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缅甸联邦第一特区卫生部

The Union of Myanmar, SR(1) Department of Health

Nephrotic Syndrome

Standard Operating Procedure (SOP)

Contents

Nephrotic Syndrome

Definition

Nephrotic syndrome is characterized by

- Edema
- Heavy proteinuria (urine protein/creatinine 20.2 g/mmol, urine protein is 3+/4+ (on dipstick or boiling test, urinary protein excretion >40 mg/m/hr)
- Hypoalbuminemia (serum albumin <2.5 g/dL)
- Hyperlipidemia (serum cholesterol >200 mg/dL) is not conventionally included as part of the diagnosis

Investigations

- Full blood count
- Urinalysis-Dipstick(proteinuria)& microscopy
- Serum albumin, cholesterol, urea and creatinine
- CXR before steroid therapy is started
- HBV, HCV, HIV screening

Renal biopsy

- Not indicated prior to start corticosteroid or cyclophosphamide therapy
- This is because 80% of children with idiopathic nephrotic syndrome have minimal change steroid responsive disease

The main indication for renal biopsy is -

  - Steroid resistant nephrotic syndrome
- Other indications
  - Persistent proteinuria and/or persistent gross haematuria
  - Persistent hypertension
  - Persistent high urea and creatinine
- Indications for renal biopsy in children with steroid sensitive nephrotic syndrome (SSNS)are-
  - Late failure to respond following initial response to corticosteroids;
  - High index of suspicion for a different underlying pathology;
  - Decreasing kidney function in children receiving calcineurein inhibitors (CNIs).

Management

General

- **Monitor**
  - Body weight
  - Blood pressure
  - Intake and output
  - Urine albumin daily
- **Diet**
  - A balanced diet consisting of 1.5-2 g/kg/day of proteins and adequate
  - calories for age is recommended
  - Fat should constitute not more than 30% total calories
  - Low salt diet
- ***Fluid restriction***
  - This is recommended in chronic edematous states
  - Fluid intake = previous day urine output + insensible loss (400 ml/m^2/day)
- ***Penicillin prophylaxis***
  - Penicillin V can be given while there is proteinuria++ or more and/or in grossly edematous children.

Dosage: Less than 5 years-125 mg bid, 5 years or above-250 mg bid

- ***Ranitidine***

Should be given while the child receiving high dose of steroid treatment.
Dosage-2 mg/kg /dose bd Po. (Maximum dose = 150 mg bd)

- ***Albumin/plasma***

The clinical indications for albumin/plasma infusion are

  - Clinical hypovolaemia
  - Symptomatic massive edema

- Dosage-1 g/kg 20% Albumin (5 ml/kg) over 4-6 hours
- Give 1 mg/kg of IV Frusemide mid-infusion

- If clinically shocked, give 10 ml/kg 4.5% Albumin
  Children should be closely monitored during albumin infusions, and where possible they should be administered during working hours

- ***Vaccination***
  The following vaccines should be given in nephrotic syndrome, during remission and preferably when the child is not receiving oral daily steroid
  - Pneumococcal vaccine
  - Hepatitis B if not given before
  - Varicella vaccine (Live vaccines can be administered 6 weeks after cessation of corticosteroid therapy)

Specific Treatment

Treatment of initial presentation of nephrotic syndrome

Prednisolone

- Longer initial courses of prednisolone are associated with a lower incidence of relapse, and therefore a 12-week initial course is recommended
- 60 mg/m?/day (2 mg/kg) (maximim 60 mg in single or divided doses) for 4weeks
- 40 mg/m?/on alternate days (1.5 mg/kg) (maximum 40 mg) as a single morning dose for 4 weeks
- Reduce dose by 5-10 mg/m? each week for another 4 weeks
  (Alternate-day treatment is not stopped abruptly at 12 weeks, but tapered over the next 2-4 months)

Response to treatment

- Most children will respond to steroid treatment within 2-4 weeks
- A remission is defined as 3 or more days of trace or negative on dipstick testing

