A Case Study on Telmisartan Induced Acute Kidney Injury

Kavya Surendran*, Beenu Maria Joseph, Jobin Kunjumon Vilapurathu

Department of Pharmacy Practice, Nirmala College of Pharmacy, Muvattupuzha, Kerala, INDIA.

ABSTRACT

Telmisartan is a widely used antihypertensive drug that effectively lowers blood pressure. In this report, we present the case of a patient who developed acute kidney injury after taking an ARB inhibitor, Telmisartan. A 40-year old, male patient who is known case of Congestive heart failure and dilated cardiomyopathy got admitted to the emergency department with breathlessness and cough. He was diabetic for the past four years and was on Insulin. He was also hypertensive for the past 11 years and was on Telmisartan. All his blood parameters except renal function tests (blood urea, creatinine, potassium, sodium) were normal during hospitalization. Cardiac markers (d-dimer and troponins) were within normal limits, but the ECG report revealed sinus tachycardia and left ventricular hypertrophy. Echocardiography report showed Global left ventricular hypokinesia, dysfunction of the left ventricle, moderate pulmonary arterial hypertension, moderate mitral regurgitation, dilated left arterial and ventricular enlargement. Chest X-ray showed cardiomegaly. High Blood pressure was controlled with ARB Inhibitor-Telmisartan. Uncontrolled hypertension caused a change in dose during admission, which could explain the sudden kidney injury. The drug was discontinued abruptly and switched over to an alpha-blocker- Prazosin. A decrease in serum creatinine levels indicated improvement in the patient's condition in the following days. Hence, we bring your attention to the possibility that all aged patients with or without a compromised cardiac function must undergo careful monitoring to prevent such adverse events due to the drug (Telmisartan). Also, it is prudent to consider the possibility of cardio-renal syndrome for fewer unwanted events.

Key words: Angiotensin receptor blockers, Telmisartan, Acute kidney injury, Angiotensin receptor blockers, Kidney function.

INTRODUCTION

AKI is a sudden decline in kidney function, associated with a range of adverse outcomes, particularly an increase in subsequent admission with heart failure.[1] Common risk factors for AKI include diabetes, chronic kidney disease, high Blood pressure, and failure of the heart with reduced ejection fraction.[2] ACEIs and ARBs are the widely used treatment strategies for various types of cardiovascular diseases like heart failure (HF), hypertension (HTN), stroke, aortic regurgitation (AR), and myocardial infarction (MI).[3] The highest mortality rate and morbidity rate among all cardiovascular diseases is hypertension.[4] According to the American Diabetes Association, patients with both diabetes and hypertension as co-morbidity should begin treatment with either ACE-I or ARBs. But these agents have different effects on cardiovascular events.[5] Because of their effectiveness in treating hypertension and CCF RAAS inhibitors have also been extensively used to treat diabetic nephropathy and anti-proteinuric effects in glomerulopathies. Even though it is considered a renal-protective drug, ACEIs and ARBs may cause AKI.[6,7] Many ill patients

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Address for correspondence:
Miss. Kavya Surendran,
Pharm D Intern, Department of Pharmacy Practice, Nirmala College of Pharmacy, Muvattupuzha-686661, Kerala, INDIA.
Email id: kavyas0025@gmail.com

www.ijopp.org

are more likely to suffer from pre-renal kidney failure. About 9% of hospitalized patients and 50% of ICU patients resulted in AKI.[8] Among those hospitalized patients, around 21% had pre-renal AKI.[9] Here, this case report describes the effects of an adverse drug reaction on a patient with Telmisartan, who developed acute kidney injury (pre-renal) following a change in dose with no prior history of such adverse event.

