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Understanding Drug-Induced Nephrotoxicity: Types, Risk Factors, And Innovative Biomarkers-A Review

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Abstract

Exposure to medications and exogenous toxins, the kidney's ability to detoxify and excrete waste products fails, a condition known as nephrotoxicity. One study found that drug-induced conditions are reported in 60 percent of hospitalised patients. Understanding the various types of nephrotoxcity such as proximal renal tubular acidosis, rhabdomylosis, crystal nephropathy, acute tubular necrosis, and glomerulonephritis allows us to detect the modern biomarkers (proteinuria, KIM-1&NGAL, type 4 collagen, etc.) that aid in the early diagnosis of the disease due to the low sensitivity of the primitive biomarkers such as blood urea nitrogen and serum creatinine levels are detectable at later stage of progression. A pharmacist's involvement in managing drug-induced nephrotoxicity is discussed in this review along with information on signs, risk factors, types of nephrotoxicity, biomarkers, prevention and treatment.

Keywords: Nephrotoxicity; Exogenous Toxins; Glomerular Nephritis; BUN (Blood Urea Nitrogen); SCr (Serum Creatinine); Crystal Nephrotoxicity; NSAIDs(Non-Inflammatory Antisteroidal Drugs); ATN (Acute Tubular Necrosis); Acute and Chronic Interstitial Nephritis

Abbreviations

BUN: Blood Urea Nitrogen; SCr: Serum Creatinine; ATN: Acute Tubular Necrosis; NSAIDs: Non-Inflammatory Antisteroidal Drugs; AIN: Acute Interstitial Nephritis; NGAL: Neutrophil Gelatinase Associated Lipocalin; KIM-1: Kidney Injury Molecule 1.

Introduction

The kidneys are vital organs present in all vertebrates that performes specific functions such as maintaining electrolyte balance ,regulating blood pressure and excretion [1]. Nephrotoxicity is the term used to describe the impairment of kidney function caused by drugs, chemicals, or exogenous toxins, which causes inflammation in the glomerulus, proximal tubules, and surrounding cellular matrix. Glomerular nephritis, acute nephritis, and chronic nephritis are some of the diseases caused by nephrotoxicity [2]. Drug-induced conditions are reported in 60 percent of hospitalised patients [3].

Signs of Nephrotoxicity

- Reduced urination [4].
- Fluid retention-related edoema.

- Elevated blood pressure.
- GFR decline less than 60 ml/min/1.73m2.
- Alteration in BUN & SCr levels .
- Shortness of breath.
- Excessive fatigue.
- Nausea.
- Pain or pressure in chest.
- Irregular heartbeat.

In a few cases, it also affects other organ systems such as the liver, heart and others. It is detectable using biomarkers.

Risk Factors

1. Patient specific [5]:

- Age: Older than 60 years.
- Genetic variation.
- Ethinicity .
- Obesity.
- Exposure to multiple nephrotoxins.

2. Disease specific:

- Underlying renal insufficiency (GFR<60 ml/min/1.73m2).
- Hypertension.
- Sepsis.
- Volume depletion.
- Liver dysfunction.
- Hypokalemia
- Hypomagnesaemia.
- Chronic kidney disease.
- Heart failure .
- Hyperuricemia.
- Renal transplantations .
- Cancers.

Types of Neprotoxicity

There are several types of nephrotoxicity, including acute and chronic nephritis, nephrotic syndrome, glomerular nephritis, crystal nephropathy, acute tubular necrosis, rhabdomyolysis, and proximal renal tubular acidosis as follows:

Acute and chronic interstitial nephritis: An inflammatory infiltration in the kidney interstitium is a hallmark of the renal lesion known as acute interstitial nephritis (AIN), which often results in a reduction in kidney function . Most frequently, pharmacological therapy is used to induce it which may leads to chronic interstitial nephritis.

