Hyperemesis Gravidarum

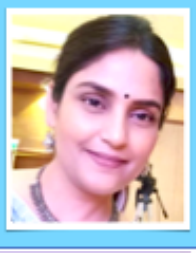
The Problem of surging Hormones and its management.

Dr Alpesh Gandhi
President FOGSI

DR Anita Singh
Vice President
FOGSI

EDITOR : Dr Rakhi Singh
Chairperson Endocrinology Committee FOGSI.

Editor :Dr Anita Rajorhia,
Consultant and HOD,
Sardar Vallabh Bhai Patel hospital, New Delhi.

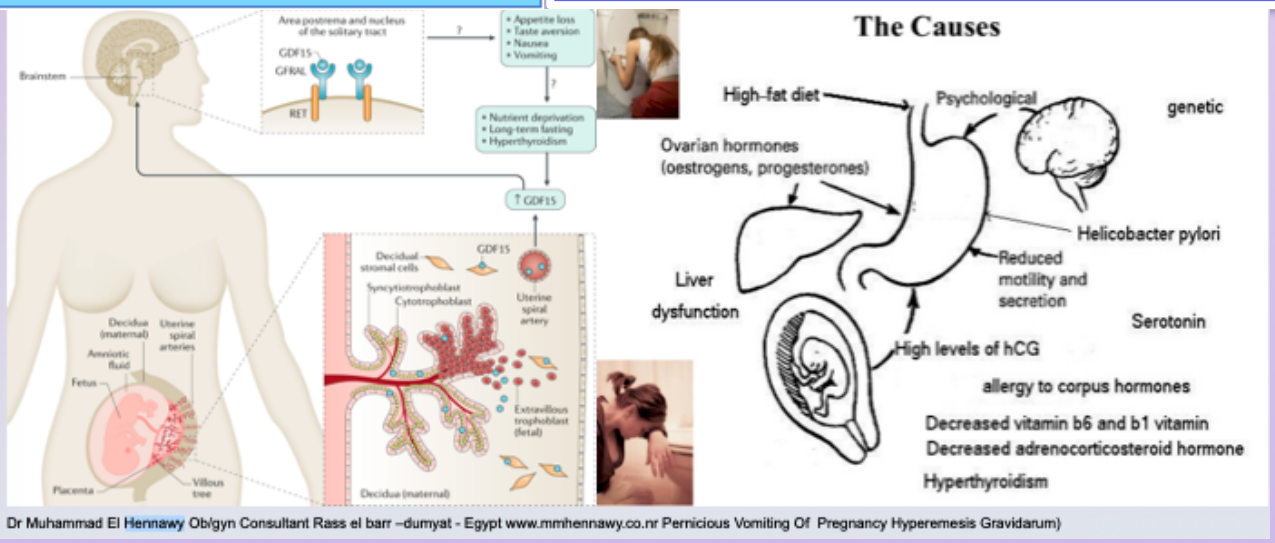


Author: Dr Anshu Raina
Senior Consultant at Kailash hospital Greater Noida.

Introduction

Hyperemesis Gravidarum is a complex condition with multifactorial etiology characterized by prolonged and severe nausea and vomiting with the triad of dehydration, electrolyte imbalance and more than 5% of weight loss from pre pregnancy level.

Symptoms are more severe in multiple pregnancies, molar pregnancies which are associated with excessively high level of HCG. If not managed adequately, can cause significant morbidities including malnutrition, electrolyte imbalances, thrombosis, Wernicke's Encephalopathy, depressive illness and poor pregnancy outcome in the form of low birth weight, preterm birth, small for gestational age baby



Dr Muhammad El Hennawy Ob/gyn Consultant Rass el barr –dumyat - Egypt www.mmhennawy.co.nr Pernicious Vomiting Of Pregnancy Hyperemesis Gravidarum)

Incidence

It varies from 0.3% to 3.6% of all pregnancies. It is more common in westernized societies and urban areas than rural areas.

