

Management of Nephrotic Syndrome

1. Introduction

- Incidence 2-4/100,000. Boys > girls 3:2; age of onset 2-6 years
- 80% of cases in children is due to minimal change (MCD) of which 80% will respond to steroid treatment
- 20% of cases due to Focal Segmental Glomerulosclerosis (FSGS) and Mesangiocapillary Glomerulonephritis (MCGN). These children are older, majority do not remit and have a poorer outcome.
- SSNS = Steroid Sensitive Nephrotic Syndrome; of these $\geq 70\%$ will relapse
- Progression to ESRF is rare and majority will achieve long-term remission in later childhood
- Morbidity and mortality are secondary to complications and side effects of the drugs

2. Definitions

| Condition | Symptoms |
|--------------------|---|
| Nephrotic Syndrome | Abnormality of glomerular permeability results in: <ul style="list-style-type: none"> • Proteinuria $> 40\text{mg}/\text{m}^2/\text{hour}$ (+++) • Hypoalbuminuria ($< 25\text{g}/\text{l}$) • Protein/creatinine ratio $> 200\text{mg}/\text{mmol}$ • Oedema |
| Remission | Urinary protein excretion $< 4\text{mg}/\text{hour}/\text{m}^2$, Albustix O-trace for 3 consecutive days. |
| Relapse | Urinary protein excretion $> 40\text{mg}/\text{m}^2/\text{hour}$ or Albustix +++ for 3-5 consecutive days or ++++ on one occasion having previously been in remission. |
| Frequent Relapses | ≥ 2 during the first 6 months after the initial episode, ≥ 4 relapses within any 12-month period. |
| Steroid Dependence | 2 consecutive relapses occurring during steroid therapy or within 14 days of stopping it. |
| Steroid Resistance | No response to daily prednisolone at $60\text{mg}/\text{m}^2$ after 4 weeks. |

3. Differential Diagnosis of Generalized Oedema

Renal

- Nephrotic
- Nephritic (oligo/anuria, hypertension, oedema)
- Acute renal failure

Non-Renal

- Severe cardiac failure
- Chronic liver disease
- Protein – losing enteropathy

4. Specific Points to include in Clinical Assessment

| History | Other History |
|--|--|
| Antecedent illness Fluid intake Urine output | Previous chicken pox History of atopic disease Immunizations |

Examination

- Assess hydration
- Height (pls document), weight, blood pressure
- Look for ascites, pleural effusions, dependent oedema
- Look for signs of acute complications e.g.
 - Hypovolaemia
 - Infection
 - Thrombosis (arterial and venous)

5. Investigation

| Blood | Urine |
|---|---|
| FBC U + E, Albumin, CRP, creatinine Complement C ₃ + C ₄ Varicella antibody titres Hepatitis serology B + C (If indicated – ASOT, ANA, Ds DNA) | Dipstick analysis Early morning protein/creatinine ratio MC + S Urine electrolytes |

Other

- Consider renal USS if atypical features or suspect renal vein thrombosis

Indication for Renal Biopsy + Referral to Nephrologist

- Atypical presentation
 - Age < 1 + > 12 years
 - Persistent hypertension
 - Persistent renal impairment (not due to hypovolaemia)
 - Frank haematuria
 - Low complement C₃
 - Rash and arthropathy
- Failure to respond to steroids (before starting 2nd line drugs)
- Severe complications
- Frequent relapses and steroid dependency
- Unacceptable steroid side effects

6. General Management

- Admit all newly diagnosed children
- Inform registrar/consultant
- Look out for hypo/hypervolaemia. Check urinary sodium
- Test all urine for blood + protein and frequent BP
- Daily weights- look out for diuresis + weight loss when oedema improves
- Accurate fluid balance charts – do not fluid restrict.
- Start treatment penicillin for 7/7 (erythromycin if allergic)
- Do not prescribe NSAIDS
- Low salt diet
- Mobilization to reduce risk of venous thrombosis

7. Parent Information

- Explain importance of compliance
- Steroid card
- Diary of urine results and medication and teach use of Albustix
- All killed vaccines are safe except meningococcal C with possible increased risk of relapse.
- Ensure Pneumococcal vaccine given to all, once in remission and off steroids
- Prophylactic steroids for intercurrent sepsis and surgery up to 3/12 after stopping steroids
- No live oral polio vaccine to household contacts during immunosuppression
- Warn about contact with chicken pox
- Explain about prophylactic penicillin (125mg <5years, 250mg) during relapses and until proteinuria has cleared
- No live vaccine if child has received daily prednisolone for more than 1 week in previous 3/12 or any other immunosuppressive drug

