Worcestershire Acute Hospitals NHS Trust

Nephrotic Syndrome (PIP)

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The following guidance is taken from the Partners In Paediatrics (PIP)

NEPHROTIC SYNDROME

RECOGNITION AND ASSESSMENT

Definition

- Oedema
- Hypoalbuminaemia: plasma albumin <25 g/L
- Heavy proteinuria, defined as:
  - dipstick 3+ or more, or
  - urinary protein >40 mg/m^2/hr, or
  - early morning protein:creatinine ratio >200 mg/mmol
- Hypercholesterolaemia

Symptoms and signs

Oedema

- Peri-orbital, pedal, sacral, scrotal
- Also ascites or pleural effusion

Cardiovascular – can be difficult to assess due to oedema

Assess for hypovolaemia carefully

- Child with diarrhoea and vomiting and looks unwell
- Abdominal pain: strongly suggestive
- Poor peripheral perfusion and capillary refill >2 sec
- Pulse character: thready, low volume, difficult to palpate
- Tachycardia or upward trend in pulse rate
- Hypertension may be an early sign, hypotension a late sign
- Jugular venous pressure (JVP) low

Muffled heart sounds suggest pericardial effusion

Respiratory

- Tachypnoea and recession: suggest pleural effusion

Abdomen

- Swelling and shifting dullness: suggest ascites
- Tenderness with fever, umbilical flare: suggest peritonitis
- Scrotal oedema: stretching can cause ulceration or infection

Investigations

Femoral blood sampling is contraindicated because of risk of thrombosis

Urine

- Urinalysis
- Early morning urine protein:creatinine ratio first morning after admission
  - normal value <20 mg/mmol; nephrotic >200 mg/mmol, usually >600 mg/mmol
  - low urine sodium (<10 mmol) suggests hypovolaemia

Baseline bloods

- U&E and creatinine
- Albumin
- FBC
- Immunoglobulins G, A and M
- Complement C3 and C4
- Zoster immune status: as a baseline
- Hepatitis B and C serology

Second-line tests

Request only if features suggestive of more aggressive nephritis (hypertension, macroscopic haematuria, high creatinine, no response to corticosteroids)

- Anti-streptolysin O titre and anti-DNase B
- Anti-nuclear antibodies
- Anti-dsDNA antibodies

Interpretation

- High haematocrit suggests hypovolaemia
- Raised creatinine or urea suggests hypovolaemia, tubular plugging or other nephritis
- Serum cholesterol and triglycerides: often elevated
- IgG usually low
- C3 normal

Differential diagnosis

- Minimal change disease (95%)
- Focal segmental glomerular sclerosis (FSGS)
- Multisystem disorders (e.g. HSP, diabetes mellitus, SLE)
- Congenital nephrotic syndrome very rare and seen in under 2s

IMMEDIATE TREATMENT

General

- Admit
- Strict fluid balance monitoring
- daily weight: **mandatory**
- Avoid added salt, but a low salt diet not indicated
- Manage hypovolaemia – see Complications
- seek **senior advice before volume resuscitation**, as risk of volume overload

Fluid restriction

- Restrict to insensible losses e.g. 300 mL/m2 plus urine output
- If not tolerated, aim for:
- 600 mL/day in children aged <5 yr
- 800 mL/day in children aged 5–10 yr
- 1000 mL/day in children aged >10 yr

Medication

- Prednisolone 60 mg/m2 oral once daily (maximum 80 mg), in the morning (see BNFc for surface area)

Phenoxymethylpenicillin (penicillin V) for pneumococcal prophylaxis (**presentation only**)

- If oedema upsetting to patient or causing discomfort, add furosemide 1–2 mg/kg oral or 1 mg/kg IV over 10 min
- may intensify hypovolaemia, in which case use albumin 20%: discuss with **consultant or specialist centre**
- If disease severe, especially with hypovolaemia, as judged by poor perfusion, high Hb, thrombophilia, or abdominal pain, treat with:
- dipyridamole to reduce risk of thrombotic complications. Discuss need for heparin/warfarin with paediatric nephrologist
- Give omeprazole for gastro protection whilst on high dose steroids

COMPLICATIONS

Hypovolaemia

- Abdominal pain, looks unwell, tachycardia, poor perfusion, high Hb
- Seek **senior advice before volume resuscitation**, as risk of volume overload
- give sodium chloride 0.9% 10 mL/kg

Do not confuse 4.5% albumin with 20% as the latter is hyperosmolar and can easily cause fluid overload

- Start dipyridamole
- Looks unwell, abdominal pain and vomiting
- Low JVP, rising urea and creatinine, and poor response to diuretics
- Treatment: check with consultant first

