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Guideline for Management and Treatment of Hyperemesis Gravidarum

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Approved By:	**Obstetrics, Gynaecology and Integrated Sexual Health Guideline Group**
Date Approved:	**28th July 2022**
Version:	
Operational Date:	**1st August 2022**
Date for Review:	**4th August 2025**
Distribution:	**Nursing, Midwifery and Medical Staff at Cwm Taf Morgannwg University Health Board**
Freedom of Information Status:	**Open**

Guideline Definition

Clinical guidelines are systematically developed statements that assist clinicians and patients in making decisions about appropriate treatments for specific conditions.

They allow deviation from a prescribed pathway according to the individual circumstances and where reasons can be clearly demonstrated and documented.

Minor Amendments

If a minor change is required to the document, which does not require a full review please identify the change below and update the version number

Type of Change	Why Change Made	Page Number	Date of Change	Version 1 to 1.1	Name of Responsible Person

Equality Impact Assessment Statement

This Procedure has been subject to a full equality assessment and no impact has been identified.

Purpose and Scope

There is variation in the management of women who have nausea and vomiting of pregnancy **(NVP)** or hyperemesis gravidarum **(HG)** with an occasional lack of understanding of its severity and options for treatment and support.

The aim of this guideline is to provide evidence-based or best clinical practice information regarding the diagnosis and subsequent management of NVP and HG across community, ambulatory day care and inpatient settings. It gives advice for multidisciplinary professionals involved in the care of women with these conditions, including how to counsel and support women before, during and after their pregnancies.

Introduction

Nausea and vomiting (NVP) affects up to 80% of pregnant women. NVP - defined as symptom of nausea and/or vomiting during early pregnancy where there are no other causes. It resolves spontaneously in most women by 16 to 20 weeks gestation. Women should be reassured that nausea and vomiting are not usually associated with a poor pregnancy outcome.

The following interventions appear to be effective in reducing symptoms and can be advised / prescribed within the primary care setting:-

- 'Ginger' in various forms
- acupressure/acupuncture

Hyperemesis Gravidarum (HG) is a condition when there is protracted NVP with the triad of more than 5% pre-pregnancy weight loss, dehydration and electrolyte imbalance. HG is the severe form of NVP, which affects about 0.3-3.6% of pregnant women and requires hospital admission.

Biochemical abnormalities occur secondary to vomiting, starvation and dehydration e.g. ketosis, electrolyte imbalance, vitamin deficiency.

Severe cases are characterised by weight loss, tachycardia, hypotension, oliguria, neurological disorders (Wernicke's encephalopathy) that are secondary to thiamine deficiency. The intravenous fluid containing Dextrose may precipitate Wernicke's encephalopathy hence, it must be avoided. Jaundice may happen in severe HG due to hepatic necrosis.

Maternal Assessment is to be consistent in all clinical areas:-

Features in the history, examination and investigations to monitor severity and other causes	
History	• Previous history of NVP/HG • Qualify severity using PUQE score: nausea, vomiting, hypersalivation, spitting, loss of weight, inability to tolerate food and fluids, effect on quality of life • History to exclude other causes: - Abdominal pain - Urinary symptoms - Infection - Drug history

	- Chronic Helicobacter pylori infection
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 as 1+ or more • MSU • Urea & Electrolytes - hypokalaemia/hyperkalaemia - hyponatraemia - dehydration - renal disease • Full blood count - Infection - Anaemia - haematocrit • Blood glucose monitoring - exclude diabetic ketoacidosis if diabetic • Ultrasound scan - confirm viable intrauterine pregnancy - exclude multiple pregnancy and trophoblastic disease • In refractory cases or history of previous admissions, check: - TFTs: hypothyroid/hyperthyroid - LFTs: exclude other liver disease such as hepatitis or gallstones, monitor malnutrition - Calcium and phosphate - Amylase: exclude pancreatitis - ABGs: exclude metabolic disturbances to monitor severity

Differential Diagnosis

Peptic ulcers, cholecystitis, gastroenteritis, hepatitis, pancreatitis, genitourinary conditions such as urinary tract infection or pyelonephritis, metabolic conditions (hypercalcaemia, Addison's disease, hyperparathyroidism), neurological conditions, drug-induced nausea and vomiting

PUQE score for assessment

Pregnancy-Unique Quantification of Emesis (PUQE) score system

Pregnancy-Unique Quantification of Emesis (PUQE) scoring					
In the last 24 hours:					
How long have you felt nauseated or sick?					**Score**
Not at all (1)	0-1 hours (2)	2-3 hours (3)	4-6 hours (4)	> 6 hours (5)	
How many times have you vomited or thrown up?					
0 times (1)	1-2 times (2)	3-4 times (3)	5-6 times (4)	> 7 times (5)	
How many times did you have retching or dry heaves without bringing anything up?					
0 times (1)	1-2 times (2)	3-4 times (3)	5-6 times (4)	> 7 times (5)	
				Total (max.15)	

- *Mild (≤ 6): for management in the community*
- *Moderate (7-12): for management in the community or in hospital as a Day Case.*
- *Severe/HG (13-15): for hospital admission*

Conservative management in the community

For mild NVP with PUQE score </=6

Patients are managed in the community by midwife/GP with following advice. This advice can also be given on discharge from hospital.

