

Glomerulonephritis

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Glomerular diseases

- Collection of diseases that affect the filters of the kidney and are mediated by different immunologic pathogenic mechanisms, resulting in varied clinical presentation and therapeutic outcomes.
- The signs and symptoms associated with glomerular diseases are commonly nephritic (reflecting inflammatory injury) or nephrotic (reflecting noninflammatory injury) and are characterized by hematuria and proteinuria.

Glomerular diseases

- They are categorized into two broad clinical phenotypes: Nephritic syndrome or Nephrotic syndrome.
- Nephritic syndrome reflects glomerular inflammation and results in gross hematuria.
- Nephrotic syndrome results in few cells or cellular casts in the urine.

Glomerular diseases

- The presence of RBC casts on urine microscopy is highly indicative of glomerulonephritis or vasculitis.
- The presence of proteinuria indicates a defect of the size- and/or charge-selective barriers within the glomerular basement membrane (GBM).

Sign&Symptoms: Nephritic Syndrome

- O Hematuria, dysmorphic RBC and RBC casts
- O Hypertension and edema, particularly as kidney function declines
 - O Proteinuria, usually < 3 g/day
 - O Abnormal eGFR (elevated SCr)

Sign&Symptoms: Nephrotic Syndrome

- O Edema
- O Weight gain from fluid retention
- O Fatigue
- O Proteinuria > 3.5 g/day/ $1.73m^2$
- O Hypoalbuminemia
- O Hyperlipidemia
- O Lipiduria

Nonpharmacologic Therapy

- O Dietary measures involve restriction of sodium intake to 50-100 mEq/day, protein intake of 0.8 to 1 g/day and a low-fat diet of less than 200-mg cholesterol per day.
- O Plasmapheresis or plasma exchange therapy may be used to remove immune factors in select cases.

Nonpharmacologic Therapy

- O Whole blood is removed from the body and centrifugation is used to separate the cellular elements from the plasma. The cells are then infused back to the patient after resuspension in saline or plasma substitute. The plasma proteins, presumably including the pathogenic immune factors, are removed from the patient.

Pharmacologic Therapy

Immunosuppressive Agents

○ Immunosuppressive agents, alone or in combination (corticosteroids/cytotoxic), are commonly used to alter the immune processes that are responsible for several of the glomerulonephritis.

Pharmacologic Therapy

- Cyclosporine and tacrolimus can reduce lymphokine production by activated T lymphocytes, and it may decrease proteinuria by improving the perm selectivity of the GBM.
- Mycophenolate mofetil is useful in some glomerulonephritis because of its effects on T- and B-lymphocytes.
- Rituximab is used for B-cell depletion and is a useful agent in antibody-mediated kidney disease.

Pharmacologic Therapy

- Corticosteroids as a result of their immunosuppressive and anti-inflammatory activities reduce the production and/or release of many substances that mediate the inflammatory process, e.g. prostaglandins, leukotrienes, platelet-activating factors, tumor necrosis factors, and interleukin-1.
- Cytotoxic agents, e.g. cyclophosphamide, chlorambucil or azathioprine are commonly used to treat glomerular diseases.

Pharmacologic Therapy

Diuretics

- Large doses of the loop diuretic, e.g. 160 to 480 mg of furosemide, may be needed for patients with moderate edema.
- A continuous IV infusion or intermittent IV boluses of a loop diuretic may be employed.

Pharmacologic Therapy

Diuretics

- In some cases, a thiazide diuretic or metolazone may be added to enhance natriuresis.
- In patients with morbid edema, albumin (25%) infusions may be used to expand plasma volume and increase diuretic delivery to the renal tubules, enhancing diuretic effect.

Pharmacologic Therapy

Antihypertensive Agents

- Optimal control of hypertension for patients with glomerular disease is important in reducing both the progression of kidney disease and the risk for CVD.
- ACEIs and ARB
- Dihydropyridine CCB
- Non-dihydropyridine CCB

Pharmacologic Therapy

Antiproteinuria Agents

- Dietary protein restriction reduces proteinuria and may minimize kidney function deterioration.
- Renin-Angiotensin-Aldosterone System Blockade: Disruption of RAS by ACEI, ARB and mineralocorticoid receptor blockers (spironolactone) can all decrease proteinuria.

Pharmacologic Therapy

- NSAIDs probably reduce proteinuria through prostaglandin E₂ inhibition, resulting in a reduction in intraglomerular pressure, a decrease in GFR and restoration of the barrier size selectivity of the GBM.
- Because of their potential for nephrotoxicity and proteinuria, esp. patient with CKD, long-term use of an NSAIDs for renoprotection is not commonly prescribed.

Pharmacologic Therapy

NSAIDs

○ Indomethacin and meclofenamate have similar efficacy to ACEIs, and combined treatment with an ACEI results in additional proteinuria reduction. However, adherence to a low-sodium diet or concurrent use of a diuretic is needed to maximize the antiproteinuric effect.

Pharmacologic Therapy

Statins

- Therapy is especially needed for those with concurrent atherosclerotic cardiovascular disease, or with additional risk factor e.g. smoking and HTN.
- HMG-CoA reductase inhibitors are considered the treatment of choice and statins can reduce CV risk.

Pharmacologic Therapy

Statins

- Meta-analysis studies showed that statins appear to reduce kidney function decline and slow the progression of proteinuria moderately.
- Statins should be used to treat the dyslipidemia in patients with persistent nephrotic syndrome.

Pharmacologic Therapy

Anticoagulants

- Renal vein thrombosis, pulmonary emboli, or other thromboembolic events are serious and common complications of nephrotic syndrome.
- Anticoagulants may be beneficial for patients with membranous nephropathy.