Childhood Nephrotic Syndrome

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Preface

These guidelines are intended to help the primary care physician manage typical nephrotic syndrome patients and do not cover the management of atypical and steroid-resistant patients. Managing nephrotic syndrome (NS) in children is a collaborative effort between the primary care physician and pediatric nephrologist.1

The incidence of NS in children is low, about 2 to 7 cases per 100,000,2,3 so pediatricians and family physicians will likely encounter few children with NS. Once a child has been found to have nephrotic syndrome, early referral to pediatric nephrologist is recommended.

Definition, Assessment, Diagnosis, and Complications

- Definition: heavy proteinuria that is severe enough to cause hypoalbuminemia, edema, and usually hypercholesterolemia
- Assessment
  - Insidious onset edema
    - Starts in periorbital region and becomes more generalized with gravity-dependent movement of fluid
    - Signs and symptoms of pleural effusion, ascites, scrotal, and vulval edema
  - Peak age at 2-3 years
    - Fifty percent (50%) of patients between 1 and 4 years-of-age
    - >75% are under 10 years-of-age
- Diagnosis
  - Physical examination evidence of
    - Periorbital, pretibial, sacral, scrotal, or vulval edema
    - Ascites
    - Plural effusion

    - Laboratory
        - Urinalysis
        - First morning urine protein and creatinine ratio (mg/mg); a ratio >2 is nephrotic
        - Serum electrolytes, BUN, creatinine, and glucose
        - Cholesterol and albumin level; serum albumin <2.5 mg/dL and high cholesterol
        - Antinuclear antibody (ANA), complement C3, C4
        - Hepatitis C and B serologies
        - HIV screening
    - Imaging; chest x-ray if suspicion of pleural effusion
    - Kidney biopsy
        - Not required unless patient <1 year-of-age or >12 years-of-age
        - Recommended in steroid-resistant patients before initiating more potent immunosuppressive treatment
- Complications
    - Obesity and growth failure mainly caused by steroid therapy
    - Dyslipidemia
        - Generally improves in remission
        - Rarely requires anti-lipid therapy except in steroid-resistant or persistent dyslipidemia
    - Thromboembolism
    - Hypertension
    - Infection

Steroid Therapy Treatment

- Prednisone or prednisolone
    - In tablet or liquid forms
    - In younger children, liquid formulations help in accurate dosing;
    - Some formulations more palatable than others
- Dosages
    - High dose: prednisone or prednisolone at 2mg/kg/day (60 mg/M2/day) in 1-2 divided doses for 6 weeks; maximum daily dose of 60 mg
    - Maintenance dose: 1.5mg/kg or 40 mg/m2 every other day in the morning for 6 weeks
    - Weaning dosage: reduce by 15%-20% every 1-2 weeks until stopped
- Side effects
    - To minimize side effects, take steroids after meals, and may prescribe antacids or H2 blockers.
    - Discuss with patient and family weight gain, hyperactivity, increased infection risk, etc.
- Treatment of relapse
    - Initial or infrequent relapse
        - Give prednisone 2mg/kg /day until urine protein negative or trace for 3 consecutive days
        - Follow with prednisone 1.5 mg/kg/day on alternate days for 4 weeks
    - Frequent relapse
        - Give prednisone 2mg/kg/day until proteinuria negative or trace for 3 consecutive days.
        - Follow with prednisone 1.5 mg/kg/day for 4 weeks on alternate days and

then taper over 2 months.
- Refer to nephrologist for further management

Other Therapies

- Prophylactic anticoagulation may be indicated in certain situations related to thromboembolism
- Hypertension
  - Monitor blood pressure
  - If blood pressure persistently >95th percentile for gender, height, and age, refer to pediatric nephrologist
- Supportive therapy
  - Monitor growth
  - Maintain vigilance to treat infections
  - Prophylactic antibiotics not recommended for infection
  - Avoid long bed rest.
  - Salt restriction recommended for all NS patients
  - Fluid restriction recommended for severe and symptomatic fluid overload; avoid intravascular contraction that can lead to thromboembolism
  - Loop and thiazide diuretics can be used in symptomatic edematous patients after assessment by pediatric nephrologist; avoid intravascular contraction that can lead to thromboembolism
  - Intravenous 25% albumin and diuretics can be used in symptomatic edematous patients; this therapy is administered in patients admitted to the hospital under pediatric nephrologist supervision

Terms to Define Response

- Remission: negative or trace proteinuria on dipstick for 3 days
- Relapse: dipstick shows 2+ proteinuria for 3 days OR 3-4+ proteinuria and edema after remission
- Frequent relapse: ≥2 relapses within first 6 months after initial response or ≥ 4 relapses in any 12-month period.
- Steroid dependent: ≥ 2 consecutive relapses during taper OR within 14 days of steroid cessation
- Steroid resistance: failure to achieve remission after 6 weeks of full daily dose

Vaccination in Nephrotic Syndrome

- Especially important for children with nephrotic syndrome
  - At risk for infections due to nephrotic syndrome itself and immunosuppression
  - Particularly susceptible for pneumococcal infection
  - Children with nephrotic syndrome have lowest protection when in relapse.
- Immunize
  - With 23-valent and 13-valent conjugated pneumococcal vaccines
  - Immunosuppressed or actively nephrotic patient and household contacts with inactivated influenza vaccine yearly
- Defer immunization with live vaccine
  - Until prednisone dose <2mg/kg/day (maximum 20 mg)
  - For 3 months from completion of therapy with cytotoxic meds

        - For 1 month from completion of other daily immunosuppression
    - Varicella
        - Immunize if not immune
        - Non-immune patient will need immunoglobulin if exposed to varicella
            - Consider intravenous acyclovir for immunosuppressed children at the onset of chicken pox lesions.
            - Refer immunosuppressed patients to pediatric nephrologist

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

References

References

References

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3. Hogg R, Portman RJ, Milliner D, Lemley KV, Eddy A, Ingelfinger J. Evaluation and Management of Proteinuria and Nephrotic Syndrome in children: recommendations from a pediatric nephrology panel established at the National Kidney Foundation conference on proteinuria, albuminuria, risk, assessment, detection and elimination (PARADE). Pediatrics 2000;105(6):1242-9.