Pathophysiology- Multifactorial

1. Hormonal Stimulation: -
   - HCG – High HCG levels (Twins, GTT)
   - High Estrogen Level- Increased E2 causes a decrease in GI motility and gastric emptying altering GI pH and encourages sub-clinical H. Pylori infection.
   - Progesterone Excess- Relaxation of Gastric Sphincter and Impaired Gastric Motility.
   - Thyroid hormone- Physiological gestational transient thyrotoxicosis. Raised FT3 and low TSH found in 66% of Hyperemesis Gravidarum.
2. Dietary Deficiency- Low Carbohydrate Intake, Vit B6 and B1 deficiency
3. Psychogenic
4. Genetic
5. Allergic or Immunological Basis
6. Liver Dysfunction
7. Vestibular System Dysfunction

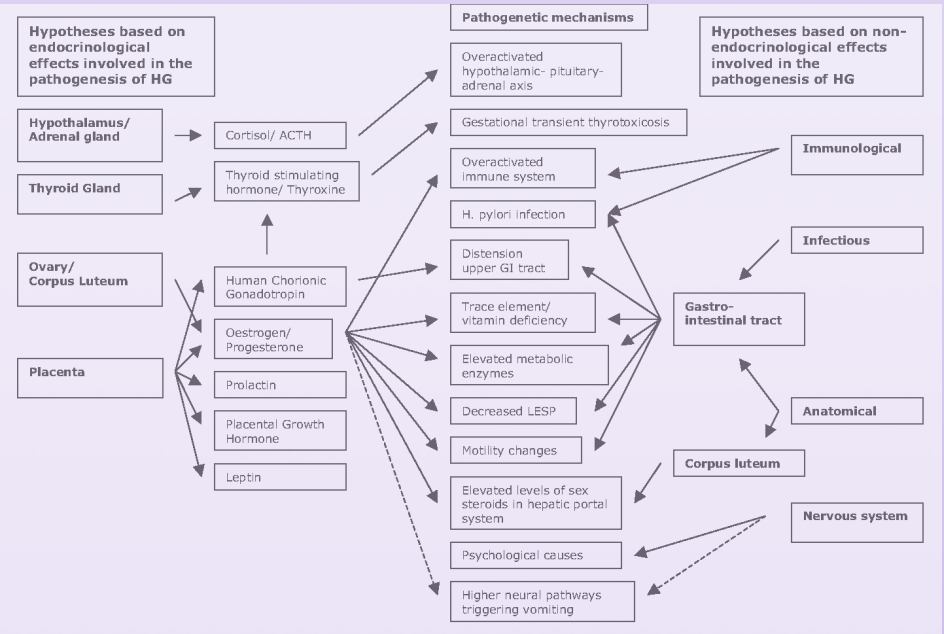


Figure 7. Interactions between endocrine influences, target organs, and functions that might be involved in the pathogenesis of hyperemesis gravidarum (HG)

Risk Factors: -

- Younger Nullipara
- Under and Overweight Women
- Multiple pregnancies
- Molar Pregnancy
- GI disorders
- H. Pylori infection
- Socio-Economic Factors- Marital Status, Lower Education
- Anxious and Highly Stressed Pregnant Women
- Migraine
- ENT Problems
- Known case of heartburn
- Diabetic
- Genetics
- History of Hyperemesis Gravidarum in previous pregnanci
- Family History of Hyperemesis Gravidarum
- History of Motion Sickness
- Female Fetus

History

- Quantify the severity using PUQE scores
- Nausea, Hyper-secretion
- Retching, Vomiting
- Loss of Weight
- Inability to tolerate food and fluids
- Effects on quality of life
- History of pain
- Abdominal Urinary Symptoms
- Drug History
- Chronic H. Pylori Infection