Complications

- **Hypovolaemia**
  - Hypovolaemia is a common finding in children with nephrotic syndrome. Clinical assessment can be very difficult.
  - The following are recognised as markers, but it is important to remember a child may still be hypovolaemic in the absence of all of these
    - Capillary refill time >2 seconds
    - Toe-core temperature gap >2C
    - Hypotension, but paradoxical hypertension in early stage
    - Persistent tachycardia

Infections

Thrombosis

  - Common sites include- Renal vein, femoral and mesenteric arterial thrombosis, deep vein thrombosis of calf veins, saggital sinus and cortical venous thrombosis
  - Renal vein thrombosis is suspected-oliguria, haematuria, or flank pain especially following an episode of dehydration
  - Saggital sinus and cortical venous thrombosis- following episodes of diarrhoea, present with convulsions, vomiting, altered sensorium, and neurological deficits

Investigaton of thrombosis

Ultrasonography, doppler studies, and cranial magnetic resonance imaging (MRI)

Treatment

- Require urgent treatment
- Correction of dehydration and other complications

There is no role for prophylactic treatment with anticoagulants inpatients with hypoalbuminemia and edema

Table 6.2 Clinical features and management of infections

Infection	Clinical features	Common organism	Antibiotics & durationof treatment
Peritonitis	Abdominal pain, tenderness distension; diarrhoea, vomiting, ascitic fluid >100 leukocytes/mm'. >50% neutrophils	S. pneumoniae S. pyogenes Esch. coli	Cefotaxime 50 mg/ kg/dose 8 hourly or Ceftriaxone 25-50 mg/kg/dose 12 hourly for7-10 days or Ampicillin 25 mg/kg/dose 6 hourly and Gentamicin 2.5 mg/kgdose 8 hourly for 7-10days
Pneumonia	Fever, cough, tachypnea, intercostal recessions, crepitations	S. pneumoniae H. infuenzae S. aureus	Oral: Amoxicillin 25mg/kg/dose tds or Co-amoxiclav (1-6 year -5 ml of 125/31 suspension tds, 6-12year-5 ml of 250/62 suspension tds orErythromycin 12.5 mgkg/dose qid for 7-10days
Cellulitis	Cutaneous erythema, induration tenderness	Staphylococci Group A streptococci H. infuenzae	Cloxacillin 25 mg/kg/dose 6 hourly andCeftriaxone 25-50 mg/kg/dose 12 hourly for 7-10 daysCo-amoxiclav lV 30m/kg (max. 1.2 g) every 8 hours
Fungal infection	Pulmonary infiltrates, persistent fever unresponsive to antibiotics, sputum/urine showing septate hyphae	Candida Aspergillus	Skin mucosa: Fluconazole 6 mg/kg/dose stat then 3 mg/kg/dose od for 10 daysoral or IV Systemic: Amphotericin IV 0.5. 1.5 mg/kg/day over 6-24 hour for 14-21 days

Treatment of Relapse Nephrotic Syndrome (Up to 60-70 %)

Prednisolone

Prednisolone treatment should be restarted once a relapse has been diagnosed.

- 60 mg/m2 daily (2 mg/kg/day) single or divided dose until the urine is negative or trace for 3 days then,
- Reduce to single morning dose of 40 mg/m2 (1.5 mg/kg/day) alternate days for 4 weeks then,
- Stop or taper the dose over 4-8 weeks. Total of 12 weeks is found to have less relapse
- Daily prednisone should be given till remission during episodes of upper respiratory tract and other infection.
- Daily prednisolone to reduce the risk for relapse in children with FR and SDSSNS already on alternate-day prednisone.

Breakthrough proteinuria may occur with intercurrent infection and usually does not require corticosteroid therapy if the child has no edema and remains well.

