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Journal

Proceedings of the UCLA Department of Medicine, 19(1)

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Publication Date

2015-09-25

CLINICAL VIGNETTE

Atenolol as a Possible Cause of Acute Kidney Injury In A Patient With Chronic Kidney Disease

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Case Report

A male in his 60s with hypertension and chronic kidney disease presented with a severe creatinine of 8.1. His baseline creatinine had increased from 1.8 to 3.4 over the past 3 years and was last measured at 4.8 two months prior to admission. The patient reported good urinary output and denied dysuria, hematuria, urgency, nausea, or vomiting. His only complaint was chronic lower back pain. Medications on admission included atenolol 25 mg, nifedipine 90 mg, and hydrocodone 5 mg/acetaminophen 325 mg. Potassium and phosphorus were within normal limits, and magnesium was slightly low at 1.4 mg/dL. Urinalysis was unremarkable, and renal ultrasound did not reveal obstruction or hydronephrosis. Upon admission, the atenolol was switched to metoprolol. With only supportive care, creatinine dropped about 1 point per day for two days of hospitalization. The patient left against medical advice on day 3 with a creatinine of 4.4, which was close to his baseline.

Discussion

Chronic kidney disease (CKD) is a major public health problem resulting in significant morbidity, mortality, and health cost. CKD is defined as GFR less than 60 mL/min/1.73 m^2 or evidence of kidney damage for 3 months. In the US, 1 in 10 adults has CKD with the most common etiologies of diabetes mellitus, hypertension, and glomerulonephritis.[1] In addition to renal protection, one key component in the management of CKD is controlling hypertension to decrease the likelihood of cardiovascular events and progression of kidney disease. CKD patients often have other health issues like heart disease or diabetes and are on many medications. This puts them at-risk for polypharmacy and adverse drug effects, such as drug induced acute kidney injury.

CKD patients are also at higher risk of developing AKI. In a study of 104 patients with acute on chronic renal failure, about 35% appeared to be drug-related.[2] Nephrotoxicity contributes to up to 60% of all in-hospital cases of AKI with the most common agents being aminoglycosides, amphotericin B, vancomycin, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, NSAIDs, vasopressors, and calcineurin inhibitors.[3] Other types of nephrotoxic tubular injury include osmotic nephrosis induced by hypertonic solutions and tubular obstruction by drug precipitation.

Renally excreted drugs can exert direct toxic effects on renal tubules, cause cellular injury and death in acute tubular necrosis, or induce inflammation in the renal interstitium in acute interstitial nephritis.[3] Nephrotoxic acute tubular necrosis is typically a dose-dependent, non-inflammatory phenomenon that occurs more frequently in patients at high risk for renal injury such as those with pre-existing renal disease. Here we describe a case of AKI in a patient with CKD, which may have been associated with use of the beta-blocker atenolol.

This case highlights the importance of having a high index of suspicions for renal excreted medications that could potentially be nephrotoxic in patients with CKD. About 20% of chronic dialysis patients receive beta blocker therapy.[4] There are different types of beta-blockers with varying beta-selectivity, cardioselectivity, routes of excretion, lipid solubility, calcium-blocking activity, and vasodilatory properties. These differences may determine how well an agent will work and how tolerable it will be in patients with CKD. Additionally, a patient's metabolic profile including factors like serum potassium and glycemic control may also affect response to a specific beta blocker. Nonselective beta blockers, such as propranolol, decrease GFR and renal blood flow by lowering cardiac output, resulting in reflexive increase in sympathetic activity and systemic and renal vascular resistance via alpha-1-receptors.[5] In addition, blockade of beta-2-vasodilation results in unopposed alpha-1 vasoconstriction that may exacerbate renal dysfunction in hypertensive patients. Beta-1-selective agents metoprolol and atenolol were the first blood pressure-lowering agents to be used in studies with patients with renal disease and were shown to dramatically decrease rate of decline of renal function.[5] Beta-1 selective agents do not produce a significant reduction in GFR or renal blood flow but do increase renal vascular resistance.[5] With the advent of more potent antihypertensives and renal protectants such as ACE inhibitors, several studies have questioned the usefulness of beta-blockers as primary tools to treat hypertension in patients with CKD.[6]

This is particularly true of the beta blocker atenolol. Atenolol is a hydrophilic agent primarily excreted by the kidneys and needs to be reduced by one-half to three-quarters of its normal dose in patients with diminished renal clearance, whereas other lipophilic beta blockers like metoprolol do not need to

be dose adjusted.[5] One study reported that long-term atenolol therapy was associated with a significant increase in urinary protein excretion.[7] Additionally, once daily atenolol is believed to have relatively weak blood pressure lowering effects due to its pharmacokinetic profile and half-life.[8,9] The combination of atenolol's low lipophilic profile and relatively weak effect on cardiovascular protection decreases utility in chronic kidney disease patients with hypertension.[6] In this case report, we highlight subacute on chronic kidney injury, which improved with withdrawal of atenolol. While control of hypertension in CKD is crucial, one must be cautious with renally excreted drugs such as the beta blocker atenolol.

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Submitted May 26, 2015