INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Case Study

NSAID Induced Acute Kidney Injury (AKI): A Case Study

Adithya S. L.[1], Swaminath G. Iyer[2], Neehar M. Shanavas[3], Shaiju S. Dharan[4], Dhanya Dharman[5]*

[1]*Pharm D Intern (Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Thiruvananthapuram, Kerala, India)*
[2]*Fifth Pharm D (Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Thiruvananthapuram, Kerala, India)*
[3] *Consultant Gastroenterologist (NIMS Medicity, Neyyattinkara, kerala, India)*
[4] *Principal, HOD (Department of Pharmacy Practice, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Thiruvananthapuram, Kerala, India)*
[5]*Associate professor (Department of Pharmacy Practice, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Thiruvananthapuram, Kerala, India)*

ARTICLE INFO

Received: 24 March 2024
Accepted: 28 March 2024
Published: 30 March 2024
Keywords:
Blood Urea Nitrogen, NSAIDs, Cyclooxygenase, Hepato Renal Syndrome, Drug-induced Acute Kidney Injury.
DOI:
10.5281/zenodo.10899139

ABSTRACT

Acute Kidney Injury, previously known as Acute Renal Failure, denotes a sudden and often reversible reduction in the kidney function, measured by increased creatinine or decreased urine volume. Although immediately after a renal insult, blood urea nitrogen or creatinine levels may be within the normal range, the only sign of Acute Kidney Injury may be a decline in the urine output. Acute Kidney Injury can lead to the accumulation of water, sodium, and other metabolic products. The crude odds ratio for Kidney Injury in non-steroidal anti-inflammatory drug users compared to non-users ranged from 1.12-5.25 and was greater than 1. Renal cell damage is more prominent in patients taking non-steroidal anti-inflammatory drugs. The major etiological factors contributing to Acute Kidney Injury are infections, drug induction, obstructive uropathy, dehydration, snake bite, cardio renal syndrome. The current case report features a patient who was admitted to the Gastroenterology department from outpatient basis due to an elevation in her serum creatinine level (4.7 mg/dL).

INTRODUCTION

Non steroidal anti- inflammatory drugs (NSAIDs) are one of the most commonly used Over the Counter (OTC) drugs. NSAIDs exert their anti-inflammatory effect via Cyclooxygenase (COX) inhibition. Their common adverse effects include

***Corresponding Author:** Dhanya Dharman
Address: *Associate professor (Department of Pharmacy Practice, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Thiruvananthapuram, Kerala, India)*
Email : dhanyadharman07@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

gastrointestinal ulcers, cardiac toxicity, bleeding diathesis, allergic reactions and renal complications, with acute kidney injury [2, 3] being the most common form of NSAIDs – induced renal injury. NSAIDs can reduce renal blood flow, cause tubular obstruction through crystal deposition, and induce direct cytotoxicity and cell- mediated immune injury mechanisms leading to the occurrence of AKI [4]. Other manifestations include hypertension, oedema, hyponatremia, hyperkalemia, nephritic syndrome, papillary necrosis and interstitial nephritis. The major signs and symptoms of AKI include swelling on legs, ankles, and around the eyes, fatigue or tiredness, decreased urine output, confusion, lower abdominal pain. These incidences of AKI are mainly determined as per the stage which it was belonged to. Mostly AKI has 3 stages [5] (Table 1). Etiological factors contributing to AKI differs and which includes infections, cardio renal syndrome, drug use, obstructive condition of the urinary tract, dehydration, etc (Figure 1). In this article we report a known case of CLD who developed AKI (Grade III) by taking NSAIDs. Thereby rapidly withdraw the suspected drug which causes the reaction.

STAGES	DEFINITION
STAGE 1	Creatinine ≥1.5 times baseline or increase of ≥0.3mg/dL within any 48 hours period, or urine volume <0.5ml/kg for 6- 12 hours.
STAGE 2	Creatinine ≥2.0 times baseline or urine volume <0.5ml/kg for ≥12 hours.
STAGE 3	Creatinine ≥3.0 times baseline or increase to ≥4.0mg/dL or cute dialysis, or urine volume <0.3ml/kg for≥24 hours.

Table 1: Staging of Acute Kidney Injury according to current kidney Disease Improving Global Outcomes definition.

