Drug Management in Nausea and Vomiting and Hyperemesis Gravidarum in the first trimester of pregnancy.

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Abstract

Nausea and vomiting in pregnancy (NVP) affects up to 80% of pregnant women,1 which is one of the most common indications for hospital admission during pregnancy, with typical stays of between 3–4 days.

NVP is defined as the symptom of nausea and/or vomiting during the first trimester of pregnancy where there are no other causes. It represents a continuous spectrum of severity, ranges from the nausea and vomiting that occurs in most pregnancies to severe disorder of hyperemesis (HG). HG is defined as persistent vomiting and severe nausea during pregnancy, which is sufficient to produce weight loss (greater than 5% of the body mass), fluid and electrolyte disturbances, dehydration, acidosis from malnutrition, and ketonuria.

The etiological theories for NVP and HG range from the fetoprotective and genetic to the biochemical, immunological, and biosocial. They are primarily thought to be associated with rising levels of beta-human chorionic gonadotropin (hCG) hormone, and conditions with higher hCG levels, such as trophoblastic disease and multiple pregnancies

The risk factors for HG among pregnant women are younger maternal age, first pregnancy, multiple pregnancy, and gestational trophoblastic disease.

The initial treatment for NVP is often conservative, including dietary changes and emotional support. The woman is advised to rest, eat small, and have frequent meals that are high in carbohydrate and low in fat; and avoid any food or smell that trigger symptoms. Drinking regular, small amounts of water, or other clear fluid can also be helpful.

In terms of the pharmacological treatments for NVP and HG, Cochrane review, and other systematic reviews and meta-analyses have reported on the safety and efficacy of many antiemetics for use in NVP and HG, with no increased risk of teratogenesis or other adverse pregnancy outcomes.

Drugs use in NVP includes antihistamines (H1 receptor antagonists) such as promethazine, cyclizine, and phenothiazines with prochlorperazine and chlorpromazine, and dopamine antagonists including metoclopramide23 and domperidone. Because different drug classes may have different mechanisms of action and therefore synergistic effects, combinations of drugs from different classes should be used in women who does not respond to a single antiemetic. Furthermore, persistent vomiting may mean that oral doses of antiemetics are not absorbed and therefore the intravenous, rectal, subcutaneous, or intramuscular routes may be necessary and more effective.

The commonly used drugs in NVP and HG by adopting the evidence-based approach are:

Antihistamine (H_1 recepter antagonists) antiemetics have the best safety profile of all the commonly used drugs, so it should be the first-line of treatment for NVP and HG. Promethazine and cyclizine have been shown to be safe and effective treatments for NVP and HG.

If antihistamine antiemetics does not work, phenothiazines can be used which also have good safety and efficacy data for management of NVP and HG. Examples are Prochlorperazine and Chlorpromazine.

If antihistamine antiemetics and phenothiazines are not able to control the symptoms of NVP and HG, metoclopramide, and domperidone are also safe and effective alternative treatments. It can be used as an add-on therapy.

Due to the risk of extrapyramidal effects with metoclopramide, it should not be used as the first-line therapy. A review of metoclopramide conducted by the European Medicines Agency's Committee for Medicinal Products for Human Use, has confirmed the risks of short-term extrapyramidal disorders and tardive dyskinesia, particularly in young people. The review recommends metoclopramide should only be prescribed for short-term use (maximum duration of 5 days).

There is evidence that ondansetron is safe and effective for the management of NVP and HG, but because data are limited, it should be used as third-line therapy.

Corticosteroids should not be used until conventional treatment with intravenous fluid replacement and regular antiemetics has failed. Studies have shown that corticosteroids have resulted in dramatic and rapid improvement in case series of women with refractory HG.

Pyridoxine is not recommended for HG. There is no association between the degree of NVP at 12 weeks and vitamin B6 levels measured at 15 weeks. A Cochrane review6 concluded that there is lack of consistent evidence that pyridoxine is an effective therapy for NV.

Most women admitted to hospital with HG are hyponatraemic, hypochloraemic, hypokalaemic, and ketotic. The 0.9% sodium chloride with 20 or 40 mmol potassium chloride or Hartmann's solution re appropriate intravenous (IV) fluids to be infused for patients with NVP or HG. Dextrose or dextrose/ saline IV fluids are not recommended, as dextrose may precipitate Wernicke's encephalopathy in thiamine-deficient states.

Thiamine supplementation should be given to all women who are diagnosed with NVP and HG. The inability to eat can lead to thiamine deficiency which results in Wernicke's encephalopathy and subsequently Korsakoff's psychosis. Give 5 mg orally once a day, only for patients who are less than 12 weeks' gestation. As the women have severe vomiting and nausea symptoms, dose higher than the normal dose (400 micrograms once a day) is used. Recurrent intractable vomiting may lead to gastroesophageal reflux disease, oesophagitis, or gastritis. Histamine H_2 receptor antagonists or proton pump inhibitors are safe to be used for women developing these medical problems. Patients with HG are at an increased risk of developing deep vein thrombosis (DVT) due to dehydration and their lack of mobility. Thromboprophylaxis with low-molecular-weight heparin should be considered in severe cases of HG.

Recent Publications (minimum 5)

1. The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum Green-top Guideline, No. 69. 1st ed. UK Royal College of Obstetricians and Gynaecologists website Available at https:// www.rcog.org.uk/.
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3. Sarris I, Bewley S, Agnihotri S. Oxford specialty training: training in obstetrics and gynaecology. 1st ed. Oxford University Press;2009:116.
4. Einarson TR, Piwko C, Koren G. Quantifying the global rates of nausea and vomiting of pregnancy: a meta-analysis. J Popul Ther Clin Pharmacol 2013;20:171–183.
5. Lacasse A, Lagoutte A, Ferreira E, Bérard A. Metoclopramide and diphenhydramine in the treatment of hyperemesis gravidarum: effectiveness and predictors of rehospitalisation. Eur J Obstet Gynecol Reprod Biol 2009;143:43–49.
6. Gazmararian JA, Petersen R, Jamieson DJ, Schild L, Adams MM, Deshpande AD, et al. Hospitalizations during pregnancy among managed care enrollees. Obstet Gynecol 2002;100:94–100.
7. Atanackovic G, Wolpin J, Koren G. Determinants of the need for hospital care among women with nausea and vomiting of pregnancy. Clin Invest Med 2001;24:90–93.: pathogenesis and treatment. Semin Liver Dis 1998; 18:281.



Christina Leung completed two Bachelor degrees in England, BSc Management Sciences followed by the BPharm Pharmacy. Following the registration as a pharmacist in the UK, she worked in different London Teaching Hospitals for 16 years. In UK, she specializes in Paediatrics (especially in PICU and Paediatric Liver), Obstetrics and Gynaecolog, and also organ transplant medicines, She published a number of articles including drugs use in paediatric liver diseases in the UK and management of vomiting in pregnancy and hyperemesis gravidarum. Ms Leung is also a registered pharmacist in Hong Kong. Currently, She is now one of the Pharmacists working in a Hospital Authority Hospital in Hong Kong

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