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A SINGLE DOSE OF TELMISARTAN+CHLORTHALIDONE CAUSED ACUTE KIDNEY INJURY

Internal Medicine

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ABSTRACT

ARB- diuretics combinations are commonly used antihypertensive drugs, which are typically used when one medication is ineffective at properly controlling blood pressure. Telmisartan is a nonpeptide AT1 angiotensin II receptor antagonist. This binding prevents angiotensin II from binding to the receptor thereby blocking the vasoconstriction and the aldosterone secreting effects of angiotensin II, thereby decreasing blood pressure. Chlorthalidone inhibits sodium and chloride reabsorption in cortical diluting segments of the ascending loop of Henle, causing increased excretion of sodium, chloride, and water. ARBs can cause nephrotoxicity by altering intraglomerular hemodynamics and decreasing GFR, and diuretics synergies this effect. In our presentation, a 74 year old male patient who was taking Telmisartan regularly, accidently took a single dose of his wife's Telmisartan-Chlorthalidone medication mistakenly and developed elevated creatinine. 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 revealed sinus tachycardia and left ventricular hypertrophy. Echocardiography report showed Global left ventricular hypokinesia, dysfunction of the left ventricle, moderate pulmonary arterial hypertension, dilated left atrial and ventricular enlargement, IWMI, RWMA (EF=26%). Chest X-ray showed cardiomegaly. High Blood pressure was controlled with Nebivolol. Accidental ingestion of antihypertensives - telmisartan and chlorthalidone, would explain the sudden kidney injury. The drug was discontinued abruptly. A decrease in serum creatinine levels indicated improvement in the patient's condition in the following days. Hence, we draw your attention to the likelihood that all elderly patients, regardless of whether they have an impaired cardiac function, need to undergo rigorous monitoring in order to prevent such drug-related adverse effects (Telmisartan+Chlorthalidone). Also, it is prudent to consider the possibility of cardio-renal syndrome for fewer unwanted events.

KEYWORDS

INTRODUCTION

Drug-induced kidney damage accounts for 19% of AKIs in a hospital setting. [(1)]. As the kidney functions as an excretory organ for the majority of drugs, it is susceptible to drug induced injuries. Telmisartan and chlorthalidone combination is used to treat hypertension, and thus reduces the workload of heart and arteries. Thereby reduces the complications caused by hypertension. Telmisartan is a class of Angiotensin receptor blocker, which functions by blocking the hormone's receptors, specifically the AT1 receptors present in the kidneys, blood arteries, and heart. It functions by obstructing the angiotensin II in the body that constricts blood vessels. So telmisartan relaxes the blood vessels, lowers BP and increases supply to the heart. Chlorthalidone are thiazide-like diuretics, which lower blood pressure by reducing the body's water content by increasing urine flow. ARB is considered the first line of treatment for hypertension according to many guidelines and is an effective treatment approach for many CVDs. But ARB can induce AKi though it is considered safe for the kidney. Diuretics would work synergistically to cause AKI when used with ARB [(2)(7)]

Case

This is a case of a 74 year old male who is a known case of systemic hypertension, type II diabetes mellitus, coronary artery disease, history of cerebrovascular event, dyslipidemia, hypothyroidism and parkinson's disease, presented to the Emergency department with alleged history of accidental intake of antihypertensive medications - Tab Nitrolong 2.6mg, Tab Telmikind CT 40mg, Tab Nebistar 5 mg on the day of admission at around 9:30 AM. No history of syncope, loss of consciousness or giddiness following ingestion. He was conscious and oriented at the time of admission in hospital. Physical examination showed no evidence of pedal edema or dehydration His BP was 110/70 mm Hg, heart rate was 80, saturation 98% in room air and systemic examinations were all normal. Routine blood investigations were done which showed normal counts and other parameters were within normal limits, but his creatinine levels were elevated (Table-1). There was no history of smoking or alcohol consumption. His height was 156 cm and weighed 60 kg with an ideal BMI of 21 kg/m2. He was on a diabetic and low sodium diet. His medications included syndopa plus, Aspirin 75 mg 0-1-0, Clopidogrel 75 mg 0-1-0, Inj. Insulin 25/50 32-0-26, Thyroxine 75 mcg 1-0-0 levetiracetam 500 mg BD, Atorvastatin 20 mg 0-0-1, Tolterodine+Tamsulosin 0-0-1, Ranolazine 500 mg 1-0-1. All these medications were used for years, but did not have any complications or kidney damage. The creatinine raise is suspected to be due to Tab. Telmikind CT (Telmisartan + Chlorthalidone), as no other causes like recent administration of other nephrotoxic drugs or NSAIDS or h/o hypotension, blood or fluid loss, organ failure or allergic reactions were noted. He was started on IV fluids and all antihypertensives were stopped. During the course of hospital stay, his BP was hourly monitored and there were no episodes of hypotension. The renal function tests were repeated and were found to be normal after cessation of ARB- diuretic drug. He became symptomatically better and discharged with advice to follow up on OP basis for restarting hypertensive drugs. The combination of Telmisartan and Chlorthalidone together was suspected of causing the reversible acute kidney injury in the absence of other probable reasons. Another indicator that the medicine may be the cause of the ailment, was that the patient's condition improved clinically after stopping the same medication. However, rechallenging was not done

Table- 1: Creatinine range of the patient from the day of admission to discharge. Day 1 is the creatinine value on the day of admission, i.e, when the drug was accidently consumed. Day 2 is the value after 1 day and day 3 is at discharge, when the range showed a decreasing trend.

Parameters	Day 1	Day 2	Day 3
Creatinine	1.29	1.43	1.40

DISCUSSION

Acute kidney injury is the rapid decline in kidney function due to damage to the kidney.[(4)] Our study focussed on Diuretic- ARB combination associated with acute kidney injury. Both ACEi and ARBs lower glomerular filtration pressure by causing vasodilation of the renal efferent arterioles. Reduced efferent vascular tone during hypovolemia reduces GFR, ultimately increasing AKI [(3)]. During AKI, tubular necrosis occurs which initiates repair under recovery phase of AKI. Due to insufficient tubular epithelial regeneration, nephrons were lost and the GFR elevated.The potential cause of altered GFR appears to be intrarenal RAS activation. [(5)] Treatment with ACEi and ARB is widely believed to be a risk factor for AKI, particularly during acute illness. [(6)] Diuretics would cause AKI when used with other medications including antibiotics, contrast media, ACEI/ARB, NSAIDs, etc. The histological lesion of AKI caused by diuretics may primarily manifest as tubular epithelial cell vacuolar degeneration. [(7)]. So, there is a synergistic effect of both telmisartan and hydrochlorothiazide in increase of creatinine level.

CONCLUSION

The study concluded that a single dose of telmisartan-chlorthalidone caused an elevated creatinine level in susceptible elderly patients and withdrawal of the drug led to remarkable improvement with renal function returning to normal. Drug induced kidney injury is a common and probable cause or contributory factor in acute kidney injury. But it is often preventable and treatable, if diagnosed early. Physicians and pharmacists should be aware that even a single dose of this drug can affect the renal function. In this case, it is important for counseling the elderly to take the correct medication at the correct dose and time as the prevalence of medication error rises in patients with polypharmacy, particularly elderly.

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