times a day
- If symptoms still persist, continue pyridoxine with a different antiemetic from the list above
- If still no satisfactory response, try ondansetron (category B1) tablet or wafer 4–8 mg, 2–3 times a day
- Patients unable to tolerate tablets or wafers, use one of the following:
 - metoclopramide (category A) 10 mg intramuscular or intravenous, every eight hours
 - ondansetron (category B1) 4–8 mg intravenous, every 8–12 hours
 - prochlorperazine (category C) 25 mg rectally, 1–2 times daily or prochlorperazine (category C) 12.5 mg intramuscular, every 8 hours
 - promethazine (category C) 12.5–25 mg intramuscular, every 4–6 hours
- If vomiting continues, consider treatment in hospital and rehydration with intravenous fluids
- Prednisolone (category A) 50 mg orally daily for 3 days, then 25 mg daily, then reducing by 5 mg daily

Mirtazapine

Mirtazapine, an antidepressant which blocks 5-HT₃ receptors, may be an alternative when other antiemetics fail to treat hyperemesis. Two small case series^{14,15} and three case reports¹⁶⁻¹⁸ describe significant improvement in symptoms of hyperemesis gravidarum which are resistant to other medicines.

Corticosteroids

Corticosteroid use should be limited to women with intractable nausea and vomiting during pregnancy. Women should have regular medical follow-up to ensure steroids are not taken for lengthy periods. Corticosteroids are best avoided in the first 10 weeks of pregnancy due to a possible association with cleft lip and palate.⁹

Other treatments

Antacids, ranitidine and proton pump inhibitors are recommended to treat acid reflux or bloating, as

these conditions can exacerbate nausea and vomiting in pregnancy.⁸

Women with prolonged vomiting may be at risk of thiamine deficiency. Thiamine replacement (100 mg daily oral or intravenous) should be considered in these women.

Conclusion

Nausea and vomiting in pregnancy is very common and there is a wide range of suggested treatments. Dietary and lifestyle changes ought to be implemented first, but pharmacological treatment should not be withheld because of fear of harming the baby. Expert clinical guidelines are available for prescribers who can be assured that early treatment will enhance the quality of life for pregnant women and their families. <

Conflict of interest: none declared

Obstetric drug information services in Australia

| State | Service | Phone |
|---|--|---|
| All states | Medicines Line (NPS MedicineWise) | 1300 633 424 |
| Australian Capital Territory | Drug Information Canberra Hospital | 02 6244 3333 |
| New South Wales | MotherSafe Royal Hospital for Women Randwick | 02 9382 6539 1800 647 848 (toll free NSW) |
| Queensland (health professionals only) | Queensland Medicines Advice and Information Service Brisbane | 07 3646 7098 |
| South Australia | Women's and Children's Hospital Adelaide | 08 8161 7222 |
| Victoria | Medicines Information Service Royal Women's Hospital Melbourne | 03 8345 3190 |
| | Drug Information Service Monash Medical Centre | 03 9594 2361 |
| Western Australia | Women's and Children's Health Services Perth | 08 9340 2723 |

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FURTHER READING

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