- Rest plenty
- Eat something dry and plain, such as bread, before getting out of bed slowly.
- Eat frequent, small portion meals, which are low in carbohydrates/fat but high in protein.
- Take sips, drink in small amounts more frequently; suck on ice
- Ginger and peppermint
- Sea sickness/acupressure bands
- Avoid iron-containing supplements
- Suggest support groups, such as Pregnancy sickness support Pregnancy sickness (nausea and vomiting of pregnancy and hyperemesis gravidarum) | RCOG

Criteria for Ambulatory/Treatment in AAU/Emergency Setting

For moderate NVP with PUQE score </= 13 *and* no complications (dehydration, electrolyte imbalance, weight loss) *and* not refractory to anti-emetics

Treatment Regimen for ambulatory care

1) Rapid Hydration- 1L Hartmann's over 1 hour, followed by

1L Hartmann's over 2 hours

2) Anti-emetics-

1st line: Cyclizine 50mg IM/IV or Promethazine 25mg IM

2nd line: Prochlorperazine 12.5mg IM or Metoclopramide 10mg IM/IV
Ondansetron 4-8mg IV (as a last resort in 1st trimester only after counselling the patient re: birth defects in the baby) Ondansetron (Zofran®) (mothertobaby.org)

3) Reassess by Midwife / SHO / Registrar
4) Woman can be discharged if she shows clinical improvement in symptoms and tolerates light diet
5) Give regular anti-emetics (TTH)

- Oral Cyclizine 50mg 8hrly / Prochlorperazine (preferably Buccastem 3-6mg BD (placed between the upper lip and gum, and left to dissolve)
- Metoclopramide 10mg 8hrly (Maximum for 5 days)
- Ondansetron 8mg 12hrly up to 5 days (counselling of pt required in 1st trimester)

6) Give either Thiamine 50mg 8hrly (oral) or Pabrinex IV (1pair of ampoules diluted in 100mls Normal saline over 30 mins) once a week can be considered.
7) Allow patient to go home with information leaflet
8) Arrange follow up in DAU in 2 days by telephone or appointment by midwife
9) Admit to ward if-

- vomiting persists
- abnormal electrolytes or liver function tests
- if the women remains unwell

Criteria for Inpatient Management

- continued nausea and vomiting and inability to keep down oral antiemetics or failed ambulatory management
- continued nausea and vomiting associated with ketonuria and/or weight loss greater than 5% of body weight, despite oral antiemetics
- confirmed or suspected comorbidity e.g. urinary tract infection and inability to tolerate oral antibiotics.

Treatment for Inpatient care

- Allow water to keep mouth moist.
- Continue intravenous fluid.– 1L Hartmann's solution 6 hourly

- Consider Normal Saline (0.9%) solution + potassium chloride supplements 20-40 mmol if potassium is <3.2 mmol/L
- Daily U+E's whilst on Intravenous fluids
- Daily urinalysis for ketones
- Regular anti-emetic treatment 6-8hourly.

Cyclizine 50 mg IV/IM 8 hourly for 48 hrs **Alternatively** Promethazine 25mg at bed time increase to 25mg 8hrly (PO/IM/IV) following day if necessary

And / or

↓

Prochlorperazine12.5 mg IM/IV 8 hourly for 48 hrs **alternatively**
Chlorpromazine 10-25mg 4-6hrly PO/IV/IM

and / or

↓

Metoclopramide 10 mg IM /IV/PO 8 hourly for 48 hrs (maximum 5 days)

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If not responding to the above treatment
Ondansetron 8 mg IM / IV 12 hourly for 48 hrs (only after counselling pt in first trimester re: birth defects in the baby)
Domperidone 10mg 8hrly oral (be aware of the cardiac side effects) Treatments for pregnancy sickness and hyperemesis gravidarum (pregnancysicknesssupport.org.uk)

- Corticosteroids:

If not responding to antiemetics then consider steroids after discussion with Consultant
(Hydrocortisone 100mg IV 12hrly x 24 hrs followed by
Prednisolone 40mg to 50mg OD orally x 7 days)
If symptom returns then continue oral prednisolone 40-50mg max daily

Reduce by 5mg weekly or earlier (The dose gradually tapered until the lowest maintenance dose that controls the symptoms)

Continue up to 20 weeks gestation.

Wean off steroids gradually over 2 weeks (when given for >10 days).

