South Australian Perinatal Practice Guidelines

Hyperemesis in Pregnancy

Introduction

- Nausea and vomiting are among the earliest symptoms of pregnancy
- The term hyperemesis gravidarum is used when symptoms are severe enough to require hospital admission and rehydration. Women with hyperemesis are usually ketotic and unable to maintain adequate oral hydration
- Hyperemesis gravidarum affects about 0.5 to 10 women per 1,000 pregnancies (Hod 1994)

Pathogenesis

Hormonal

- High levels of Human chorionic gonadotrophin (hCG) and oestrogen have been implicated in hyperemesis in some but not all studies (Kauppila 1979; Soules 1980; Goodwin 1992)

Mechanical

- There is a fall in lower oesophageal pressure, decreased gastric peristalsis and gastric emptying in pregnancy (Walsh 1996)

Emotional

- Various psychological and social factors are associated with hyperemesis, but it is debatable whether these are consequences of the condition, rather than causal (Deuchar 1995; Naeff 1995)

Diagnosis and investigations

- The diagnosis of hyperemesis is only made after exclusion of other pathology
  - Obtain detailed history including any maternal disease or conditions related to nausea and vomiting
  - Clinical assessment for signs of dehydration
  - Exclude maternal disease, molar or multiple pregnancy
- Investigations are required to determine the degree of physiological disturbance and to exclude significant pathology if indicated by history and examination
  - Ward urinalysis, microurine and culture
  - Blood for urea, electrolytes and serum creatinine
  - Blood sugar if diabetic
  - Liver function tests (specific hepatitis serology if indicated)
  - Thyroid stimulating hormone, free T4 level to exclude thyrotoxicosis
  - Serum amylase if pancreatitis considered
  - Obstetric ultrasound to confirm ongoing pregnancy and exclude multiple pregnancy or hydatidiform mole
  - Abdominal erect and supine x-rays if suspected bowel obstruction

Exclusion of other pathology before diagnosis of hyperemesis gravidarum

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Possible cause	Investigations if indicated by history and examination
Urinary tract infection	Urinalysis, microurine, urine culture
Gastroenteritis	Stool culture
Drug induced vomiting	
Multiple pregnancy	Obstetric ultrasound
Hydatidiform mole	Obstetric ultrasound
Diabetic ketoacidosis	Urinalysis, electrolytes, blood sugar level
Hepatitis	Liver function tests, specific hepatitis serology
Addison's disease	Electrolytes, creatinine
Thyrotoxicosis	Thyroid stimulating hormone, free T4 level
Pancreatitis	Serum amylase
Bowel obstruction	Erect / supine abdominal X-ray with appropriate shielding
Raised intracranial pressure	MRI or CT head

Management

- Hyperemesis gravidarum may result in:
  - Hyponatraemia
  - Hypokalaemia
  - A metabolic hypochloraemic alkalosis
  - Ketonuria
  - Raised haematocrit
  - Increased specific gravity of the urine
  - Wernicke's encephalopathy (rare)

Treatment options and evidence of treatment efficacy

Intravenous rehydration

- This is the most important component of management
- No study has compared different fluid replacements for nausea and vomiting of pregnancy (ACOG 2004)
- Use electrolyte solutions containing sodium and potassium to correct the hyponatremia + / - hypokalemia (either sodium chloride 0.9 % or Hartmann's)
- Glucose and vitamins, especially thiamine, may be included as a treatment option when prolonged vomiting is present (ACOG 2004)

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Precaution:

- Intravenous glucose increases Vitamin B1 requirements. In cases of severe nausea and vomiting of prolonged duration (> 3 weeks and gestation > 10 weeks), this may precipitate Wernicke's encephalopathy (Bergin 1992; Chiossi et al. 2006). Administer thiamine supplements (100 mg once daily either orally or intravenous) before giving intravenous glucose to prevent this

Nasogastric feeding and Total Parenteral Nutrition (TPN)

- Enteral or parenteral nutrition should be considered for any pregnant woman who cannot maintain her weight because of vomiting (ACOG 2004)
- Intravenous thiamine supplementation 100 mg daily is advised for women with hyperemesis gravidarum of longstanding duration receiving parenteral carbohydrate solution or nutrition (Chiossi et al. 2006)
- In a small study, nasogastric feeding has been successfully compared with parenteral nutrition in terms of clinical efficacy and cost (Hsu 1996). If tolerated, it may be effective before resorting to TPN
- Small observational studies have supported the safety of TPN in pregnancy, and its role in temporarily aiding maternal and fetal nutrition in hyperemesis (Zibell-Frisk 1990)
- TPN should be arranged in consultation with the appropriate specialists

Pharmacological treatments

Antiemetics

- A meta-analysis of 12 controlled studies involving over 1,500 women demonstrates a significant reduction in nausea using antiemetic medication with no increase in miscarriage or fetal abnormality (Jewell 2004)
- Metoclopramide (Maxolon) – 10 mg tablets, one tablet taken three times a day. Side effects may include extrapyramidal signs and oculogyric crises
- Doxylamine (Restavit) – 25 mg tablets, one at night. Doxylamine with Vitamin B6 (Diclectin) is the only medication approved in Canada for nausea and vomiting in pregnancy (Category A)
- Promethazine theoclate (Avomine) – 25 mg morning and night. Side effects include sedation
- Prochlorperazine (Stemetil) – Suppositories, 25 mg once or twice daily for severe, persistent and uncontrolled hyperemesis gravidarum, not relieved by the above treatment
- Promethazine and prochlorperazine – Category C for use in pregnancy, as when used in large doses late in pregnancy, they have been associated with extrapyramidal side effects in the infants after birth

