Background

Management of hyperemesis gravidarum

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Guidelines on the Management of Hyperemesis Gravidarum

Nausea and vomiting are common features of the first trimester, experienced by up to 80% of women. The symptoms are usually benign and are overcome by the 14th week of pregnancy. Occasionally the vomiting becomes more severe or protracted, requiring admission to hospital. This condition is known as hyperemesis gravidarum which can be defined as intractable vomiting associated with loss of more than 5% of pre pregnancy weight, dehydration, electrolyte disturbances, or need for hospital admission. This affects 0.3-3.6% of all pregnancies. There is a high risk of recurrence in subsequent pregnancies.

Hyperemesis gravidarum is a diagnosis of exclusion, rarely starts after 12 weeks gestation, and if a woman presents with vomiting after this time, alternative causes should be sought. Consider diabetic ketoacidosis as an alternative diagnosis in a ketotic woman with diabetes.

Complications

- Hyperemesis is associated with hyponatraemia, hypokalaemia, low serum urea, raised haematocrit and ketonuria with a metabolic hypochloraemic alkalosis. If severe, a metabolic acidaemia may develop.

- In two-thirds of patients, there may be abnormal thyroid function tests with a biochemical thyrotoxicosis and raised free thyroxine levels with or without a suppressed thyroid stimulating hormone level. These patients rarely have thyroid antibodies and are euthyroid clinically. The biochemical thyrotoxicosis resolves as the hyperemesis improves and treatment with antithyroid drugs is inappropriate.

- Liver function tests are abnormal in up to 40% with the most likely abnormality being a rise in transaminases. Bilirubin levels can be slightly raised but without jaundice, and amylase levels can be mildly raised too. These abnormalities improve as the hyperemesis resolves.

- Rarely severe hyponatraemia producing pontine demyelination (central pontine myelinolysis) which can result in pyramidal tract signs, spastic quadriplegia and altered levels of consciousness. Do not correct hyponatraemia rapidly as rapid correction is associated with risk of central pontine myelinolysis. If sodium less than 110 mmol/l aim to increase sodium by 0.5mmol/hour.

- Wernicke’s encephalopathy, as a result of acute nutritional thiamine (vitamin B1) deficiency, can develop in severe cases. Wernicke’s encephalopathy may also be precipitated by dextrose-containing fluids (oral or IV). Avoid dextrose infusion for fluid replacement especially in presence of abnormal LFTs.

- Peripheral neuropathy and megaloblastic anaemia are also possible and are a result of deficiencies in pyridoxine (Vitamin B6) and cyanocobalamin (Vitamin B12).

- Thrombosis

Pregnancy outcomes are usually good, but an increased incidence of Low Birth weight, prematurity and small for gestational age has been reported.
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Management

History

Quantify severity
History to exclude other causes: abdominal pain, urinary symptoms, infection, drug history

Examination

Temperature
Pulse
Blood pressure
Oxygen saturations
Respiratory rate
Abdominal examination
Weight
Signs of dehydration
Signs of muscle wasting
Other examination as guided by history

Investigation

Urine dipstick: – quantify ketonuria, check for infection
MSU
Urea and electrolytes
Full blood count
Blood glucose monitoring: – if diabetic
Ultrasound scan on first admission to confirm viable intrauterine pregnancy and exclude multiple pregnancy and trophoblastic disease
TFTs in refractory cases
LFTs

Treatment

1. Inpatient management should be considered if there is at least one of the following:
   a. continued nausea and vomiting and inability to keep down oral antiemetics
   b. continued nausea and vomiting associated with ketonuria and/or weight loss (greater than 5% of body weight), despite oral antiemetics
   c. Confirmed or suspected comorbidity (such as urinary tract infection and inability to tolerate oral antibiotics).

2. Weigh patient on admission, then twice weekly.

3. Intravenous fluids
   a. Suitable fluids are
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- Normal Saline eg Sodium chloride 0.9% (150mmol/L sodium) or Hartmann’s.

Avoid glucose as it can precipitate Wernicke’s encephalopathy.

- Titrate to daily Na, K, and fluid requirements. Consider potassium replacement if hypokalaemia, using Sodium chloride 0.9% 500ml + 20mmol potassium or Sodium chloride 0.9% 500ml + 40mmol potassium.

- The rate of rehydration depends on severity but usually initially aggressive rehydration with 1000mls over 2 hours (no potassium) and subsequently 1000mls over 4-8 hours, having reviewed the U+E.

- NB Refer to consultant any women with renal or cardiac failure or complex congenital heart disease as aggressive hydration is contraindicated.