- Daily fluid balance chart including the vomits and urine output
- Omeprazole 20-40mg daily (PO)
- Vitamin supplement- Thiamine 50 mg PO TDS or Pabrinex IV (1pair of ampoules diluted in 100mls Normal saline over 30 mins) once a week
- Thromboprophylaxis – TEDS and LMWH
- Slowly introduce other oral fluids and light diet if nausea settles
- Parenteral or enteral feeding will be considered following a Dietetic review, if the patient remains unresponsive to medical treatment
- Regular oral anti-emetic if appropriate when tolerating food
- Daily medical review

Safety and efficacy of pharmacological agents

Anti-emetics

There are safety and efficacy data for first-line anti-emetics such as antihistamines (H1 receptor antagonists) and phenothiazines and they should be prescribed when required for NVP and HG (Appendix 2).

Clinicians should use anti-emetics with which they are familiar and should use drugs from different classes if the first drug is not effective. 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 do not respond to a single anti-emetic. Furthermore, persistent vomiting may mean that oral doses of anti-emetics are not absorbed and therefore the intravenous, rectal, subcutaneous or intramuscular routes may be necessary and more effective.

Women should be asked about previous adverse reactions to antiemetic therapies.

Drug-induced extra-pyramidal symptoms and oculogyric crises can occur with the use of phenothiazines and Metoclopramide. If this occurs, there should be prompt cessation of the medications. Metoclopramide is safe and effective, but because of the risk of extrapyramidal effects it should be used as second-line therapy. Metoclopramide should only be prescribed for short-term use - maximum dose of 30 mg in 24 hours or 0.5 mg/kg body weight in 24 hours (whichever is lowest) and a maximum duration of 5 days. Intravenous doses should be administered by slow bolus injection over at least 3 minutes to help minimise these risks.

There is evidence that ondansetron is safe and effective, but because data is limited it should be used as second-line therapy.

A Cochrane review (5) and other systematic reviews and meta-analyses (34–36) and birth registry data (36) have reported on the safety and efficacy of many anti-emetics for use in NVP and HG with no increased risk of teratogenesis or other adverse pregnancy outcomes. These drugs include:
antihistamines (histamine H1 receptor antagonists) such as promethazine, cyclizine, cinnarizine, doxylamine and dimenhydrinate; phenothiazines including prochlorperazine, chlorpromazine, perphenazine; and dopamine antagonists including metoclopramide and domperidone.

Thiamine

Thiamine supplementation (either oral or intravenous) should be given to all women admitted with prolonged vomiting, especially before administration of dextrose or parenteral nutrition.

Pyridoxine

Pyridoxine is not recommended for NVP and HG.

Corticosteroids

Corticosteroids have resulted in dramatic and rapid improvement in case series of women with refractory HG. Corticosteroids should not be used until conventional treatment with intravenous

fluid replacement and regular anti-emetics has failed. The suggested dose is intravenous hydrocortisone 100 mg twice daily, and once clinical improvement occurs convert to oral prednisolone 40–50 mg daily, with the dose gradually tapered until the lowest maintenance dose that controls the symptoms is reached. In most cases prednisolone needs to be continued until the gestational age at which HG would have typically resolved and in some extreme cases this occurs at delivery.

Rehydration Regime

Normal saline with additional potassium chloride in each bag with administration guided by daily monitoring of electrolytes is the most appropriate intravenous hydration.

The most important intervention is likely to be appropriate intravenous fluid and electrolyte replacement. There is no evidence to determine which fluid regimen is most appropriate but given that most women admitted to hospital with HG are hyponatraemic, hypochloraemic, and hypokalaemic and ketotic, it seems appropriate to use normal saline and potassium chloride.

Dextrose infusions are **not appropriate** unless the serum sodium levels are normal and thiamine has been administered. Dextrose-containing solutions can precipitate Wernicke's encephalopathy in thiamine-deficient states hence, each day intravenous dextrose is administered, and high doses of parenteral thiamine (e.g. 100 mg) should be given to prevent Wernicke's encephalopathy.

Complementary Therapies

Ginger

Ginger may be used by women wishing to avoid anti-emetic therapies in mild to moderate NVP. No increased risk of major malformations has been reported with use of ginger.

Acupressure and Acupuncture

Women may be reassured that acupressure and acupuncture are safe in pregnancy. Acupressure may improve NVP. Acupressure applied by finger pressure or wristband and electrical stimulation at PC6 (located about 2.5 finger breadths up from the wrist crease on the inside of the forearm) have been shown to reduced NVP.

Hypnosis

Hypnotic therapies should not be recommended to manage NVP and HG**.**

Discharge Criteria

- If the woman has tolerated at least two meals without vomiting
- Follow up as outpatient or by phone within two days at DAU
- Inform Team Midwife and G.P by discharge letter.
- Arrange follow up at A.N.C. in 2/52 from discharge and serial fetal growth scan in severe cases.
- Consider eliminating precipitating factors and offer reassurance of self-limiting condition and no specific fetal risk factors.

References

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RCOG patient information leaflet: https://www.rcog.org.uk/en/patients/patient-leaflets/pregnancy-sickness/