Pregnancy-Unique Quantification of Emesis and nausea

Circle the answer that best suits your situation in the last 24 hours

1. On average in a day, for how long do you feel nauseated or sick to your stomach?

>6 hours 5 points	4–6 hours 4 points	2–3 hours 3 points	≤1 hour 2 points	Not at all 1 point

2. On average in a day, how many times do you vomit or throw up?

≥7 times 5 points	5–6 times 4 points	3–4 times 3 points	1–2 times 2 points	Not at all 1 point

3. On average in a day, how many times have you had retching or dry heaves without bringing anything up?

≥7 times 5 points	5–6 times 4 points	3–4 times 3 points	1–2 times 2 points	Not at all 1 point

Total score (sum of replies to 1, 2 and 3): mild NVP ≤6; moderate NVP, 7–12; severe NVP ≥13.

Dean Caitlin R, Shemar Manjeet, Ostrowski Gillian A U, Painter Rebecca C. Management of severe pregnancy sickness and hyperemesis gravidarum BMJ 2018

Symptoms

- Nausea
- Vomiting
- Enhanced Olfactory Senses
- Food and fluid intolerance
- Lethargy

Signs

- Dehydration
- Tachycardia
- Anemia
- Ketonuria
- Weight Loss

Examination

- Assessment of General Condition
- Vitals, Signs of Dehydration
- Abdominal and Other Examinations as per History of Individual Patient

Investigation

Mild Case

1. Urine Ketones
2. Complete Blood Count
3. Serum Electrolytes

Severe Cases

1. Urine Analysis- Dark Color, Oliguria, Acidic PH, High Specific Gravity with Acid Reaction, Presence of Ketones, Diminished or Absent Chlorides.

2. Serum Electrolytes
3. Blood for Urea and Creatinine
4. Complete Blood Count
5. Blood Sugar
6. Liver function test
7. TSH & T4
8. ABG (Arterial Blood Gases)
9. Obstetric USG to confirm pregnancy and exclude GTD
10. Other tests depending on patient's general conditions and specific history

Differential diagnosis

- Pregnancy Related- Multiple Pregnancies, Trophoblastic Disease, Acute Fatty Liver of Pregnancy, HELLP Syndrome, Pre-Eclampsia, Pre-Mature Contractions
- Genitourinary- UTI, Uraemia, Molar Pregnancy
- Gastrointestinal- Gastric/Peptic Ulcer, Reflux Oesophagitis, Pancreatitis, Bowel Obstruction
- Endocrine- Hyperthyroidism, Addison's Disease, Diabetes Ketoacidosis
- CNS- Intracranial Tumors, Vestibular Disease
- Others- Eating disorders, Drug Intoxication, Iron Exposure

Management

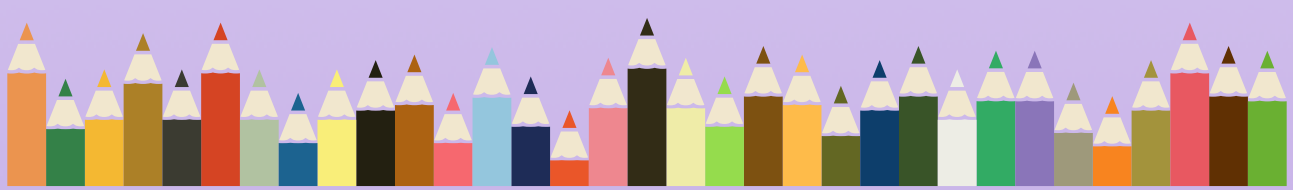
1. OPD Care can be considered for PUQE score less than 13 (ideal for less than 6, or maybe 7-10)

2. IPD Care is needed in patients

    - Symptoms are severe despite 24-hours of medication.
    - Evidence of dehydration and ketosis.
    - Hyperemesis Gravidarum unable to keep down with Oral Antiemetic.
    - Hyperemesis Gravidarum with Ketonuria, weight loss more than 5% despite oral Antiemetics
    - Confirmed or suspected co-morbid conditions associated with Hyperemesis like diabetes, peptic ulcers, chronic esophagitis and UTI.