Rarely does acute nephritis require medical intervention to heal. In chronic interstitial nephritis to remove harmful proteins and extra fluids, it typically necessitates medicine and special treatments. Blood pressure monitoring and routine kidney examinations are often part of the treatment for chronic nephritis. Antibiotics(penicillin),NSAIDS,proton pump inhibitors causes interstitial nephritis [6-9] .

Corticosteroid therapy, which can treat acute interstitial nephritis, should be administered within two weeks of the biopsy. Methyleneprednisolone (250-500mg) was given first, followed by prednisone (1mg/kg/day for 1.5 months). In patients with> 75 percent interstitial nephritis, corticosteroid therapy should be avoided [6].

Nephrotic syndrome: A low serum albumin level, edoema, and proteinuria in the nephrotic range are all components of nephrotic syndrome. In a single spot urine collection, nephrotic-range proteinuria is defined as the presence of 2 g of protein per gramme of urine creatinine or the loss of 3 grammes or more of protein per day into the urine [7].

The medicines that cause nephrotic syndrome are penicilliamine, antirheumatics (bucilliamine, gold), NSAIDs, antibiotics, and radio contrast agents [8].

Glomerulonephritis: Glomerulonephritis is an inflammation of the kidneys' tiny filters, (glomeruli). The physiological fluid by which glomeruli remove waste and surplus fluid from the bloodstream is urine. Glomerulonephritis may appear suddenly, develop steadily over time, or be acute or chronic [10]. Drugs that cause glomerulonephritis include naproxen, penicillin G, lithium.

crystal nephropathy: In the renal tubules, medications that are insoluble in human urine form precipitate. This precipitates the formation of crystals, resulting in crystal nephrotoxicity. Sulfadiazine, acyclovir, indinavir, triamterne, and ciproflaxcin are some of the medications that cause crystal nephropathy [11].

Acute tubular necrosis (ATN): Lack of blood flow and oxygen to kidney tissue cells brought on by exposure to exogenous toxins or drugs results in cell death [12]. NSAIDs, antibiotics (including Amphotericin B), aminoglycosides, vancomycin, piperacillin, and radio contrast agents are all known to cause ATN [13].

Rhabdomyolysis: It is a syndrome with a high risk of death brought on by the use of exogenous poisons or medications. Myoglobin, a protein that harms the kidneys, is released into the extracellular space as a result of the breakdown of muscle tissue [14]. Drugs like salicylates, antihistamines, and statins can all lead to rhabdomyolysis [15].

Proximal renal tubular acidosis: It happens when the kidneys do not properly remove acids from the blood into the urine. Acidosis occurs when the acid level in the blood becomes

too high. A certain amount of acid in the blood is normal, but too muchacid can disrupt many bodily functions [16].

Amphotericin B,lithium, analgesics,ifosamide, and toluene are examples of drugs that cause proximal tubular acidosis [17].

Nephrotoxic Medications:

The most often utilised drugs are listed in Table 1 [3]:

1	Acetaminophen	Chronic interstitial nephritis , Acute tubular necrosis.
2	Acyclovir	Proximal renal tubular acidosis ,crystal nephropathy.
3	Amphotericin B	Acute tubular necrosis,proximal renal tubular acidosis.
4	Aminogiycosides	Acute tubular necrosis.
5	Analgesics	Proximal renal tubular acidosis .
6	Antihistamines	Rhabdomylosis.
7	Benzodiazepines	Rhabdomylosis.
8	Cisplatin	Chronic interstitial nephritis.
9	Ciproflaxcin	Crystal nephropathy.
10	D-pencilliamine	Nephrotic syndrome .
11	Furosemide	Acute interstitial nephritis .
12	Gold	Glomerulonephritis & nephritic syndrome.
13	Indinavir	Acute interstitial nephritis, Crystal nephropathy.
14	Interferon –alpha	Glomerulonephritis.
15	Lithium	Chronic interstitial nephritis,
		Glomerulonephritis&Rhabdomylosis.
16	Methotrexate	Crystal nephropathy.
17	Naproxen	Acute and chronic interstitial nephritis,Acute tubular necrosis & Glomerulonephritis.
18	Omeprazole	Acute interstitial nephritis .
19	Penicillin G	Glomerulonephritis.
20	Pantoprazole	Acute interstitial nephritis.
21	Ranitide	Acute interstitial nephritis
22	Statins	Rhabdomylosis.
23	Sulfonamides	Acute interstitial nephritis,crystal nephropathy.
24	Tetracycline	Acute tubular necrosis.
25	Vancomycine	Acute interstitial nephritis.