- salt-poor hyperosmolar albumin **20%** 0.5–1 g/kg (2.5–5 mL/kg) over 2–4 hr with furosemide 1–2 mg/kg IV midway through infusion over 5–10 min (maximum 4 mg/min)
- regular observations for signs of circulatory overload (e.g. raised JVP, tachycardia, gallop rhythm, breathlessness, low SpO_2)
- often required daily: liaise with specialist centre

Peritonitis

- Difficult to recognise
- steroids may mask signs, including fever, or cause leucocytosis
- Abdominal pain
- consider hypovolaemia and appendicitis: request early surgical opinion
- Obtain blood culture and peritoneal fluid (for Gram stain and culture) if possible, then start piperacillin with tazobactam (Tazocin®) IV pending culture results
- if penicillin allergic discuss with microbiologist or consultant in infectious diseases

Cellulitis

- Commonly caused by haemolytic streptococci and pneumococci – treat promptly

Thrombosis

- Renal vein: an important differential in abdominal pain
- Cerebral vasculature
- Pulmonary vein
- Femoral vein: femoral blood sampling contraindicated
- A fall in platelets, rise in D-dimers and reduced PTT are suggestive
- USS with Doppler study to look at perfusion and to image renal vein and IVC can be helpful
- If in any doubt, seek advice from paediatric nephrologist regarding investigation/management

DISCHARGE POLICY AND SUBSEQUENT MANAGEMENT

- Discharge once in remission
- defined as trace/negative urine protein for 3 days
- patients with normal BP and stable weight who are well may be allowed home on ward leave with **consultant approval**. Normally twice weekly review will be required until in remission
- Arrange plan of care with patient and carers – see **below**
- Outpatient review in 4 weeks

New patients

- Prednisolone 60 mg/m^2 (maximum 80 mg) once daily for 4–6 weeks
- Then 40 mg/m^2 (maximum 40 mg) alternate days for 4–6 weeks
- gradually reduce dose aiming to stop after 3–4 weeks
- Response usually apparent in 7–10 days
- No response after 4 weeks daily steroid 60 mg/m^2 suggests corticosteroid resistance

Relapsing patients

- 3 consecutive days of 3+ or more early morning proteinuria, having previously been in remission = relapse
- Start prednisolone 60 mg/m^2 (maximum 80 mg) once daily
- continue until nil or trace proteinuria for 3 days
- then 40 mg/m^2 (maximum 40 mg) alternate days for a further 4 weeks, gradually reduce dose aiming to stop after 3 weeks
- If relapses frequent despite alternate-day prednisolone, discuss with paediatric nephrologist

Oral prednisolone

- While on prednisolone 60 mg/m^2 once daily advise to:
- carry a corticosteroid card
- seek prompt medical attention for illness, especially zoster contacts (if not zoster immune)

Other management

- Urine testing
- teach technique and provide appropriate dipsticks
- test only first daily urine sample
- keep a daily proteinuria diary and bring to **every** clinic attendance

- Corticosteroid diary with instructions regarding corticosteroid dosage

Infectious precautions

- Avoid live immunisations for 3 months after completion of treatment with high-dose corticosteroids
- Benefit of inactivated vaccines can be impaired by high-dose corticosteroids and so a similar delay advisable where possible
- where not possible because of frequent relapse, give INACTIVATED vaccines after a shorter delay and check for an antibody response
- Continue phenoxymethylpenicillin (penicillin V) (**presentation only**) prophylaxis until oedema has resolved (if penicillin allergic give azithromycin)
- If zoster non-immune (VZV IgG negative) and on high-dose corticosteroids, give IM zoster immunoglobulin (obtain from local Public Health England laboratory)
- after definite zoster contact. A contact is infectious 2 days before onset of rash until all lesions crusted over
- can be given up to 10 days after exposure. Contact consultant microbiologist on duty (or local virology laboratory) for release of VZIG
- at first sign of illness give aciclovir IV
- varicella vaccine (live vaccine) available and should be given if a suitable opportunity arises between relapses
- Give pneumococcal vaccine if child has not received pneumococcal conjugate vaccine – see **BNFc** for schedule

Refer for paediatric nephrologist advice if:

- Corticosteroid-resistant disease
- non-responsive after 4 weeks of daily prednisolone, but start discussions with specialist centre in third week, or if relapses frequently
- Corticosteroid-dependent disease
- 2 consecutive relapses during corticosteroid treatment or within 14 days of cessation
- Significant corticosteroid toxicity
- Aged <1 yr or >12 yr at first presentation
- Mixed nephritic/nephrotic picture: macroscopic (not microscopic) haematuria, renal insufficiency or hypertension
- Low complement C3/C4
- ANA +ve