Aim of IPD Management

- Correction of dehydration and electrolyte imbalance.
- Prophylaxis against recognized complications.
- Provision of symptomatic relief.



1. **IV Fluids** - NS & Hartmann's Solution (Preferably if Ketotic or Fluid Intolerant)

AVOID Dextrose solution as: -

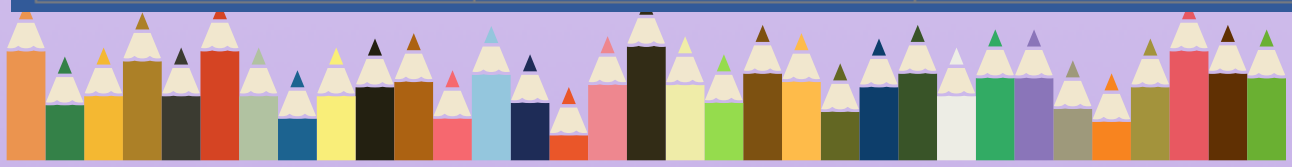
- It cannot correct commonly associated hyponatremia.
- High concentration of dextrose solution precipitate Wernicke's Encephalopathy.
- Avoid double strength saline even in cases of severe hyponatremia

2. **Antiemetic Therapy**
   - Antiemetics are safe and recommended liberally in Hyperemesis Gravidarum.
   - Patients on antiemetic-better pregnancy outcome due to better nutrition.

Class of Drugs	Antiemetics
Phenothiazine	Prochlorperazine (stemetil/buccastem) Chlorpromazine
Dopamine Antagonists	Metoclopramide Domperidone
5-HT3 (serotonin) antagonist	Ondansetron
Antihistamines (H1 receptor antagonist)	Cyclizine Promethazine (Phenergan) Meclozine

Group 1	Drug	Dose	Route
First Line	Cyclizine	50mg T.D.S	PO, IM or IV
Second Line	Prochlorperazine (Stemetil)	12.5 mg T.D.S 3-6 mg BD	IM Sublingual
Third Line	Metoclopramide	10 mg T.D.S	PO, IM, or IV

Group 2		
Promethazine (Phenergan)	25mg a Day	IM/Oral
Chlorpromazine	10-25mg T.D.S 25mg T.D.S	PO
Domperidone	20 mg QID 30-60mg QID	PO PR