Risk factors for frequent relapses

- Age <3 years onset
- Relapse in first 6 months
- Delayed onset of remission in the first episode

Treatment of Frequent Relapses

Low dose alternate day prednisolone

Following treatment of a relapse, prednisolone is gradually tapered to maintain the patient in remission on low dose alternate day steroid treatment 0.5-0.7 mg/kg(<10-15 mg/alt days) which is administered for 9-18 months.

Close monitoring of blood pressure, growth and features of steroid toxicity is essential.

Referral to/discussion with pediatric nephrologist

- Frequent relapsers
- Steroid dependency (Two consecutive relapses occurring during the period of steroid taper or within 14 days of its cessation)
- Steroid toxicity
- Steroid resistant (Failure to achieve remission in spite of 4 weeks of 2 mg/kg daily dose prednisolone therapy)

Indication for Immune Modulators Therapy

- If the dose of prednisolone to maintain the remission is higher or
- If features of corticosteroid toxicity are seen

Immunosuppressant drugs must be given under consultation and guidance of nephrologists

Levamisole

Indications

- Frequently relapsing or steroid-dependent nephrotic syndrome with unacceptable steroid side-effects, due to MCNS.
- ***Dosage***-2.5 mg/kg on alternate days for 6 months-1 year
- Check full blood count monthly for first 3 months to detect reversible neutropenia
- Beware of levamisole dependence (>2 years)
- Co-treatment with prednisolone at a dose of 1.5 mg/kg on alternate day for 2-4 weeks and gradually reduced by0.15-0.25 mg/kg every4 weeks to a maintenance dose of 0.25-0.5 mg/kg for 6 or more months.

Cyclophosphamide

- ***Indication***
  - Frequent relapses
  - Steroid dependent
- Dosage-2-2.5 mg/kg/day od for 8-12 weeks or equivalent (maximum cumulative dose 168 mg/kg)
- FBC should be monitored weekly for the first few weeks of treatment ancfortnightly for next 8 weeks.
- Stop drugs if:
  - Febrile illness
  - WBC count <3.0X10°/L
  - Platelets count <100 X10° /L
- Prednisolone is co-administered at a dose of 1.5 mg/kg alternate for 4 weeks followed by 1 mg/kg for next 8 weeks and tapered over next 2-3 months.

Cyclosporin

- ***Indications***
  - Steroid-resistant and steroid-dependent patients with MCNS who has failed cytotoxic therapy with alkylating agents such as cyclophosphamide and with normal renal function
- Nephrotic syndrome due to FSGs with normal renal function
- Dose 3-6 mg/kg/d in two divided doses with maintenance of lower levels after a child has been in stable remission for 3-6 months, aiming to minimize cyclosporine nephrotoxicity
- Usually for 1 year may be useful as a steroid sparing agent
- Monitor BP and Urine output, serum creatinine, renal function and drug level if possible

Mycophenylate Mofitil (MMF)

- ***Indication***
  - Patients who are still relapsing on steroid and cyclosporine
  - In those with cyclosporine toxicity
- Dosage-600 mg/m/day bid have been used.
- FBC should be monitored for leucopenia.
- ***Side effects*** - Gastro-intestinal intolerance, mainly diarrhoea.