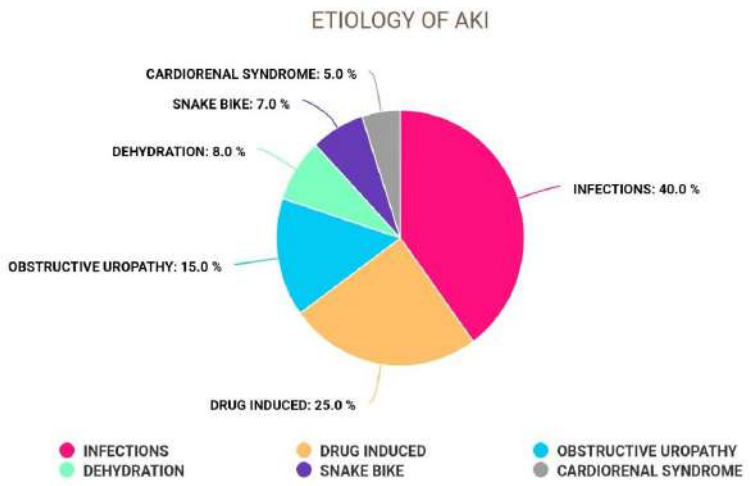

Figure 1: Etiology of Acute kidney Injury (AKI)

CASE REPORT:

A 53-year-old female patient came to the Gastroenterology department for her routine review. On evaluation, serum Creatinine shows acute elevation (4.7mg/dL). She had a past medical history of Chronic Liver Disease (CLD) for 8 months and Hypothyroidism for the past 2 years. And was on medical treatment with TAB. URSODEOXYCHOLIC ACID 300mg, PROTEIN SUPPLEMENTS 30gm, and DIETARY SUPPLEMENTS 500+400mg, HEME IRON POLYPEPTIDES 12mg, TAB. THYROXINE 100mcg. She was admitted to the hospital with the chief complaints of abdominal

pain and pedal oedema 8 months back. And show alterations in renal function and thought to be as Hepato Renal Syndrome (HRS). On taking her family and social history, came to know about the intake of ACECLOFENAC and PARACETAMOL tablet for toothache. Thus concluded this case as NSAID induced AKI. She was admitted 12 days in the hospital. Admission examination showed: Blood pressure of 120/80mmHg, heart rate of 72beats/min, no abnormalities in the auscultation of the lungs, Oxygen saturation at rate of 97 %, no murmur in the heart, pallor positive, no abdominal tenderness. The patient was anaemic. ESR, SGOT, SGPT, ALP, Urinary epithelial cells and pus cells were found to be elevated than normal limits. Albumin level monitored on LFT was below the limit. It is declined to 2.8 mg/dL. Urea (58 mg/dL) and serum Creatinine (4.7mg/dL) on the day of admission was declined. Due to the elevation of urinary pus cells and epithelial cells, urine culture is done and it is sterile. USG of abdomen and pelvis was taken, and it shows mildly coarsened hepatic echo texture with Splenomegaly and bilateral Grade I parenchyma echoes. Serum urea, Creatinine and levels were monitored for 11 days for her hospital stay (Table 2). PTINR was monitored for 4 days (Table 3).

(Table 2): Determination of Serum Urea and Creatinine for the first 11 days of hospital stay

PARAMETERS (mg/dL)	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9	DAY 10	DAY 11
SERUM UREA	58	72	76	80	81	79	73	63	56	52	44
CREATININE	4.7	4.9	4.9	4.6	4.0	3.3	2.9	2.8	2.6	2.6	2.3

(Table 3): Determination of PTINR value on Day 2, Day 6, Day 7, and Day 8

DAYS	TEST	CONTROL	INR
DAY 2	22.2	13.6	1.680
DAY 6	27.5	13.6	2.110
DAY 7	26.4	13.6	2.02
DAY 8	27	13.6	2.07

She was treated with vasopressin agonist (INJ. TERLIPRESSIN 1mg), Proton pump inhibitor (TAB. PANTOPRAZOLE 40mg), Hepatoprotective agent (TAB. UDILIV 300mg), and Rifamycin antibiotic (TAB. RIFAXIMIN 550mg). During nephrologist's consultation, it was advised to give ALBUMIN – TERLIPRESSIN infusion. So INJ TERLIPRESSIN changed from 1mg Q6H to BD. Also added TAB. SODIUM BICARBONATE 500mg, TAB. FOLIC ACID 5mg, and Inj. ACETYL CYSTEINE 1.2gm, and Inj. HUMAN ALBUMIN was given on daily basis. Potassium and sodium level declination found on the eight day and was corrected with Ivf. NORMAL SALINE 500ml with Inj POTASSIUM CHLORIDE 40mEq. Creatinine levels gradually declined. She was clinically stable and discharged after 12 days of hospital stay.