CASE REPORT

A 40-year-old male patient reported to the medical emergency department with progressive worsening of breathlessness with cough. He was found to have a blood pressure of 170/100 mm Hg and hypoxic without experiencing any chest pain upon presentation. There was no sign of dehydration or pedal edema on physical examination. All the other systemic findings were remarkable and denied any signs of fever. He had no known family history of cardiovascular disorders or kidney disease. The patient had a medical history of congestive cardiac failure. Hypertension and diabetes type 2 were other risk factors for the past 11 years and for the past four years, respectively. He was feeling unwell for the past three days. There was no history him smoking; he is an ex-alcoholic and stopped the consumption a year ago. His height was 156 cm and weighted 60 kg with an ideal BMI of 21kg/m^2. His diet was diabetic. His medications include T. Digoxin 0.25 mg 5 days/ week, T. Telmer 20mg, Inj. Human Mixtard 10U-0-0. Additionally, he had dilated cardiomyopathy with severe mitral regurgitation and was off medications. Complete hemogram results revealed an elevated blood urea level (31.7%). All the other parameters were normal. Cardiomegaly was found on a chest X-ray and ECG reports were suggestive of Sinus Tachycardia and left ventricular hypertrophy. There was marked systolic dysfunction of the left ventricle revealed by echocardiography, as well as global hypokinesia of the left ventricle, moderate pulmonary arterial hypertension, dilated left arterial and ventricular enlargement. Upon admission, the patient's condition deteriorated and he was subsequently hospitalized in a cardiac intensive care unit. From the subjective and objective data, the patient was diagnosed with Acute decompensated heart failure, severe left ventricular dysfunction, hypokalemia, and Telmisartan induced acute kidney injury.

As initial symptomatic management, the physician suggested Intravenous Furosemide along with NTG Infusion. Later, he began to feel better. No growth was observed in blood cultures. Due to an uncontrollable rise in blood pressure, the dose of Telmisartan was increased from 20 mg to 40 mg per day. Routine blood tests revealed a rise in creatinine levels by 0.5 mg/dL (from 1.3 mg/dL to 1.8 mg/dL) within 48 hr. The renal function tests were repeated and were abnormal [Table 1]. Because of the decline in potassium levels, adequate supplementation was provided by adding potassium-sparing diuretics (Spironolactone 25 mg) and potassium supplement (KCl 30 mL/ day). The sodium levels were also lower. It was corrected with Tolvaptan 15 mg/day. The blood sugar levels were within the required range. A Nephrology consultation was done to evaluate the condition. Telmisartan was discontinued and switched to Prazosin 1.5 mg/ day. The blood pressure levels normalized accordingly and the dose of NTG was reduced and Prazosin was continued. Sodium bicarbonate 500 mg BD was prescribed along with the repeated monitoring of creatinine levels. The patient received care from all potentially nephrotoxic agents, and the patient was continuously monitored to ensure that he was improving. The loop diuretic was continued as per cardiac indication along with balancing adequate hydration. The patient improved symptomatically and the creatinine levels declined abruptly as the value reached near the normal limit (1.5 mg/dL). As part of his discharge, he has been prescribed the following medications: T. Prazosin 2.5 mg OD, T. Sodium Bicarbonate 500 mg B.D, T. Lasix 60 mg OD. He was instructed to follow up in one week. During the follow-up period, his renal parameters were normal and, were recovering slowly. In the absence of other suspected causes, Telmisartan was suspected of causing the pre-renal acute kidney injury. The clinical improvement of patient condition after discontinuation of the same drug was also a crucial finding to suspect the drug as a causative agent for this condition. But, the drug Telmisartan was not rechallenged to this patient.

DISCUSSION

One of the most common complications associated with hospitalization is acute kidney injury. It has consistently been depicted that AKI worsens chronic kidney disease (CKD) and end-stage renal disease (ESRD) as well as increases the risk of death long term.[10] Patients who got