Table 1: Drugs List.

Evaluation of Nephrotoxicity & It's Biomarkers

It is assessed using a simple blood and urine test. Nephrotoxicity is determined by changes in blood urea nitrogen levels, serum creatinine levels, glomerular filtration rate, and creatinine clearance.

These biomarkers have low sensitivity and determine the disease at a later stage of disease progression , necessitating the development of novel biomarkers for early detection, such as NGAL (neutrophil gelatinase associated lipocalin), KIM-1 (kidney injury molecule1), Transferrin, clusterin, proteinuria, cytokines (interferons, interleukins, tumor necrosis factor), cystatin & alpha 1-microglobulin etc [2].

Prevention & Treatment of Nephrotoxicity:

- Minimal consumption of NSAIDs and other analgesics [4,17].
- Using substitute medications.

- Changing the medication's dosage.
- Because of risk factors, avoid using medications that induce nephrotoxicity.
- Using medications that are non- nephrotoxic.
- Urinary alkalinization may help to prevent renal failure triometerene, suilfonamide, or methotrexate.
- It is treated by adequate hydration and fluid volume maintenance.
- CorticoSteroid therapy implementation.
- keeping electrolyte balance.
- Stop taking any medications that cause nephrotoxicity.

The Pharmacist's Role in Management of Nephrotoxicity:

As follows, pharmacists play an important role in the management of drug-induced nephrotoxicity [18-20]:

- Pharmacists must learn about more drugs from patients on a regular basis in order to prescribe non-nephrotoxic drugs.
- Pharmacist should review the medications already prescribed and make a list of the nephrotoxic medications.
- During ward round participation, pharmacists must actively participate in prescribing to ensure compliance with the nephrotoxic medication list.
- The pharmacist must advise on drug dosage and frequency.
- A pharmacist is the person who investigates potential causes of drug-induced nephrotoxicity.
- By implementing proper pharmaceutical care, pharmacists can successfully manage druginduced nephrotoxicity.
- The pharmacist must identify the contraindicated medication by taking into account risk factors such as age, comorbidities, etc and then prescribe the drugs .
- This inclusion would support theoretical insights and strengthen the article's utility for healthcare professionals.

Experimental Studies

Including data from clinical studies involving patient groups exposed to common nephrotoxic drugs, such as NSAIDs, aminoglycosides, or vancomycin, would provide valuable insights. These studies can focus on monitoring biomarkers like KIM-1 (Kidney Injury Molecule-1), NGAL (Neutrophil Gelatinase-Associated Lipocalin), and proteinuria, which are crucial for the early detection of nephrotoxicity. For instance, longitudinal data tracking changes in biomarker levels in response to drug exposure could validate their diagnostic value.

Case Studies

Real-world case studies involving patients who developed nephrotoxicity after receiving specific medications would add practical perspectives. Detailed accounts could include clinical presentations, progression of kidney damage, and treatment responses. For example, a case study documenting a patient treated with vancomycin could illustrate how early intervention using modern biomarkers influenced the outcome.

Comparative Analysis

A comparative analysis of treatment outcomes between standard care approaches and interventions guided by novel biomarkers could be incorporated. For instance, comparing patients who were monitored using traditional biomarkers (e.g., serum creatinine) versus those monitored with advanced tools like KIM-1 could demonstrate the efficacy of innovative diagnostic methods.