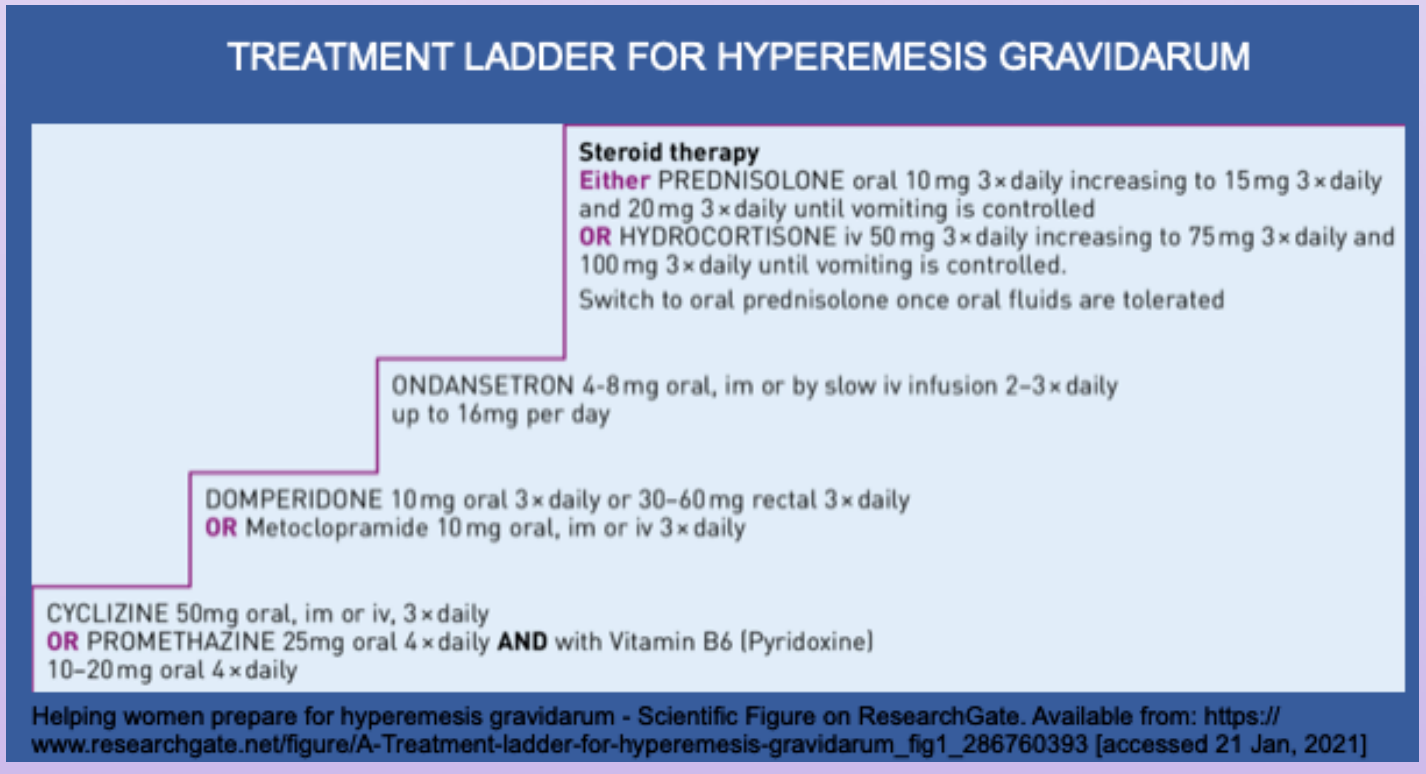
First line	• Cyclizine 50 mg PO, IM or IV 8 hourly • Prochlorperazine 5–10 mg 6–8 hourly PO; 12.5 mg 8 hourly IM/IV; 25 mg PR daily • Promethazine 12.5–25 mg 4–8 hourly PO, IM, IV or PR • Chlorpromazine 10–25 mg 4–6 hourly PO, IV or IM; or 50–100 mg 6–8 hourly PR
Second line	• Metoclopramide 5–10 mg 8 hourly PO, IV or IM (maximum 5 days' duration) • Domperidone 10 mg 8 hourly PO; 30–60 mg 8 hourly PR • Ondansetron 4–8 mg 6–8 hourly PO; 8 mg over 15 minutes 12 hourly IV
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

Management of Hyperemesis Gravidarum RCOG 2016

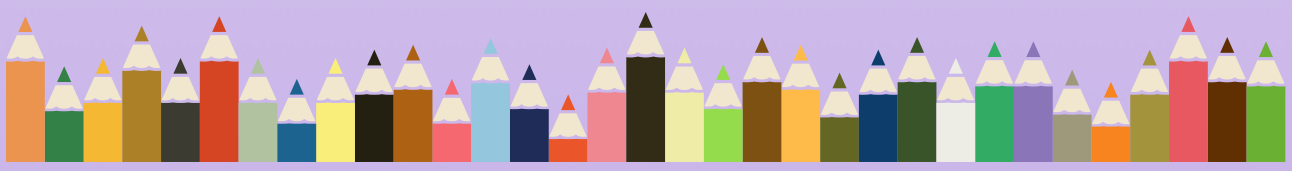
3. Cortico Steroids Treatment

Indication: -

- Intractable hyperemesis which is not responding to antiemetic
- IV Hydrocortisone 100mg BD for 48 hours
- Oral Prednisolone 30-40mg per day for 1 week than tapered gradually (5mg reduction every week.