Table 1: Renal Function Tests

Parameters	Day 1	Day 2	Day 3	Day 4
Urea	31.7mg%	26.6mg%	31.6mg%	27.0mg%
Creatinine	1.3 mg%	1.5mg%	1.8mg%	1.5mg%
Sodium	131meq/L	124meq/L	138meq/L	136meq/L
Potassium	3.5meq/L	3.2meq/L	3.3meq/L	3.8meq/L

discharged after an episode of AKI have a 40% increased risk of death, two years after hospitalization compared with those patients who do not develop AKI.[11] The most common cause of AKI is drug-induced. Blocking the Renin-Angiotensin System (RAS), including drugs that inhibit the conversion of angiotensin to angiotensin and drugs that block the angiotensin receptor, causes AKI from reduced renal perfusion. AKI may also result when RAS blockers are initiated in patients with renal artery stenosis.[12] Preferably, an increase of up to 30% is acceptable upon initiation of RAS blocker therapy; but, a more substantial elevated serum creatinine, or the initiation of these agents in conditions of decreased renal perfusion, may result in AKI.[13]

The latest shreds of evidence regarding the adverse drug events with ARBs are alarming. Acute kidney injury caused by the ARB inhibitor-Telmisartan should be considered and dealt caution. Studies and researches that focus on the adverse events of ARBs (Telmisartan) had to be performed to generate a strong signal. These agents cause renal dysfunction in situations in which angiotensin II-dependent efferent arteriole vasoconstriction is essential to maintain the intraglomerular capillary pressure.[14] So, blockade of the renin-angiotensin system in such instances may lead to a sharp and abrupt decline in GFR.[15] Apart from withdrawing the offending drug Telmisartan, fluid therapy, Vasopressor drugs like Noradrenaline, Vasopressin, and Terlipressin, and Diuretics are effective to manage fluid overload and also electrolyte disturbances in AKI. Other therapeutic strategies include Levosimendan, a drug that has both vasodilatory and inotropic actions. Calcifediol and calcitriol are also used for the treatment of early renal failure primarily due to the high rates of AKI seen in patients with Vitamin D deficiencies. In addition to these therapies, renal replacement therapies are also used to treat AKI.[16]

Accordingly, we conclude that before initiation of ACEI, ARB, and renin inhibitor therapy in the elderly population, renal function should be carefully evaluated before beginning the treatment, and periodically thereafter, so that modifiable risk factors can be controlled. As soon as the causative drug is removed from the body, renal function usually improves, confirming the functional pattern of the injury. Our case report contends that Telmisartan was crucial in contributing to the patient's deteriorating heart failure condition as well as AKI 1. His serum creatinine levels eventually improved to 1.2 mg/dL after the discharge despite 1.8 mg/dL after 3 drug changes.

CONCLUSION

An acute kidney injury occurs when the kidneys are unable to remove waste products from the blood. Both structural damage and functional loss are included in this term. It is a very common complication among those patients hospitalized for heart failure and contributes to adverse outcomes. Pre-renal AKI requires proper identification to prevent long-term adverse events. Proper identification of the patient requires consideration of specific clinical manifestations at the time of admission. It develops rapidly over a few hours or days and occurs commonly in those who are critically ill or already hospitalized. ARB inhibitors-induced AKI is commonly observed in patients with heart failure. In addition, it is important to consider the possibility of the cardio-renal syndrome and manage this appropriately with proper dose selection based on the patient's condition. To minimize the risk of an ARB-induced AKI, it is essential to apply adequate diagnostic criteria and to make an early diagnosis, as well as to discontinue the drug and initiate alternative treatment.

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CONFLICT OF INTEREST

The authors declare that there is no conflicts of interest.

ABBREVIATIONS

ARBs: Angiotensin receptor blockers; **ACEIs:** Angiotensin converting enzyme inhibitors; **AKI:** Acute kidney injury; **HF:** Heart failure; **HTN:** Hypertension; **AR:** Aortic regurgitation; **RAAS:** Renin angiotensin aldosterone system; **ESRD:** End stage kidney disease; **GFR:** Glomerular filtration rate.

Authors Contributions

The first author (Kavya Surendran) drafted the manuscript, the second author (Beenu Maria Joseph) collected the case and references for the manuscript, and the third author (Jobin Kunjumon Vilapurathu) reviewed and edited the manuscript.

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