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AN OVERVIEW OF NEPHROTOXICITY IN THE ELDERLY POPULATION

Acute kidney injury (AKI) is not unique to any specific patient population, but the incident is increasing among the elderly population. Drug-induced kidney injury can present itself in four different ways: acute kidney injury, glomerular disorders, tubular disorders, and nephrolithiasis/ crystalluria. Generally, nephrotoxicity is defined as a 50% or 0.5mg/dL increase in serum creatinine over 24 – 72 hours after at least 24 – 48 hours of drug therapy. The most common medications associated with drug-induced kidney injury include antibiotics, chemotherapy, contrast dye, and agents that block the renin angiotensin system. Education and awareness are fundamental to prevention and early detection of kidney injury. Beyond supportive measures, there is no recognized treatment; however, in most cases, drug-induced kidney injury is reversible with discontinuation of the offending agent. This issue of *CLIPs* briefly summarizes an article that evaluates the prevalence, causes, and therapy of drug-induced kidney injury in the elderly population. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Khan S, Loi V, Rosner MH. Drug-induced kidney injury in the elderly. *Drugs Aging*. 2017 Aug 16. doi: 10.1007/s40266-017-0484-4. [Epub ahead of print]

Introduction

- Elderly patients are at increased risk of developing acute kidney injury due to exposure to nephrotoxic medications, comorbidities, structural and functional changes to the kidneys related to age, and the kidneys' decreased ability to regenerate.
- Drug-induced kidney injury can be characterized based on when symptoms develop after drug exposure as acute (1 – 7 days), subacute (8 – 90 days), or chronic (> 90 days).
- Drug-induced kidney injury accounts for 8 – 60% of all cases of acute kidney injury (AKI), 19 – 54% of AKI in the elderly.
- Elderly patients > 70 years are 3.5 times more likely to develop AKI than younger patients.

Risk Factors

- Structural and functional changes to the kidneys are part of the normal aging process.
- Changes in body composition affect volume of distribution.
- Comorbid disease states of hypertension, diabetes mellitus, heart failure, and coronary disease.
- Polypharmacy is much more common in the geriatric population. The use of multiple medications increases the risk of drug-drug interactions, as well as, adverse drug reactions.
- Baseline chronic kidney disease and a decrease in drug excretion increase risk of acute kidney injury.

Diagnosis

- There is not one standard set of criteria for diagnosing acute kidney injury (Risk, Injury, Failure, Loss, End-stage renal disease criteria (RIFLE), Acute Kidney Injury Network (AKIN), Kidney Disease: Improving Global Outcomes guidelines (KDIGO)).
- All three defining standards are based on changes in serum creatinine and urine output.
- Criteria used for diagnosis are located in Table 1.

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Table 1: Characteristics of acute kidney injury

RIFLE criteria		
Risk	SCr 1.5 – 1.9 times baseline or eGFR decrease ≥ 25%	UOP < 0.5 mL/kg/h for > 6h
Injury	SCr 2 – 2.9 times baseline or eGFR decrease ≥ 50%	UOP < 0.5 mL/kg/h for > 12h
Failure	SCr ≥ 3 times baseline or eGFR decrease ≥ 75% or SCr ≥ 4mg/dL; acute rise ≥ 0.5 mg/dL	UOP < 0.3 mL/kg/h for 24 h or anuria for 12h
Loss	Persistent acute renal failure with complete loss of function > 4 weeks	
End-stage renal disease	Need for RRT > 3 months	
AKIN Criteria		
Stage 1	SCr 1.5 – 2.5 times baseline or increase ≥0.3 mg/dL	UOP < 0.5mL/kg/h for > 6h
Stage 2	SCr > 2 – 3 times baseline	UOP < 0.5 mL/kg/h for > 12h
Stage 3	SCr > 3 times baseline or SCr > 4mg/dL with acute increase of > 0.5 mg/dL	UOP < 0.3 mL/kg/h for 24h or anuria for 12h
KDIGO criteria		
Stage 1	SCr 1.5 – 1.9 times baseline within the prior 7 days or ≥ 0.3 mg/dL increase within 48h	UOP < 0.5 mL/kg/h for > 6h
Stage 2	SCr 2 – 2.9 times baseline within the prior 7 days	UOP < 0.5 mL/kg/h for >12h
Stage 3	SCr ≥ 3 times baseline or increase to ≥ 4 mg/dL within the piror 7 days	UOP < 0.3mL/kg/h for 24h or anuria for 12h

SCr: serum creatinine; UOP: urine output; RRT: renal replacement therapy

Pathogenic Mechanisms

- Altered glomerular hemodynamics can be caused by diuretics, NSAIDs, ACE inhibitors, ARBs, calcineurin inhibitors, or SGLT-2 inhibitors.
- Tubular Cell Toxicity (Acute Tubular Necrosis and Tubulopathies) is most commonly associated with antibiotics (aminoglycosides, amphotericin B, and vancomycin), chemotherapy (cisplatin), contrast dyes, and bisphosphonates.
- Glomerular injury is characterized by profound proteinuria and microscopic hematuria and often caused by NSAIDs, lithium, or pamidronate.
- Thrombotic microangiopathy is associated with antiplatelet or anti-neoplastics like gemcitabine.
- Acute interstitial nephritis accounts for 3 – 15% of all drug-induced AKI cases, occurs 7 – 14 days after therapy, NSAIDs, proton pump inhibitors, beta-lactam antibiotics, rifampin, quinolones, sulfonamides, and loop diuretics. Self-limiting, reversible.
- Crystal-induced nephropathy and tubular obstruction is caused when drugs form a precipitate in the urine. Often this is a result of dehydration. Medications associated with this cause of AKI are acyclovir, high-dose methotrexate, indinavir, and sulfonamides.

Prevention

- Calculate an accurate baseline eGFR before administering any medications to ensure proper dosing.
- Identify potential nephrotoxic medications or combinations and closely monitor.
- Prescribed medications should be administered at the lowest effective dose for the shortest duration necessary. Monitor renal function and hemodynamics often.

Treatment

- Discontinue the drug causing harm. Provide supportive therapy.
- Renal replacement therapy has been shown to be safe and effective in the elderly population; however, it should be reserved for extreme cases.

Conclusion

- Elderly patients are at an increased risk of developing AKI, and with an aging population this is becoming an increasing issue. Prevention is vital, so medications and kidney function should be closely monitored prior to and during medication therapy.

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An overview of nephrotoxicity in the elderly population. *CLIPs- Current Literature and Information for Pharmacists.* 2017 Oct 2;21(10):1-2.