Helping women prepare for hyperemesis gravidarum - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/A-Treatment-ladder-for-hyperemesis-gravidarum_fig1_286760393 [accessed 21 Jan, 2021]

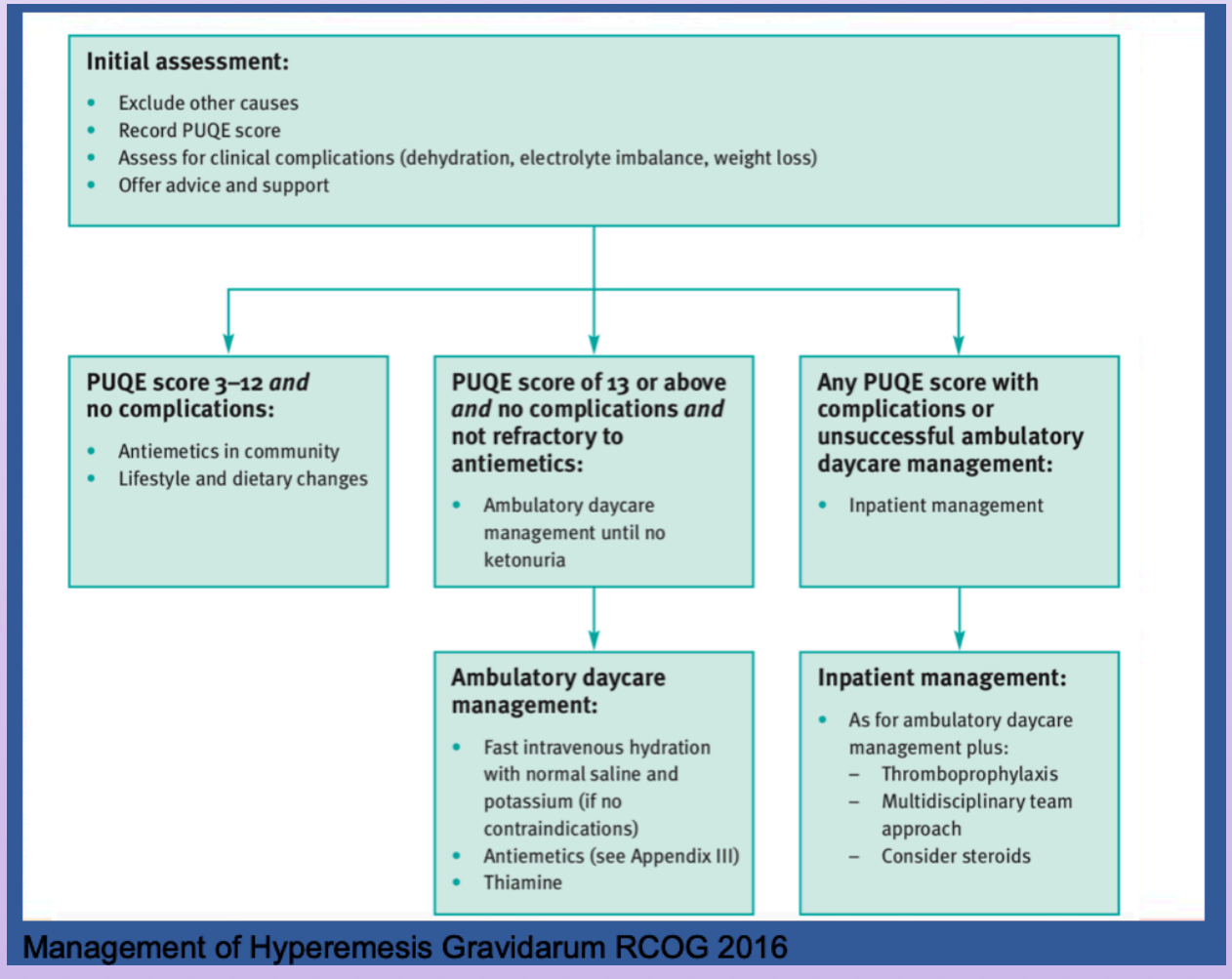


4. Other supportive treatment

- Vitamin supplementation specially Thiamine (50mg PO once daily) or Pabrinex IM/IV 2 ampules twice weekly to prevent Wernicke's Encephalopathy.
- Anti-Reflux Measures H2 blockers such as Ranitidine and proton pump inhibitors (Omeprazole)
- Diet and Lifestyle (Small Frequent dry meal, learn to avoid certain scents which make the patient, intolerable)
- Avoid Mental Stress and try to keep mind occupied
- Use of ginger traditionally done in India needs extensive study.

The option for severe hyperemesis who failed to response to above measures: -

- Enteral Nutrition
- Parenteral Nutrition
- Rarely Termination of Pregnancy

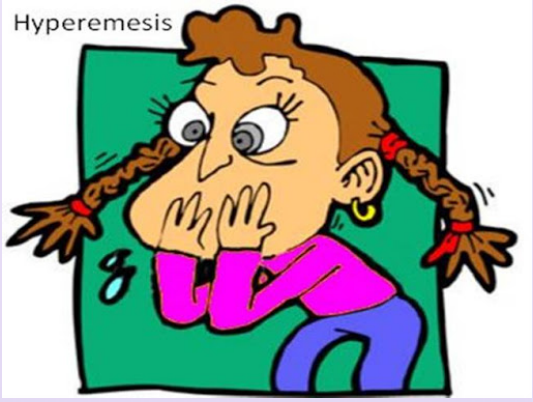


Management of Hyperemesis Gravidarum RCOG 2016

Complications

1. **Maternal Complications**

- Extreme Electrolyte Imbalance
- Drug Induced Extrapyramidal Symptoms
- Oculogyric Crisis
- Wernicke's Encephalopathy
- Excessive addition of sodium



2. **Fetal Complications**

- Fetal Loss
- IUGR
- All Problems of Maternal Malnutrition (Low Birth Weight Baby, Small for Gestational Age, Premature Infants)

Conclusion

1. Hyperemesis Gravidarum is a complex and multi-factorial condition with significant adverse effects on a quality of life.
