Guidelines on the Management and Investigation of Haemolytic Uraemic Syndrome

Renal Unit
Royal Hospital for Sick Children
Yorkhill Division

Please note: the following guidelines have not been assessed according to the AGREE (Appraisal of Guidelines for Research and Evaluation) criteria. This will take place at the next review of this guideline.
1. Introduction

The following guideline has been developed and is regularly reviewed by clinicians within the Renal Unit at Yorkhill. These guidelines are based on current evidence and best practice relating to the Investigation and Management of Haemolytic Uraemic Syndrome. This document is intended for use by clinicians and nursing staff in the treatment of Haemolytic Uraemic Syndrome. For further discussion of this guideline, please contact a consultant within the Renal Unit.

Haemolytic Uraemic Syndrome (HUS) is the commonest cause of acute renal failure in children in Scotland. In the majority of cases it follows infection with verotoxin producing Escherchiae Coli, the commonest subtype being 0157:H7. In the majority of these there is a preceding history of diarrhoea which is frequently bloody.

The haemolytic uraemic syndrome refers to a constellation of findings which include:

- Microangiopathic Haemolytic Anaemia
- Red cell fragmentation on Blood Film
- Acute Renal Failure

These features whilst most commonly following a diarrhoeal prodrome may also occur after infections with other organisms, drugs, pregnancy or may be familial. The investigation and management of children with this type of atypical HUS will be dealt with separately.
The bulk of this text refers to the investigation and management of patients with typical post-diarrhoeal HUS.

As a tertiary centre referrals are often made from outwith the Yorkhill campus and should be coordinated through the consultant covering the ward or the on-call consultant (out of hours).

If referrals are made directly to the ward a list of the desirable information is listed overleaf.

2. Initial Assessment and Management

Standard assessment of airway, breathing and circulation and a full history and examination should be undertaken. Attention should be paid to possibility of contact with farm animals and the presence of diarrhoea in other family members. Particular attention should also be paid to the assessment of the patients intravascular status by assessing the following:

- Thirst, Restlessness, Confusion
- Skin Turgor
- Fontanelle
- Heart Rate
- Core/Peripheral Temperature Gradient
- Capillary refill
- JVP
- Oliguria
- Blood Pressure
- Evidence of oedema

Hypovolaemia should be treated by volume expansion with 0.9% Saline, 4.5% Human Albumin Solution or Packed Red Blood cells depending on clinical status.

2.1 Initial Investigations

- Full Blood Count with film and differential - daily
- U&E’s and LFT’s - daily
- CRP
- Glucose
- Coagulation Screen
- Group and Save (or direct cross match if transfusion or theatre imminent)
- E Coli serology (clotted sample to microbiology)
- Stool culture
- Urinalysis
- Urine Culture
- Other investigations as clinically indicated e.g. CXR, Renal Ultrasound,

Establish IV access

2.2 Fluid Management

Is dependent on the patients current hydration status. In the presence of oligo/anuria and clinical fluid overload, fluids should be administered cautiously should not exceed the insensible fluid losses plus the urine output. In most cases in this scenario the aim to should be to decrease the patients fluid
overload by giving them less fluid e.g. urine output only, however this should be discussed with the resident SpR or senior SpR.

Remember Hyponatraemia is correctly treated by fluid restriction.

Hypovolaemia should be treated as mentioned previously.

For details of insensible fluid requirements see protocol entitled Investigation and management of acute renal failure.

2.3 Electrolyte Abnormalities

For details of management protocols of electrolyte abnormalities in patients with acute renal failure - see protocol entitled Investigation and management of acute renal failure.

2.4 Hypertension

Initially this is usually secondary to volume overload and therefore if the patient is unresponsive to diuretic therapy will benefit from a vasodilator. Our first choice would be Nifedipine. - see protocol entitled:– Investigation and management of acute renal failure.

2.5 Abdominal Pain/Vomiting

This is secondary to the colitis that occurs in post diarrhoeal HUS. Initial treatment of the abdominal pain should be with paracetamol, but on occasion opiate analgesia may be required. This will decrease intestinal motility and if possible should be avoided.

Do not prescribe IBUPROFEN

2.6 Altered Consciousness/Focal Neurological Signs

If these develop then immediate discussion with a senior colleague must be undertaken.

2.7 Nutrition

A nasogastric tube should be inserted at the time dialysis access is obtained or prior to this if caloric intake poor. Feeds should be commenced as continuous infusion at an initially slow rate. Choice of feed is determined by patients biochemistry and dialysis. Common feeds include Nepro and Paediatric Nutrison.
3. Indications for Dialysis

- Fluid overload resistant to Diuretic therapy
- Hyperkalaemia
- Intractable Acidosis
- Symptoms of uraemia
- Likely progression to one of the above

3.1 Choice of Dialysis Modality

Most patients will be commenced on peritoneal dialysis except those with severe colitis, cerebral HUS or profound metabolic abnormalities.