Follow Up

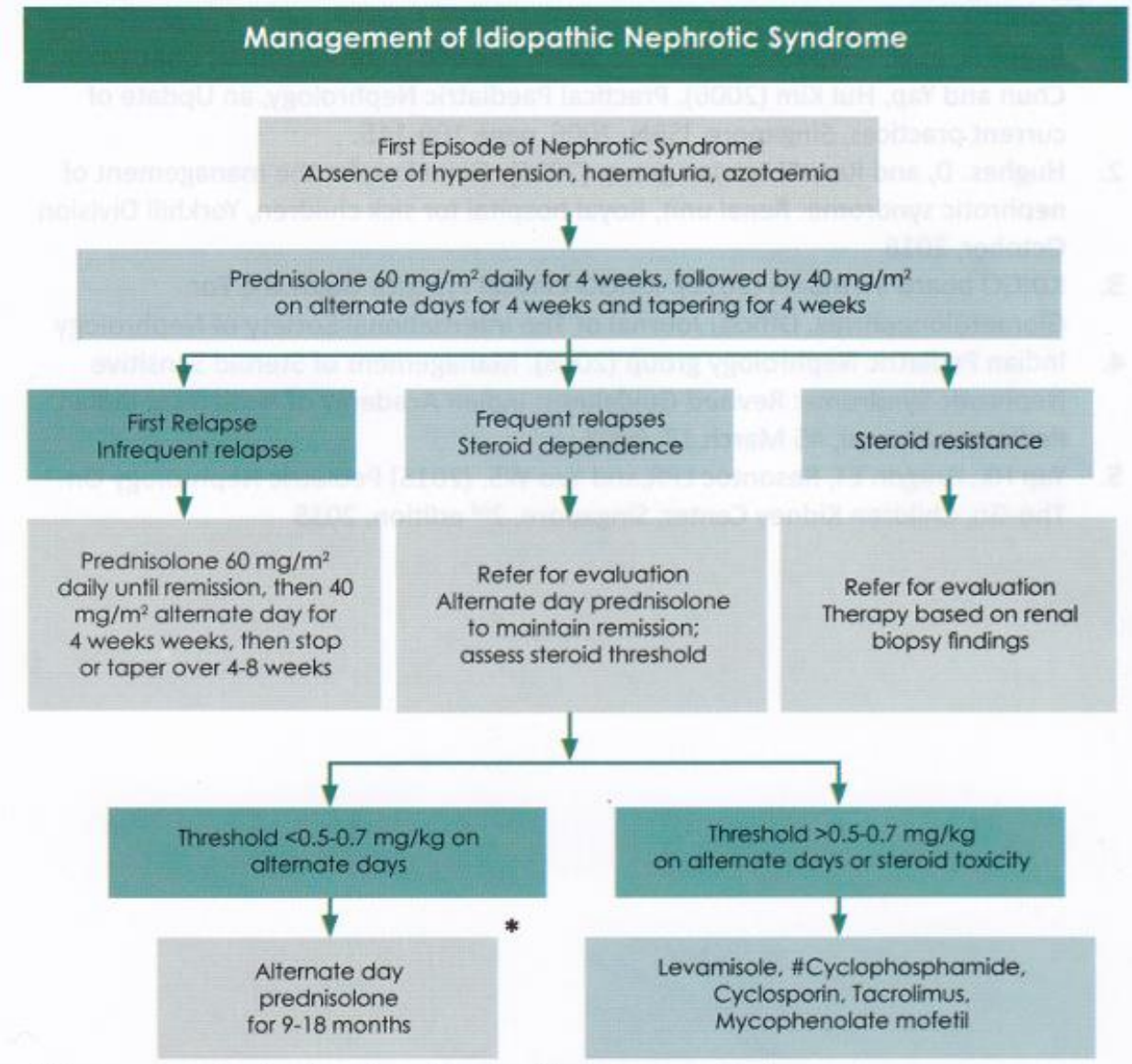
General considerations during follow up
For children on long-term steroids

- Monitor BP
- Monitor growth, height and pubertal stage
- Glycosuria
- Calcium supplements

Ophthmology review 6 monthly

Remission	Urine protein dipstick negative or trace for 3 consecutive days
Relapse	Urine protein dipstick 2^+ or more for 3 consecutive days
Frequent Relapses (FRNS)	Two or more relapses within the frst 6 months of presentation OR Four or more relapses within any 12 month period
Steroid dependent (SDNS)	Relapse occurs while on alternate day steroid therapy orwithin 28 days of stopping prednisolone therapy
Steroid resistance (SRNS)	Failure to achieve response in spite of 4 weeks prednisolone therapy
Steroid sensitive (SSNS)	Remission achieved by steroid therapy alone

*If failure to achieve remission 4 weeks duration of 60 mg/m^2/day, to consult with nephrologist



#The course of cyclophosphamide should not be repeated.
**To consult and refer to nephrologist*