Emergency Clinic Guidelines
Management of Ovarian hyperstimulation syndrome (OHSS)-GL1027

Approval

<table>
<thead>
<tr>
<th>Approval Group</th>
<th>Job Title, Chair of Committee</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gynaecology Clinical Governance</td>
<td>Chair, Gynaecology Clinical Governance</td>
<td>15th February 2019</td>
</tr>
</tbody>
</table>

Change History

<table>
<thead>
<tr>
<th>Version</th>
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</tr>
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<tbody>
<tr>
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This document is valid only on date printed
1.0 **Purpose**
The aim of this guidance is to provide high quality, efficient service and care for the patients referred to the RBH's Emergency Clinic (EC) with Ovarian hyperstimulation syndrome (OHSS). The Trust is committed to the provision that is fair, accessible and meets the needs of all individuals.

2.0 **Scope**
This guidance describes the outpatient and inpatient management of women with OHSS.

3.0 **Roles and responsibilities**
The team consists of:
- Lead Consultant for Reproductive medicine and fertility
- Lead consultant for Emergency Gynaecology/Early pregnancy
- Hot week consultant – as per rota
- Lead sister for Gynae Emergency/Early pregnancy Clinic
- Qualified nursing staff working within Emergency Gynae/Early pregnancy Clinic or working on Sonning Ward.

4.0 **Definitions**
Ovarian hyperstimulation syndrome (OHSS) is a complication of fertility treatment, which uses pharmacological ovarian stimulation to increase the number of oocytes and therefore embryos available during assisted reproductive technology (ART).

It is a syndrome characterised by ovarian enlargement, fluid accumulation in the peritoneal, pleural and rarely the pericardial cavities, resulting in intravascular volume depletion and haemoconcentration.

5.0 **Introduction**
Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic condition, seen most commonly as a result of the administration of exogenous FSH/HCG. It is a systemic disease resulting from vasoactive products released by hyper stimulated ovaries.

OHSS is potentially lethal and prompt and appropriate management is essential to prevent or curtail its serious consequences. The natural course of OHSS is one of gradual resolution over 10-14 days, unless pregnancy occurs.
5.1 Risk factors for OHSS
Risk factors for development of OHSS include:
1. Polycystic ovarian syndrome
2. Elevated baseline AMH
3. Increased ovarian volume and high antral follicle count (AFC) on baseline scan
4. Young age
5. Low BMI
6. Previous OHSS
7. High dose of FSH
8. Large number of oocytes retrieved (>25)
9. Rapidly rising and/or high oestradiol levels (>17,000 pmol/l)

5.2 Classification of OHSS
The clinical symptoms and signs exhibit a continuum of scope and severity, and the classification below incorporates this demonstrated graduation. Progression of illness is recognised when symptoms persist or deteriorate. An important sign is the development of ascites.

<table>
<thead>
<tr>
<th>Symptoms</th>
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<tbody>
<tr>
<td><strong>Mild</strong></td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
</tr>
<tr>
<td><strong>Severe</strong></td>
</tr>
<tr>
<td><strong>Critical</strong></td>
</tr>
</tbody>
</table>

- Complications are more frequent when conception does occur and a protracted and complicated course may evolve.
- Moderate OHSS in non-conception cycles is usually followed by the resolution of symptoms with menstruation, except that the ovarian cysts may take 2-4 weeks to resolve.
Mild OHSS represents mainly a chemical hyperstimulation usually of little clinical concern that resolves with the onset of menstruation and is usually managed on an outpatient basis.

## 5.3 Initial assessment and investigations

The history should seek to clarify nature, duration and severity of symptoms, and presence of risk factors and co-morbidities. Alternative diagnoses should always be considered.

Clinical examination should incorporate assessment of body weight, hydration status, heart rate and blood pressure, respiratory rate (breathing difficulty), abdominal circumference (to check for degree of distance and presence of clinical ascites), cardiovascular and respiratory systems (to check for pleural or pericardial effusion) and the abdomen.

Pelvic examination should be avoided, as this may induce ovarian cyst rupture.

The severity at presentation should be established according to above table and recorded in the clinical notes.

Diagnosis is based on clinical criteria, but the following investigations may aid in ascertaining severity and response to treatment.