4. Daily Urea and Electrolytes, HCO3 whilst on intravenous fluids

5. Anti-embolism stockings (AES) and prophylactic Dalteparin (dose based on body weight - see Trust Guideline of prophylactic anticoagulation in pregnancy AO1b – ID No: 878)

6. Anti-emetics

- These appear to be safe in the first trimester.(Grade C evidence)
- Use regularly rather than PRN whilst vomiting.
- Combinations of different drugs should be used in women who do not respond to a single antiemetic.
- For women with persistent or severe hyperemesis gravidarum, the parenteral or rectal route may be necessary and more effective than an oral regimen.

Recommended antiemetic therapies and dosages

First line

Cyclizine 50 mg PO, IM or IV 8 hourly

This should be avoided in cases of drug abuse. Side effects are drowsiness, dizziness, insomnia, blurred vision, dry mouth, constipation, tachycardia (rarely) and urticaria.

Prochlorperazine 5–10 mg 6–8 hourly PO; 12.5 mg 8 hourly IM/IV; 25 mg PR daily

Side effects of prochlorperazine are extrapyramidal symptoms, drowsiness, antimuscarinic symptoms, hypotension, and rarely cardiac arrhythmias. Avoid prochlorperazine in women with severe liver or renal impairment or epilepsy.

Promethazine 12.5–25 mg 4–8 hourly PO, IM, IV or PR

Chlorpromazine 10–25 mg 4–6 hourly PO, IV or IM; or 50–100 mg 6–8 hourly PR

Second line
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**Metoclopramide** 5–10 mg 8 hourly PO, IV or IM (maximum 5 days’ duration)

Side effects of metoclopramide are extrapyramidal symptoms especially dystonic reactions. Caution with SSRIs as CNS toxicity is recognised.

**Domperidone** 10 mg 8 hourly PO; 30–60 mg 8 hourly PR
Not to be used in women with cardiac conduction defects or severe liver disease.

**Ondansetron** 4–8 mg 6–8 hourly PO; 8 mg over 15 minutes 12 hourly IV
Side effects are constipation, headache, flushing/warmth sensation, hiccups.

**Third line**

**Corticosteroids**: hydrocortisone 100 mg twice daily IV and once clinical improvement occurs, convert to prednisolone 40–50 mg daily PO, with the dose gradually tapered until the lowest maintenance dose that controls the symptoms is reached.

The decision to start corticosteroids must be made by a consultant.

This treatment is contraindicated in patients with possible gastroduodenal ulceration. Patients must be warned about the risk of osteoporosis, infection and rarely aseptic necrosis of the hip. Fetal adrenal suppression may occur if prolonged high dose exposure. Careful consideration should be taken before starting corticosteroids in pregnancy at < 10 weeks gestation, a critical period for cleft palate formation as there is a small risk with high dose steroids.

The regimen:

a) Hydrocortisone 100mg IV bd until vomiting controlled. If there is no response after 48hr, stop treatment (abruptly) since further response is unlikely.

b) When vomiting controlled, convert to Prednisolone 40mg po daily.

c) After a week, start decreasing the dose in 5mg intervals every week whilst the vomiting is controlled. The idea is to titrate the dose such that the patient is on the lowest dose of steroids which achieves adequate symptom control.

d) Patients may need to stay on steroids throughout the pregnancy and must carry a STEROID TREATMENT card with them at all times. Patients still on steroids at the time of delivery must be give Hydrocortisone 100 mg IV 6 hourly during labour/delivery.

e) When the patient finally comes off the steroids she must reduce the dose gradually (as in c).

14. When all other medical therapies have failed, enteral or parenteral treatment should be considered with a multidisciplinary approach. In refractory cases artificial nutritional support should be considered. Referrals to the Nutrition Support team...
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can be made via ICE. Enteral (nasogastric or nasojejunal) or parenteral feeding can be considered. The MUST screening tool (available via Nutrition department on intranet) may be useful. Enteral feeding is contraindicated in women with acute vomiting due to the risk of aspiration.

15. **Vitamin supplementation** - especially thiamine (50mg po once daily) or as Pabrinex im/iv, one pair of ampoules twice weekly to prevent Wernicke’s encephalopathy) - in patients who have required I.V. fluids for more than 48 hours, or those with nutritional deficiency.

- IV Pabrinex may precipitate anaphylactic reactions. Facilities for treatment should be nearby if hyperemesis protracted check serum magnesium as response to Thiamine is poor in hypomagnesaemia

14. Anti-reflux measures. H₂ blockers such as Ranitidine and proton pump inhibitors (Omeprazole) are considered safe in pregnancy although data limited (Omeprazole is licensed for use in pregnancy)

15. Give the patient information leaflet on ‘Hyperemesis gravidarum’ (M211) to the patient on admission.

References:


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10. The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum (Green-top Guideline No. 69) June 2016