CLINICAL GUIDELINE

eGFRsupport: Nephrotic Syndrome Renal Support

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Electronic Guidelines for Renal Support (eGFRsupport): Nephrotic Syndrome

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Introduction

Nephrotic syndrome, a syndrome complicating various pathological processes and which can present in all age groups, is the combination of proteinuria, hypoalbuminaemia and oedema (+/- hyperlipidaemia and a hypercoagulable state). It is defined clinically by presence of the following:

- Urinary protein losses of >3g/day (~ urine protein:creatinine ratio >300mg/mmol)
- Serum Albumin <30g/L
- Oedema (may be mild)

Consideration of nephrotic syndrome should be given to presentations listed in in box 1

Presentation of Nephrotic syndrome

- Unexplained oedema
- New or persistent hypoalbuminaemia
- New or uncontrolled hypertension
- New presentation of deep venous thrombosis or pulmonary embolism
- Unexplained proteinuria on urinalysis

Box 1 – Important presentations of nephrotic syndrome

Assessment / Monitoring

Initial Assessment

- Dipstick urinalysis is a simple, cheap and semi-quantitative method of assessing for proteinuria and should be performed in all patients with suspected renal disease. Beware false negatives are possible in those with very dilute urine or Bence-Jones proteinuria (urinary light-chains for suspected myeloma).
- Unexplained presence of protein +/- blood may signify glomerular disease and warrant discussion with renal. All cases of visible haematuria and cases of persistent dipstick positive haematuria in those >40years should also be discussed with local urology services with a view to cystoscopic examination
- Obtain a clinical history. Check for potential causes (box 2) and attempt to discover aetiology.

Box 2 – Common causes of nephrotic syndrome

Common causes of nephrotic syndrome

- Multisystem disorders – e.g. Diabetes or SLE
- Chronic inflammatory disorders (e.g. IBD, Rheumatoid arthritis)
- Primary Glomerulonephritis
- Secondary Glomerulonephritis due to obesity, hypertension or certain drugs
- Malignancy including multiple myeloma

- Clinical examination :
  - Review patient observations: blood pressure is often high and oxygen saturations low
  - Outside of critical care areas, measurements of fluid intake/ urinary output are often inaccurate. Weigh daily during admission and whilst adjusting treatment, ideally using the same scales each time.
  - Examine daily for pulmonary oedema. Be wary of skin integrity and risk of infection.

- Investigations:
    - Quantify proteinuria by requesting a urinary protein:creatinine ratio. Send a white topped universal container of early morning urine to biochemistry.
    - Perform a glomerulonephritis screen in all (ANCA, ANA, rheumatoid factor and C3/C4), myeloma screen in those aged >60years (serum electrophoresis, immunoglobulins and Bence-Jones protein) and virology testing in those with risk factors (HBV, HCV or HIV).
    - All patients should undergo renal tract ultrasound

Nephrotic syndrome complications: protein malnutrition, hypovolaemia (often iatrogenic), acute kidney injury, thromboembolism and infection

Management

General principles

- All cases of nephrotic syndrome should be referred to renal to discuss the need for a renal biopsy. If renal function is stable and oral treatments are effective patients can be managed as outpatients.
- Oedema
    - Salt restrict to <2g daily, fluid restrict to <1.5L daily
    - Loop diuretics are used for symptomatic relief of fluid overload. Often absorption is inhibited by generalised oedema thus intravenous is required.
    - Moderate to high dose bolus dosing is used first line followed by a continuous infusion if weight loss is unachievable. Aim to lose ~1-2kg of body weight per day, using patient-predicted ‘dry’ body weight as a target.
- Hypertension
    - Uncontrolled hypertension is a risk factor for nephrotic syndrome, progressive renal disease and bleeding at time of renal biopsy.
    - Commence anti-hypertensives as tolerated to control blood pressure.
- Hyperlipidaemia
    - Refer patient to dieticians for protein and fat intake advice.
    - We do not recommend acutely commencing lipid-lowering therapy for nephrotic syndrome in the absence of a confirmed aetiology.