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Severe OHSS</th>
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<tbody>
<tr>
<td><strong>Full Blood Count</strong></td>
<td></td>
</tr>
<tr>
<td>Haematocrit</td>
<td>&gt; 55%</td>
</tr>
<tr>
<td>White cell count</td>
<td>&gt; 25000/ml</td>
</tr>
<tr>
<td><strong>Urea &amp; Electrolytes</strong></td>
<td></td>
</tr>
<tr>
<td>Hyponatraemia</td>
<td>&gt;135mmol/L</td>
</tr>
<tr>
<td>Hyperkalaemia</td>
<td>&gt; 5.0 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>&gt; 0.1 mmol/L</td>
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<tr>
<td><strong>Liver Function Tests</strong></td>
<td></td>
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<tr>
<td>Elevated enzymes</td>
<td>&lt; 25 g/L</td>
</tr>
<tr>
<td>Reduced albumin</td>
<td></td>
</tr>
<tr>
<td><strong>Coagulation</strong></td>
<td></td>
</tr>
<tr>
<td>Elevated fibrinogen</td>
<td></td>
</tr>
<tr>
<td>Reduced anti-thrombin III</td>
<td></td>
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<tr>
<td><strong>hCG</strong></td>
<td></td>
</tr>
<tr>
<td>If 10 days post oocyte retrieval</td>
<td></td>
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<tr>
<td><strong>Radiology</strong></td>
<td></td>
</tr>
<tr>
<td>Ultrasound pelvis</td>
<td></td>
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<tr>
<td>Enlarged ovaries with multiple ovarian cysts</td>
<td></td>
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<tr>
<td>Ascites</td>
<td></td>
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<tr>
<td>Ovarian vessels Doppler studies if suspected ovarian torsion</td>
<td></td>
</tr>
<tr>
<td><strong>Other (if clinically indicated)</strong></td>
<td></td>
</tr>
<tr>
<td>Arterial blood gases</td>
<td></td>
</tr>
<tr>
<td>To diagnose respiratory failure</td>
<td></td>
</tr>
<tr>
<td>D-dimers</td>
<td>Elevated</td>
</tr>
<tr>
<td>ECG</td>
<td>Pericardial effusion</td>
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</tbody>
</table>

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<table>
<thead>
<tr>
<th>echocardiogram</th>
<th></th>
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<tbody>
<tr>
<td>Chest x-ray</td>
<td>– Pleural effusion</td>
</tr>
<tr>
<td></td>
<td>– Interstitial oedema</td>
</tr>
<tr>
<td>CTPA or V/Q scan</td>
<td>– Definitive diagnosis of pulmonary embolism</td>
</tr>
</tbody>
</table>

### 5.4 Management

Management of OHSS is supportive whilst waiting for the condition to resolve spontaneously. The main aims of management are to:

- Provide reassurance and symptomatic relief to the patient.
- Avoid/treat haemoconcentration.
- Prevent thromboembolism.
- Maintain cardio-respiratory and renal function.

### 6.0 Outpatient management

Treatment for women with mild OHSS and many with moderate OHSS can be managed on an outpatient basis, as long as resolution is reported and review takes place every 2–3 days.

Counselling women regarding the signs and symptoms of progressing illness is crucial.

The areas that require coverage during outpatient management include:

<table>
<thead>
<tr>
<th>Analgesia</th>
<th>Use of paracetamol or codeine; avoid NSAIDS as these may affect renal function.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiemetic’s</td>
<td>Use those appropriate for the possibility of early pregnancy, such as prochlorperazine, metoclopramide and cyclizine.</td>
</tr>
<tr>
<td>Luteal support</td>
<td>Use of progesterone not hCG.</td>
</tr>
<tr>
<td>Hydration</td>
<td>Drinking to thirst, not to excess. Electrolyte-supplemented drinks are preferable to other beverages.</td>
</tr>
<tr>
<td>Activity</td>
<td>Avoidance of strenuous exercise and sexual intercourse, as injury or torsion to enlarged ovaries can occur. Light physical activity should be maintained to the extent possible. Strict bed rest is unwarranted and increases risk of thromboembolism.</td>
</tr>
<tr>
<td>Weight</td>
<td>Weight should be recorded daily, as well as the frequency and/or volume of urine output. Weight gain of &gt;2 pounds per day or decreasing urinary frequency should prompt urgent medical attention.</td>
</tr>
</tbody>
</table>
Bloods | Bloods to be taken at each clinical review (visit).
---|---
Ascites | If tense ascites is present and expertise exists, trans-vaginal drainage could be considered (see inpatient management).

Clinical review every 2–3 days should be arranged via 602 clinic. However, urgent clinical review is necessary if the woman develops increasing severity of pain, increasing abdominal distension, shortness of breath and a subjective impression of reduced urine output.