8. Treatment of Nephrotic Syndrome

Steroid treatment for first nephrotic illness (adapted from Guy's protocol)

Remember to give a steroid card

1. Prednisolone 60mg/m² (maximum dose 80mg) per day as a single dose or in divided doses for 28 days irrespective of whether the child goes into remission earlier than 28 days. If no response to steroids, refer to Guy's Paediatric Nephrology Unit.
2. Followed by Prednisolone 40mg/m² BSA on alternate days for a 28 day period
3. Followed by Prednisolone 30mg/m² BSA on alternate days for a 28 day period
4. Followed by Prednisolone 20mg/m² BSA on alternate days for a 28 day period
5. Followed by Prednisolone 10mg/m² BSA on alternate days for a 28 day period
6. Followed by Prednisolone 5mg/m² BSA on alternate days for a 28 day period
7. Then stop.

NB total duration = 6 months

If the child relapses during the weaning period, they are very likely to become frequently relapsing. However, a further daily course of Prednisolone (60mg/m² BSA per day) should be given, particularly if there was a precipitating factor that caused the relapse, before recourse to alkylating agents.

Treatment is currently subject of RCT. Please contact Dr Bhatti for further details.

Steroid treatment for Nephrotic Relapses (adapted from Guy's protocol)

1. Prednisolone 60mg/m² BSA per day as a single dose or in divided doses until early morning urinalysis is negative for protein or trace for 3 consecutive days
2. Followed by Prednisolone 40mg/m² (maximum dose 60mg) on alternate days for a 4 week period

Steroid treatment for Steroid Dependent Nephrotic Children (adapted from Guy's protocol)

1. Prednisolone 60mg/m² BSA per day as a single does or in divided doses until early morning urinalysis is negative for protein or trace for 3 consecutive days
2. Followed by Prednisolone 40mg/m² BSA on alternate days for a 6 day period
3. Followed by Prednisolone 30mg/m² BSA on alternate days for a 6 day period
4. Followed by Prednisolone 20mg/m² BSA on alternate days for a 6 day period
5. Followed by Prednisolone 10mg/m² BSA on alternate days for a 6 day period
6. Followed by Prednisolone 5mg/m² BSA on alternate days for a 6 day period

The new **maintenance dose** of alternate-day steroid is chosen by following the weaning schedule until the dose just above the dose at which the child relapses

Decisions about diuretics and 20% albumin use must be discussed with consultant/registrars

9. Complications – inform registrar/consultant

A. Hypovolaemia – can cause ATN and thrombosis (Peripheral and renal vein)

NB Consider if gross oedema, sepsis, D+ V, excessive diuretic use

| | |
|----------------|---|
| SYMPTOMS | <ul style="list-style-type: none"> • Abdominal pain – (? Secondary to compensatory vasoconstriction of splanchnic circulation) • Nausea, vomiting • Diarrhoea • Lethargy |
| CLINICAL SIGNS | <ul style="list-style-type: none"> • Cold feet, legs, hands • Tachycardia, poor peripheral perfusion, CRT > 25 • Hypertension/normotension (hypotension is a very late sign) • JVP not visible; toe/care gap > 3° C • No sign of intravascular fluid overload <ul style="list-style-type: none"> - Gallop rhythm not present - No cardiomegaly/hepatomegaly |
| URINE | <ul style="list-style-type: none"> • Oliguria (<1ml/kg/hr) • Random urinary Na < 10mmol/l |
| BLOOD | <ul style="list-style-type: none"> • Increased PCV, increased urea |
| TREATMENT | <ul style="list-style-type: none"> • For shock (lower BP), give 20mls/kg of 4.5% albumin (or normal saline) over 30 minutes |

B. Acute renal failure – consider RVT, refer All

C. Peritonitis

- Broad spectrum antibiotics –iv ceftriaxone (usually strep or Gram –ve)
- Please see the Trust [antibiotic guidelines](#)

D. Thrombosis

- Urinary loss of antithrombin III, increased fibrinogen

E. Gross oedema

- No indication for the use of 20% albumin infusion solely to increase serum albumin

F. Infections

- Due to urinary loss of immunoglobulins + complement
- Increased risk of pneumococcal, staphylococcal cellulites and varicella

G. Hypertension

- Persistent increase BP in absence of hypovolaemia atypical - needs further assessment
- Nifedipine 200µg/kg/dose tds may be used

[c/work/protocols2002/nephrotic syndrome- management/jan02](#)

Protocol ratified by:

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Print name:

Date:

Reviewed: November 2014

Next Review: November 2017