Ondansetron

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- Selective 5HT3 receptor agonist
- Reported as effective in two cases of intractable hyperemesis (Giukontes 1992; World 1993), but no benefit over antihistamines demonstrated in a small pilot study (Sullivan 1996). [Has been associated with chest pain and myocardial ischaemia, and myocardial infarction (Frigiero 1996)]
- Only initially prescribed for cases of severe hyperemesis gravidarum, in association with intravenous rehydration, thiamine and electrolyte correction
- Doses: 4-8 mg intravenous or orally, 8-12 hourly, available as wafers to dissolve in the mouth
- Category B1 in pregnancy

Corticosteroids

- Avoid during the first trimester because of the possible increased risk of oral clefting and restrict to refractory cases (Arsenault & Lane 2002). For further information see http://www.otispregnancy.org/files/prednisone.pdf
- Case reports of the successful use of corticosteroids in intractable hyperemesis (Nelson-Piercy 2001) are supported by a randomised controlled trial of oral methylprednisolone (16 mg three times daily, halved every three days) compared to promethazine that found the oral steroid was more effective than the antihistamine in preventing readmission (Safari 1998)
- Blood sugar levels should be monitored carefully. Occasionally, insulin may be needed to maintain normoglycaemia

Vitamins

- Studies report pyridoxine (vitamin B6) significantly reduces nausea, but there was no significant reduction in vomiting (Sahakian 1991;Vutyavanich 1995)
- Pyridoxine – 25 mg tablets, one tablet taken three times a day

Ginger powder

- One trial of 70 women comparing ginger with placebo reported ginger to be of benefit for both nausea and vomiting in pregnancy (Vutyavich 2001)
- A recent trial of 291 women compared ginger with Vitamin B6 and reported ginger to be equally effective as Vitamin B6 in relieving the severity of symptoms of nausea, dry retching and vomiting in early pregnancy (Smith et al. 2004)

Non pharmacological

- Acupuncture and acupressure are different treatment modalities and cannot be compared directly
- Acupuncture has not been shown to be effective in reducing nausea and vomiting in pregnancy (Jewell 2004)
- Two trials have reported acupressure at the P6 acupuncture point decreases nausea (Jewell 2004), although the largest study (which provided continuous data) showed no improvement in either frequency or severity of vomiting (Belluomini 1994)
- A recent study comparing both acupressure and acupuncture with sham acupressure and acupuncture reported no difference in vomiting, but women's health status improved with time (Smith et al. 2002)

Dietary changes

- Encourage the woman to eat before, or as soon as they feel hungry in order to avoid an empty stomach that may aggravate nausea
- Encourage small, frequent high carbohydrate, low fat meals

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- Some women report an improvement when eliminating spicy or fatty foods and eating salty, bland, dry or high protein snacks / meals (Newman et al. 1993; Jednak et al. 1999)
- Fluids are better tolerated if cold, clear, and carbonated or sour (e.g. ginger ale, lemonade) taken in small amounts between meals

Day admission guideline for hyperemesis gravidarum

Eligible women

- Women suffering from hyperemesis gravidarum who require hospital admission for:
  - Parenteral antiemetic treatment
  - Intravenous rehydration for ketonuria or dehydration

Assessment and management

- Medical admission
  - Assess the woman's hydration state and general well being
- Intravenous access

Investigations

At each admission:

- Ward urinalysis on admission and before discharge (document ketonuria)
- Urine for MSSU
- Blood for urea, electrolytes and creatinine

If not already done

- Ultrasound examination to exclude multiple pregnancy and gestational trophoblastic disease
- Thyroid function tests
- Dietician referral
- Social work referral, if appropriate

Treatment with intravenous fluids and antiemetics

Intravenous fluid replacement

- Usually 2 litres of either sodium chloride 0.9 % or Hartmann's will be required – administer fluid volume as per clinical assessment. The first litre may be given stat (over 30-60 minutes) and the second over 2 to 3 hours. If hypokalaemic, the woman may require potassium (oral route preferred)

Antiemetics

- **Metoclopramide** – 10 mg intravenously every 6 hours (suggest alternative if past history of dystonic reaction to metoclopramide or phenothiazines)
- **Ondansetron** - may be prescribed for cases of severe hyperemesis gravidarum, in association with intravenous rehydration, thiamine and electrolyte correction. Give 4-8 mg intravenous or orally, 8-12 hourly, available as wafers to dissolve in the mouth

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Observations

- Temperature, pulse, respiratory rate and blood pressure on admission and every two hours during intravenous fluid treatment

Discharge

- The effectiveness of treatment needs to be assessed before discharge

Medication

- The recommended discharge antiemetic treatment is pyridoxine 25 mg, orally three times a day and metoclopramide 10 mg orally every 8 hours. (If vomiting persists prochlorperazine 25 mg suppositories twice daily may be prescribed)
- Persistent vomiting requires medical review and consideration of alternative antiemetics

Follow-up / readmission

- Arrange follow-up within three days of discharge (either with GP, antenatal or day clinic) to assess if ongoing severe hyperemesis requiring further intravenous rehydration

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Useful web site:

http://www.otispregnancy.org/pdf/nvp.pdf

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