Risk Assessment Framework

Integrating clinical data to construct a risk assessment framework would be a valuable addition. This framework could stratify patients based on risk factors like age, comorbid conditions (e.g., diabetes, chronic kidney disease), and genetic predispositions. Evidence from clinical trials or observational studies could validate the framework, making it a practical tool for healthcare providers.

Treatment Outcomes and Strategies

The article could present data on the efficacy of various treatment strategies, such as:

- Corticosteroid therapy for conditions like acute interstitial nephritis.
- Adjustments in nephrotoxic drug regimens based on clinical and biomarker data.
- Outcomes of preventive strategies, such as urinary alkalinization or hydration, in mitigating nephrotoxic effects.

Conclusion

We can detect nephrotoxicity early in its progression and treat it by using modern biomarkers. A pharmacist plays an important role in identifying patients who are prescribed nephrotoxic medications and preventing them by changing dosing and frequency, changing the drug of choice, and prescribing non-nephrotoxic medication while taking risk factors such as age and comorbidities into account. This will be accomplished successfully through the implementation of pharmaceutical care that may improve patient's quality of life. Drug-induced nephrotoxicty will be treated with corticosteriod treatment. This therapy will not be used to treat patients who have >75% dug-induced nephrotoxicity.

References

1. Adam Bernstein MD (2021) Kidneys: Location, function, anatomy, pictures, and related disease.Tim Newman.

2. Sun-Young K (2012) Drug-Induced Nephrotoxicity and its Biomarkers. Biomolecules & Therapeutics. 20(3): 268-278.

3. Ghane Shahrbaf F, Assadi F (2015) Drug-induced renal disorders. J Renal Inj Prev 4(3): 57-60.

4. Thakwani J (2019) Symptoms, Signs, diagnosis, treatment &prevention of Nephrotoxicity.

5. Amoghimath S, Ishwar S (2017) Drug Induced Kidney Disease .Open Acces Journal of toxicology.

6. Dennis G, Mark A (2017) Drug-Induced Acute Interstitial Nephritis. Clin J Am Soc Nephrol 12(12): 2046-2049.

7. Sinnakirouchenan S (2023) Nephrotic Syndrome. medscape.

8. Ohno I, Rinsho N (2004) Drug induced nephrotic syndrome. Nihon Rinsho 62(10): 1919-1924.

9. Charles Konder M, Kudrimoti A (2003) Diagnosis and Management of Acute Interstitial NephritisAm Fam Physician 67(12): 2527-2534.

10. (2020) Mayo Clinic Family Health Book. In: 5th (Edn.), Glomerulonephritis, Symptoms and causes.

11. Sri Yarlagadda G, Mark Perazella A (2008) Drug-induced crystal nephropathy: an update. Expert Opin Drug Saf 7(2): 147-158.

12. Bethesda (2008) Medical Encyclopedia. Acute tubular necrosis.National libraray of medicine.

13. Muhammad Hanif O, Ramphul K (2023) Acute Renal Tubular Necrosis. National libraray of medicine.

14. Teresa Coco J, Klasner AE (2004) Drug-induced rhabdomyolysis. Curr Opin Pediatr 16(2): 206-210.

15. Guzman D (2020) Which medications may cause rhabdomyolysis.

16. Christie Thomas P (2020) Metabolic Acidosis.

17. Guo X, Nzerue C (2002) How to prevent, recognize, and treat drug-induced nephrotoxicity. Cleveland Clinic Journal of Medicine 69(4): 289-290.

18. Manyama TL, Tshitake RM, Moloto NB (2020) The role of pharmacists in the renal multidisciplinary team at a tertiary hospital in South Africa: Strategies to increase participation of pharmacists.National library of medicine 25: 1357.

19. Hannah Howell R, Brundige ML (2007) Drug-Induced Acute Renal Failure. US Pharm 32(3): 45-50.

20. Bradford McDaniel L, Michael Bentley L (2015) The role of medications and their management in acute kidney injury. Integr Pharm Res Pract 4: 21-29.