Canterbury District Health Board
Te Poari Hauora ō Waitaha

Clinical Pharmacology Bulletin

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Treatment of nausea and vomiting during pregnancy

Background

Nausea and vomiting are experienced by up to 80% of pregnant women. This is often referred to as morning sickness, although nausea and vomiting may occur at other times of the day. For the majority of pregnant women these symptoms are limited to the first trimester and are manageable, but for some, the symptoms may persist throughout pregnancy and become severe.

Around 1% of women develop hyperemesis gravidarum where vomiting and nausea may be so severe that dehydration, weight loss and metabolic compromise may occur. In these circumstances there are potentially serious health risks to the mother and the foetus necessitating hospital treatment and referral to Obstetric Services.

Symptom control of morning sickness

This can be approached in a stepwise manner based on the severity of symptoms. A combination of therapies may be useful in some patients.

Non-pharmacological management may be helpful for some women. This includes the avoidance of nausea and vomiting triggers such as dehydration, hunger, lack of sleep and, in some women, strong smells. The intake of frequent, small, carbohydrate rich meals with a low fat content has been used anecdotally for management of mild symptoms e.g. a couple of plain biscuits, dry toast or ginger biscuits.

Antiemetics are the mainstay of treatment for women with troublesome nausea and vomiting who are not successfully managed by non-pharmacological measures.

First-line agents are usually well tolerated and have a large body of data to support their use. They include the sedating antihistamine, cyclizine, and the dopamine antagonists; metoclopromide, promethazine and prochlorperazine.

Observational studies of cyclizine or promethazine exposure during the first trimester found no increase in the risk of malformations in exposed infants. Similarly, prospective studies of metoclopramide use during the first and second trimester have not shown an association with an increased risk of malformations. Prochlorperazine is effective and considered safe to use during pregnancy, despite being implicated in a number of case reports with various congenital abnormalities. More robust studies do not support these findings.

The side effects of these antiemetics are generally mild. Cyclizine, promethazine and prochlorperazine may all cause sedation, dry mouth and other adverse effects that may limit their usefulness in some patients. Metoclopramide has been reported to cause restlessness, drowsiness and fatigue in up to 10% of patients and, less commonly, dystonic reactions (0.2%).

Women with hyperemesis gravidarum may need therapy with more than one antiemetic with different mechanisms of action.

Second-line agents include ondansetron (antagonises serotonin [5HT3] receptors in the gut), which has considerably less data to support safety in pregnancy compared to the first-line antiemetics. However, the limited available data suggest that it is not associated with an increased risk of malformations. Use may be necessary in some women with severe symptoms who have failed to respond to combination therapy with first-line agents.

Complementary therapies are generally not recommended during pregnancy due to the lack of evidence to support their safety and efficacy. However, the use of these is popular as they are perceived by some people to be 'safer' than conventional treatments. Pyridoxine (vitamin B6) is used commonly and there are some data to show safety and efficacy in the treatment of morning sickness. Ginger is also suggested to be helpful. However, there are insufficient safety data to recommend its use in pregnancy in greater quantities than found in food.

Table: management of nausea and vomiting during pregnancy

	Drug (FDA category*)	Dosage	Comments	Funding status
Non-pharmacological	N/A	Small frequent carbohydrate-rich and low fat meals.	A small meal first thing (plain biscuits or dry toast) may be helpful	N/A
First-line therapy	Cyclizine (B)	25 to 50mg up to three times a day	Side effects such as sedation and dry mouth can occur	Subsidised
	Metoclopramide (B)	10mg three times a day	Side effects such as restlessness, drowsiness and rarely dystonic reactions can occur	Subsidised
	Prochlorperazine (C)	5 to 10mg two to three times a day	Side effects such as sedation, dizziness, dry mouth and dystonia can occur	Subsidised
	Promethazine (C)	10-25mg at bedtime, up to 4-6 hourly (max 100mg daily)	Side effects such as sedation and dry mouth can occur	Subsidised
Second-line therapy	Ondansetron (B)	4mg three times a day under specialist obstetrics recommendation only		Discretionary community
Complementary therapies	Pyridoxine (A)	25mg three times a day	Very large doses may be neurotoxic	Subsidised
	Ginger (C)	No data re dose or efficacy for treatment of nausea and vomiting during pregnancy		

* A - Adequate, well-controlled studies failed to demonstrate risk to foetus in the first trimester of pregnancy (and no evidence of risk in later trimesters). B - Animal reproduction studies failed to demonstrate risk to the foetus and no adequate, well-controlled studies OR Animal studies have shown adverse effect, but adequate, well-controlled failed to demonstrate risk to the foetus in any trimester. C - Animal reproduction studies have shown adverse effect on foetus and no adequate, well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnancy despite potential risks.