2. As soon as possible, accurate diagnosis and management for Hyperemesis Gravidarum is must to avoid morbidities.
3. Hyperemesis Gravidarum is diagnosed by exclusion.
4. Modified 24-hours PUQE score is also required for heartburn plan.
5. Hydration and Electrolyte management to be done with intensive monitoring care.
6. Proper treatment with individualization.
7. Needs antiemetic in a step-up pattern like Doxylamine, Promethazine, Prochlorperazine, Cyclizine
8. H1 receptor antagonists should be considered in the management of acute and breakthrough episodes of vomiting.
9. Pyridoxine monotherapy supplementation maybe considered as an adjuvant measure.
10. Corticosteroids should be avoided during the first trimester because of possible increased risks of oral clefting.
11. Use of steroids should be restricted for refractory cases.
12. Hyperemesis refractory to initial treatment needs investigation to rule out other potential causes.
13. Dietician consultation is helpful.

References: -

1. RCOG Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum, the Green-top Guidelines No.69 June 2016
2. ACOG Practice Bulletin Summary No.189 January 2018
3. Cochrane Review 2010
4. Clinical Practice Guidelines Royal College of Physician Ireland version 12
5. Lee NM, Saha.S Nausea and Vomiting of Pregnancy. Gastroenterol Clin North America 2011, 40 (2)