Appendix 8: Drug-Induced Kidney Disease

INTRODUCTION

TABLE A8-1

Drug-Induced Kidney Structural–Functional Alterations

Tubular epithelial cell damage
Acute tubular injury/necrosis Aminoglycoside antibiotics Radiographic contrast media Cisplatin, carboplatin Ifosfamide Amphotericin B Cyclosporine, tacrolimus Adefovir, cidofovir, tenofovir Pentamidine Foscarnet Zoledronate Osmotic nephropathy Mannitol Dextran IV immunoglobulin (sucrose) Hydroxyethyl starch
Hemodynamically mediated kidney injury
Angiotensin-converting enzyme inhibitors Angiotensin II receptor blockers SGLT-2 inhibitors NSAIDs Cyclosporine, tacrolimus OKT3
Obstructive nephropathy
Crystal nephropathy Acyclovir Sulfonamides Indinavir, atazanavir Foscarnet Methotrexate

- Ascorbic acid, ethylene glycol, orlistat
- Nephrolithiasis
  - Sulfonamides
  - Triamterene
  - Indinavir, atazanavir
- Nephrocalcinosis
  - Oral sodium phosphate solution

Glomerular disease

- Minimal change disease
  - NSAIDs, COX-2 inhibitors
  - Lithium
  - Pamidronate
  - Interferon-α and β
- Membranous disease
  - NSAIDs
  - Penicillamine
  - Captopril
- Focal segmental glomerulosclerosis
  - Pamidronate
  - Interferon-α and β
  - Lithium
  - Sirolimus
  - Anabolic steroids
  - Tyrosine kinase inhibitors

Tubulointerstitial disease

- Acute allergic interstitial nephritis
  - Penicillins
  - Ciprofloxacin
  - NSAIDs, cyclooxygenase-2 inhibitors
  - Proton pump inhibitors
  - Loop diuretics
- Chronic interstitial nephritis
  - Cyclosporine
  - Lithium
  - Aristolochic acid
- Papillary necrosis
  - NSAIDs, combined phenacetin, aspirin, and caffeine analgesics

Renal vasculitis, thrombotic microangiopathy, thrombosis, and cholesterol emboli

- Vasculitis and thrombosis
  - Hydralazine
  - Propylthiouracil
  - Allopurinol

Penicillamine
Gemcitabine
Mitomycin C
Methamphetamines
Cyclosporine, tacrolimus
Adalimumab
Bevacizumab
Cholesterol emboli
Warfarin
Thrombolytic agents

TABLE A8-2

Potential Risk Factors for Aminoglycoside Nephrotoxicity

(A) Related to aminoglycoside dosing
Large total cumulative dose
Prolonged therapy
Trough concentration exceeding 2 mg/L[a]
Recent previous aminoglycoside therapy
(B) Related to synergistic nephrotoxicity. Aminoglycosides in combination with
Cyclosporine
Amphotericin B
Vancomycin
Diuretics
Iodinated radiographic contrast agents
Cisplatin
NSAIDs
(C) Related to predisposing conditions in the patient
Preexisting kidney disease
Diabetes
Increased age
Poor nutrition
Shock
Gram-negative bacteremia
Liver disease
Hypoalbuminemia
Obstructive jaundice
Dehydration
Hypotension
Potassium or magnesium deficiencies

[a]The equivalent concentration in SI molar units is 4.3 µmol/L for tobramycin and 4.2 µmol/L for gentamicin.

TABLE A8-3

Recommended Interventions for Prevention of Contrast Nephrotoxicity

Intervention	Recommendation	Recommendation Grade[a]
Contrast	Minimize contrast volume/dose Use noniodinated contrast studies Use low- or iso-osmolar contrast agents	A-1 A-2 A-2
Medications	Avoid concurrent use of potentially nephrotoxic drugs (eg, NSAIDs, aminoglycosides)	A-2
Isotonic sodium chloride (0.9%)	Initiate infusion 3–12 hours prior to contrast exposure and continue 6–24 hours postexposure Infuse at 1–1.5 mL/kg/hr adjusting postexposure as needed to maintain a urine flow rate of 150 mL/hr Alternatively, in urgent cases, initiate infusion at 3 mL/kg/hr, beginning 1 hour prior to contrast exposure, then continue at 1 mL/kg/hr for 6 hours postexposure	A-1

[a]*Strength of recommendations*: A, B, and C are good, moderate, and poor evidence to support recommendation, respectively. *Quality of evidence*: (1) evidence from more than one properly randomized, controlled trial; (2) evidence from more than one well-designed clinical trial with randomization, from cohort or case-controlled analytic studies or multiple time series, or dramatic results from uncontrolled experiments; and (3) evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert communities.

TABLE A8-4

Drugs Associated with Allergic Interstitial Nephritis

Antimicrobials	
Acyclovir	Indinavir
Aminoglycosides	Rifampin
Amphotericin B	Sulfonamides
β-Lactams	Tetracyclines
Erythromycin	Trimethoprim–sulfamethoxazole
Ethambutol	Vancomycin
Diuretics	
Acetazolamide	Loop diuretics
Amiloride	Triamterene
Chlorthalidone	Thiazide diuretics
Neuropsychiatric drugs	

Carbamazepine	Phenytoin
Lithium	Valproic acid
Phenobarbital	
Nonsteroidal anti-inflammatory drugs	
Aspirin	Ketoprofen
Indomethacin	Phenylbutazone
Naproxen	Diclofenac
Ibuprofen	Cyclooxygenase-2 inhibitors
Diflunisal	
Piroxicam	
Miscellaneous	
Acetaminophen	Immune checkpoint inhibitors
Allopurinol	Lansoprazole
Interferon-α	Methyldopa
Aspirin	Omeprazole
Azathioprine	*p*-aminosalicylic acid
Captopril	Phenylpropanolamine
Cimetidine	Propylthiouracil
Clofibrate	Radiographic contrast media
Cyclosporine	Ranitidine
Glyburide	Sulfinpyrazone
Gold	Warfarin sodium

(*See Chapter 63, Drug-Induced Kidney Disease, authored by Thomas D. Nolin and Mark A. Perazella, for a more detailed discussion of this topic.*)