This decision should be made following consultation with the duty nephrologist

3.2 Peritoneal Dialysis

- Contact on-call surgical registrar and request placement of a peritoneal dialysis catheter and a small percutaneous double lumen external jugular line for sampling (5Fr x 8cm Cook – available from PICU) and also a nasogastric tube. (See protocol entitled – Acute Peritoneal Dialysis)

<table>
<thead>
<tr>
<th>Peritoneal Catheter Size</th>
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<tbody>
<tr>
<td><strong>Patient Weight</strong></td>
</tr>
<tr>
<td>&lt; 5Kg</td>
</tr>
<tr>
<td>3.5 to 7.5Kg</td>
</tr>
<tr>
<td>7.5 to 15Kg</td>
</tr>
<tr>
<td>&gt;15Kg</td>
</tr>
</tbody>
</table>

- Ensure patient cross-matched for 2 units of packed red blood cells
- Obtain U&E’s/LFT’s and FBC prior to theatre.
- Obtain consent for procedure (or request surgeon to do so)
- If platelets less than 30x10⁹ then order CMV negative matched platelets as directed by haematology.
- Prior to theatre each patient should have a loading dose of antibiotics:-
  1. **Vancomycin 15mg/kg once only (i.e. NOT TO BE GIVEN REGULARLY)**
  2. **Netilmicin 2.5mg/kg once only (i.e. NOT TO BE GIVEN REGULARLY)**

Dialysis prescription should be based on protocol entitled – Acute Peritoneal Dialysis
3.3 Haemodialysis

Haemodialysis is indicated for those with severe colitis, cerebral HUS (who may require plasmapheresis) or for those with profound metabolic derangements such as hyperkalaemia or are markedly catabolic. (See protocol entitled – Acute Haemodialysis)

- Contact the on-call surgical registrar and request placement of a haemodialysis line and the passage of a nasogastric tube.

<table>
<thead>
<tr>
<th>Haemodialysis Access</th>
<th>Internal Jugular Lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5Kg</td>
<td>6.5F x 7.5cm Hospal</td>
</tr>
<tr>
<td>5-15Kg</td>
<td>10F x 10cm Cook</td>
</tr>
<tr>
<td>15 – 40Kg</td>
<td>10F x 10cm Cook</td>
</tr>
<tr>
<td>&gt;40Kg</td>
<td>12.5F x 15cm Cook</td>
</tr>
</tbody>
</table>

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Dialysis prescription should be based on the protocol entitled – Acute Haemodialysis.

4. Atypical Haemolytic Uraemic Syndrome

Haemolytic Uraemic Syndrome may follow infection with other serotypes of E Coli and serology for these should be specifically requested if indicated. Similarly other infectious agents have been identified including Strep Pneumoniae, Klebsiella and shigella therefore other potential infectious agents should be sought.

Familial cases of HUS are also recognised and a detailed family must therefore be obtained and the parents directly questioned regarding the possibility of consanguinity.
4.1 Other potential causes

- Idiopathic
- Drug Toxicity
  - Chemotherapy, Mitomycin-C, Tacrolimus, Cyclosporin, oral contraceptives, valacyclovir, OKT3 Immune mediated
  - Quinine, Ticlodipine, Clopidorgel
- Conditioning for Bone Marrow Transplantation
- Solid organ transplantation
- Malignancy
- Hereditary e.g. Autosomal Recessive or Dominant; Inborn error of cobalamin deficiency
- Pregnancy or post partum
- AIDS and early symptomatic HIV
- Connective Tissue Disease e.g. SLE, Sjorgens, Systemic Sclerosis, antiphospholipid antibody syndrome, Scleroderma
- Other Glomerulonephritides e.g. APIGN, membranoproliferative

4.2 Possible Investigations

- Complement levels
  - Low C3
  - Factor H
  - C3 Nef
- Von Willebrand cleaving factor
- Urinary
  - Methylmalonic acid
  - Homocysteine
- Renal Biopsy
- Autoantibodies
  - Anticardiolipin, Antinuclear factor, Anti double stranded DNA, Anti-endo nuclear
- Antiplatelet antibodies
- Pregnancy Test
- HIV Test

5. Future Guideline Development

- Should any aspect of this guideline change before the planned review (i.e. new technology or changes in procedure) then this guideline should be updated accordingly.

- Future review of this guideline should make use of the AGREE document to ensure that this guideline incorporates up-to-date evidence and best clinical practice. For further information on guideline development please contact the chairperson of the Multi-Professional Clinical Practice Committee.
**Appendix: Referral Proforma**

**Patients Name**

**Date of Birth**

**Diarrhoeal Prodrome**  Yes/No  **Duration**

**Red Cell Fragmentation**  Yes/No

**Urine Output**  Normal  Reduced  Absent

**Blood Results**

**Date & Time Obtained**

<table>
<thead>
<tr>
<th>Na</th>
<th>K</th>
<th>Cl</th>
<th>Bic</th>
<th>Urea</th>
<th>Creat</th>
<th>Ca</th>
<th>Phos</th>
<th>Alb</th>
<th>Hb</th>
<th>WCC</th>
<th>Neut</th>
<th>Plt</th>
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</table>

**Hydration Status**  Normal  Hypovolaemic  Overloaded

**Blood Pressure**

**Conscious Level**

**Referring Doctor**

**Contact Telephone Number**

**Referring Hospital**

This information should be passed immediately to the appropriate consultant nephrologist.