- Hypercoagulability
    - The greatest risk of venous thrombus occurs when serum albumin is <20g/L. Use mechanical measures to reduce risk of DVT in all patients.
    - Do NOT commence anticoagulation without discussing with renal as this may delay, or substantially increase the risk from, performing a renal biopsy.

Drug therapy/treatment options

Oedema

Drug	Suggested dosage	Cautions
Furosemide	***Currently on diuretics*** Give usual dose as a stat IV dose then give usual dose daily (e.g. 80mg daily, give 80mg IV daily) Inadequate response; options: - Increase dose - add further bolus at ~2pm - commence continuous infusion ***Diuretic naïve:*** Suggested starting doses eGFR > 60mL/min: 40mg daily eGFR 30-60ml/min: 80mg daily eGFR <30mlmin: 120mg daily	Ototoxicity, hypokalaemia, hypovolaemia, acute renal decline.
Thiazide	*Only commence on specialist/senior advice* Addition of bendroflumethiazide 2.5mg or metolazone 5mg on alternate or each day	Profound hypovolaemia, hypokalaemia, hyponatraemia
Amiloride	Weak diuretic effect, beneficial in preventing hypokalaemia Amiloride 5mg daily	Hypovolaemia, hyperkalaemia,

Box 3 – Example diuretic regimes

Hypertension

Drug	Starting dose
ACE inhibitors	*Avoid whilst using high dose diuretic due to risk of hypovolaemia induced AKI* Ramipril 2.5mg daily
Beta-Blockers	Bisoprolol 2.5mg daily
Calcium channel blocker	Amlodipine 5mg daily

Box 4 – Example anti-hypertensives regimes

Other information

Sub-nephrotic proteinuria

- Proteinuria increases cardiovascular risk and is an independent risk factor in the progression of renal disease. All unexplained uPCR results >100mg/mmol should be discussed, non-urgently with renal; out-patient follow-up may be required.
- Transient proteinuria often occurs in association with a systemic inflammatory response. A repeat sample in convalescence can clarify.

New or uncontrolled hypertension

- Essential hypertension is common, often requiring up to three agents to control blood pressure.
- Secondary causes of hypertension should be considered in those resistant to therapy or presenting at a young age (age <40 years). Seek senior advice if suspected
- History, examination and specific screening investigations can provide the diagnosis in the majority of cases.

- History
  - Ask about culprit drugs, symptoms of associated systemic diseases (box 5). Consider screening questionnaire for sleep apnoea
- Clinical examination
  - Look for features of systemic disease. Perform fundoscopy
- Initial investigations
  - Blood: U&ES/ FBC/TFTs/Glucose
  - Imaging: Renal tract ultrasound for renal size/symmetry. **Consider**: ECHO (LVH/aortic coarctation) and formal renal angiogram (renal artery stenosis)
- Hormonal investigations (if indicated):
  - Aldosterone: Renin ratio (Early morning blood sample, discuss with biochemistry prior to sending)
  - Dexamethasone suppression testing (Cushing's syndrome)
  - 24 hour urinary catecholamines (Phaeochromocytoma – for episodic hypertension)

Systemic disease	Notes
Obstructive sleep apnoea	Overweight, headaches, snoring, daytime sleepiness
Renal disease	Check U&Es
Primary hyperaldosteronism	Suspect if ↑Na, ↓K
Thyroid disease	Hyper- and hypo- associated with hypertension
Cushing's syndrome	Classical appearance, consider iatrogenic
Acromegaly	Classical appearance, check visual fields
Phaeochromocytoma	Episodic hypertension, with pallor and anxiety
Aortic coarctation	Upper limb hypertension (headache, nose bleeds), lower limb claudication

Box 5 – Clues for secondary causes of hypertension