The review should include history of symptoms, clinical examination, laboratory blood test (as described above) and ultrasound abdomen if indicated.

If the woman conceives, prolonged monitoring may be appropriate, whereas, in the absence of pregnancy, resolution would be anticipated by the time of the withdrawal bleed.

### 7.0 Inpatient management

Hospital admission should be considered for women who:
- are unable to achieve satisfactory pain control
- are unable to maintain adequate fluid intake due to nausea
- show signs of worsening OHSS despite outpatient intervention
- are unable to attend for regular outpatient follow-up
- have critical OHSS.

**Features to note on examination:**
- General state of hydration.
- Chest - difficulty breathing, pleural or pericardial effusion.
- Abdomen - degree of distension / presence of ascites. NB Ileus is a common finding.
- Evidence of thromboembolism.

**Daily investigations:**
- Hb and haematocrit.
- Urea and electrolytes.
- Clotting factor screen.
- Albumin and LFTs.
Nursing observations:
- BP, pulse, temperature (4 hourly).
- Weight, abdominal girth (daily).
- Strict fluid input/output chart.
- Consider urinary catheterisation only if urine output minimal.

Basic treatment:
- Analgesia/anti-emetics - as required. Preferred drugs would be paracetamol, paracetamol + codeine and/or pethidine; but not non-steroidal anti-inflammatory agents, e.g. diclofenac sodium. Metoclopramide or stemetil for nausea or vomiting are helpful (can be given per rectum).
- Full length TED stockings - to reduce venous thrombosis risk.
- Encourage oral fluid intake if not vomiting.

Maintenance of intravascular volume:
Initially the aim is to replace fluids in the vascular compartment sufficient to allow resumption of normal urine production - >30 ml/hr. Therefore, the intravenous infusion chosen depends on the type and extent of the intravascular disturbance.
Patients with severe OHSS should receive 3 litres of N/Saline intravenously per 24hrs. They can eat and drink freely.
If serum albumin levels fall to < 30g/l then give 2 units of Human Albumin Solution 20% over 2 hours I.V.

Diuretics
Diuretics should be avoided as they remove fluid from the vascular compartment only.

Surgery
Avoid surgery if at all possible but may be necessary if there is marked haemorrhage or rupture of the cysts. These are difficult features to detect but a sudden fall in PCV without a change in other indices of haemoconcentration indicates haemorrhage.

Abdominal paracentesis
Drainage of ascites or pleural effusions is symptomatically helpful if these are marked or in the presence of respiratory distress. Paracentesis of tense ascites often increases urine output due to decreased pressure on the renal
vasculature. Abdominal paracentesis should generally be performed under ultrasound control to reduce the risk of damage to the bowel or ovaries. Be aware that the ascites may rapidly re-accumulate and that paracentesis may accelerate protein loss, but this is rarely of clinical significance and should not deter the role of paracentesis in symptom relief when ascites is excessive. Give 2 units of albumin per day of paracentesis.

**Anticoagulation**

Prophylactic daily subcutaneous heparin (tinzaparin adjusted according to weight) and TED stockings will be beneficial in severe forms of the disorder even in the absence of thromboembolism.

**Other medication**

- Cyclogest 400mg BD per vagina to be continued till pregnancy test if embryo/s was/were transferred.
- Folic acid as per pregnancy protocol.
- Antiemetic’s could be given if required.

**Termination of pregnancy**

Pregnancy has been terminated in extremely severe cases of OHSS to save the patient's life but should rarely be necessary.

### 7.1 Summary of inpatient care:

1. Daily FBC, U&E, LFT, clotting screen.
2. STRICT fluid balance chart.
3. Daily weight & girth.
4. 3 litres N/Saline every 24hrs, eat and drink.
5. Start tinzaparin and TEDs.
6. Paracentesis /chest X-ray as advised by on-call consultant.

### 8.0 References

Appendix 1:
Action to be taken by staff member when OHSS is clinically suspected.

1. Inform consultant on call of suspected diagnosis.
2. Give couple OHSS information sheet and explain diagnosis.
3. If hospital admission is not required, baseline parameters performed and the patient reviewed as clinically indicated.
4. If it is thought that the degree of OHSS is mild this may be performed by telephone, otherwise the patient should return to the IVF unit where they had treatment, so that the baseline parameters may be repeated.
5. Following admission to the gynaecology ward, the on-call team will liaise with the IVF unit for subsequent management of the patient.