DISCUSSION:

The aetiology of AKI is conceptually classified into three general categories: Pre-renal, Intra-renal and Post-renal (Table 4) [6]. This patient was admitted with elevated serum Creatinine (4.7mg/dL). The points in favour NSAID induced AKI was reduced urine output, history of taking NSAIDs, declined serum Creatinine. ALBUMIN infusion was given to correct hypoalbuminemia. Patient was admitted for 12 days in the hospital and was clinically better. On twelfth day, her serum Urea and Creatinine were 40 and 2.3 respectively. Discontinuation of the drug is important in case of drug induced diseases. Cirrhotic patients are more prone to develop drug induced AKI than normal individuals. Here the

drug was stopped due to renal impairment. NSAIDs have an inhibitory effect on both COX – 1 and COX – 2, that is enzymes that inhibit Prostaglandin (PG) synthesis. Both forms of this isoenzyme are found in the kidney [7]. Blocking one or both of these enzymes can defect different kidney functions [8,9,10]. COX – 2 derived PGs have profound effects on renal homeostasis, suggesting that selective COX – 2 inhibitors such as CELECOXIB may have the same potential for renal adverse effects as traditional non- selective NSAIDs, especially in clinical situations associated with a renal impairment such as sodium depletion, hypovolemia, cirrhosis, heart failure, Nephrotic syndrome, and CKD.

CATEGORY	ABNORMALITY	POSSSIBLE CAUSES
PRE-RENAL	True volume depletion	• Hemorrhage • Poor oral intake • GI losses (Vomiting, Diarrhea) • Third space losses (Pancreatitis, burns) • Renal losses (over diuresis) • Skin or respiratory losses
	Impaired cardiopulmonary functions	• Congestive Heart Failure • Pericardial tamponade • Pulmonary thromboembolism
	Decreased vascular resistance	• Systemic vasodilation • Sepsis • Neurogenic Shock • Anaphylaxis • Hepatorenal syndrome (HRS)
	Intra-renal hemodynamic changes	• Medications (NSAID, RAS blockers, CNIs) • Hypercalcemia
INTRINSIC	Tubular damage	• Renal ischemia • Nephrotoxins • Endogenous • Myoglobin, hemoglobin • Tumor lysis syndrome • Exogenous • Medications (contrast agents)
	Glomerular damage	• Acute glomerulonephritis • Vasculitis • Malign hypertension • Thrombotic microangiopathies
	Interstitial damage	• Infections (bacterial or viral) • Medications (antibiotics, NSAIDs)
	Vascular damage	• Renal artery/ vein thrombosis • Vasculitis (polyarteritis nodosa) • Aeroembolism
POST-RENAL	Intra-renal obstruction	• Nephrolithiasis
	Extra-renal obstruction	• BPH • Ureterolithiasis • Prostate, bladder, rectal or cervical cancer • Acute neurogenic bladder • Urethral stenosis or clotting • Retroperitoneal fibrosis

		• Renal papillary necrosis

Table 4: Medical causes of Acute Kidney Injury (AKI)

CONCLUSION:

Acute Kidney Injury (AKI) is a global public health concern associated with high morbidity, mortality, and healthcare costs. It is more common among cirrhotic or CLD patients than normal individuals. For these, treatments are needed to reduce the high morbidity and mortality and improve recovery of renal function; however, the multifactorial aetiology of AKI and the complicated clinical course of the patient have created challenges in the search for pharmacological agents that work [11.12]. Here the patient is presented with elevation in serum Creatinine levels on blood examination. The Ultrasound scan of abdomen and pelvis shows Grade I renal parenchyma echoes and mildly coarsened hepatic echo texture. Patient started with proton pump inhibitors, antibiotics, liver protectants, protein supplementation. Patient had past history of Hypothyroidism for past 2 years and taking THYRONORM and CLD for past 8 months. Her own medicines are continued on her hospital stay. In conclusion, treatment of AKI induced by ACECLOFENAC and PARACETAMOL was effective depending upon its severity. The first step physicians put forward is the discontinuation of the drug.

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HOW TO CITE: Adithya S. L., Swaminath G. Iyer, Neehar M. Shanavas, Shaiju S. Dharan, Dhanya Dharman, NSAID Induced Acute Kidney Injury (AKI): A Case Study, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 3, 1262-1267. https://doi.org/10.5281/zenodo.10899139