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Benazepril induced acute kidney injury (AKI) in a patient with congestive heart failure (CHF) and moderate chronic kidney disease (CKD): A case report

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Abstract

Angiotensin-converting enzyme inhibitors (ACEIs) was demonstrated protective effect for patients with mild to moderate chronic kidney disease (CKD). The ACEIs was usually applied to patients while his serum creatinine (Scr) levels were no more than 3.0 mg/dL. However, it could induce AKI even in the patients with mild to moderate CKD combined with CHF. We report a case of a 62-year-old male with CHF and moderate CKD (SCr: 1.9 mg/dL) who subsequently and transiently develop AKI after he was administrated benazepril 2.5mg/day. Using the Naranjo, benazepril was found to be a probable cause of AKI in the patient. ACEIs, classified as RAAS inhibitors, can induce AKI in some conditions. Attention should be given to benazepril therapy in patients with mild to moderate CKD and CHF. Routine hemodynamic examination and biochemical monitoring was suggested before and during the period of benazepril therapy.

Introduction

Heart failure (HF) is a clinical syndrome that results from highly prevalent disorders in our society, including chronic hypertension and coronary artery disease. Most guidelines promote early treatment, including the use of ACEIs to control Cardiovascular (CV) risk in patients with chronic renal failure [1-2]. ACEIs play an indispensable role in the treatment of a variety of disorders including hypertension, CHF, and in the prevention of diabetic nephropathy [3]. The renoprotective effects and independent of blood pressure control of the ACEIs, benazepril, have been demonstrated [2] However, Lin-Hua Tan [4] reported a case with reversible acute renal failure in a premature neonate with double outlet right ventricle and CHF induced by Captopril. The tolerance of ACEIs to renal need to be carefully monitored. In this paper, we described a case with CHF and moderate CKD occurred AKI induced by benazepril, which showed the application of benazepril in CHF and mild to moderate CKD still should be careful.

Case report

A 62-year-old male was urgently hospitalized because of abdominal pain, abdominal distension and shortness of breath. The abdominal pain had begun 1-month earlier and had been progressively getting worse. For the previous 10 days, his Abdominal circumference and body weight obviously increased. He had a history of hypertension, type 2 diabetes mellitus, CHF and Renal dysfunction. The prescription of Furosemide Tablets, Spironolactone Tablets and tolvaptan was orally administrated to this patient. A review of systems was negative for fever, chills, vomiting, extremity weakness or paresthesias. Physical examination revealed a temperature of 36.5°C, blood pressure of 130/70 mm Hg, heart rate of 61 beats per minute, and respiratory rate of 18 breaths per minute. Electrocardiogram (ECG)showed an sinus rhythm and Premature Ventricular Beats; Ultrasound showed a positive sign of ascites and lower limb dema. He was diagnosed with coronary heart disease (CHD), CHF, seroperitoneum, hypertension, type 2 diabetes mellitus and CKD (Scr: 1.9 mg/dL). The treatment including isosorbide mononitrate tablets, diuretic, antithrombotic and hypoglycemic agents. The urine output of the patient remained high (about >2000ml) despite the diuretic changed from furosemide to torasemide. However, the urine output unexpectedly decreased when benazepril was prescribed 2.5mg Q.d because of his CHF on hospital day12. When benazepril was discontinued, the urine output return to normal. And next, represcribed benazepril, the urine output decreased again. All his fluid volume and the related drugs were shown as table 1. Using the Naranjo, [5] benazepril was found to be a probable cause of decreased urine output in the patient with CHF and moderate CKD.

Discussion

In previous reports, urine output was often used as a marker of AKI. The patient who with decrease of urine output will be classified as "AKI".Urine output criteria may be more sensitive in identifying acute kidney injury than traditional serum creatinine criteria [6]. The decreased urine output occurred in the case we described reminded us the possible of AKI in the patient. Decreased of urine output may be associated to a decrease of GFR due to decrease of renal blood flow

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or renal perfusion pressure [7]. The most likely causes of decreased urine output include as following. The first, the technical aspects of specific surgical procedures may predispose an at-risk patient to the development of decreased urine output and/or AKI, involve urologic surgery, general and gynecologic surgery, Cardiac surgery, Vascular surgery [8], laparoscopic operations. The second, hypothermia linearly correlated with the decrease in core temperature, which importantly implicated for fluid management problem [9]. The third,direct drug toxicity include morphine sulfate, diclofenac, gentamicin and vancomycin are administered simultaneously etc. In this report, the decreased urine output seemed to be related to the direct drug toxicity, it was probably induced by benazepril according to the judgement by Naranjo method. So far, benazepril- Induced AKI in mild to moderate CKD was rarely reported in literatures.

Benazepril hydrochloride was a non-thiol ACEI which was hydrolyzed in vivo to the active metabolite benazeprilat after oral administration [10]. As the kidneys are the primary route of elimination for benazeprilat, the pharmacokinetic (PK) properties of benazepril in patients with renal impairment have been studied extensively after single and multiple dose administration. The PK profile of intact (i.e., not metabolized) benazepril was not significantly influenced by kidney function, since it is cleared from plasma mainly by biotransformation rather than renal elimination[2]. Therefore, the burden from Benazepril to kidney seems to be fewer.

Early evidence demonstrated that ACEIs slowed down the progression of chronic kidney disease in patients with baseline serum creatinine (SCr) of 1.5–3.0 mg/dl or less [11]. Benazepril was usually given to the patients with CKD (SCr<3.0 mg/dL). Hou *et al.* [12]. subsequently demonstrated that renal outcomes were also improved with benazepril treatment compared with placebo in patients with SCr levels between 3.1 and 5.0 mg/dl (i.e., very markedly advanced renal failure). Benazepril was shown to exert renoprotective effects when administered alone or in combination with other drugs [13]. In this case, the patient presented with moderate CKD (SCr: 1.9 mg/dL), which indicated to use benazepril. However, kidney injury rapidly occurred in this patient after administration of benazepril, which could be related to its' usage to patients with CHF.

For the heart failure patients with renal insufficiency, cardiac output and mean arterial blood pressure decrease, leading to decreased renal perfusion, neurohormonal and sympathetic nervous system maladaptation occurs, resulting in inappropriate activation of the RAAS. While benazepril was administrated to such patients, it expands the efferent arteriole stronger than afferent glomerular arteriole. Consequence, it might be observed a reduction in the GFR and the decreasing of urine output, despite an increase in renal plasma flow [14-15]. It mainly explained that benazepril decreased urine output in the patient with CHF and CKD.

Maybe there were some combined factors to induce decreasion of urine output. For example, this patient uses a large dosage of loop diuretic. The principal mechanism of action of Loop diuretics involves the blockade of the Na-K-2C1 transporter on the luminal side of the thick ascending limb of the loop of Henle. The pharmacodynamic properties of loop diuretics was different in patients with CHF. The expression of the Na-K-2Cl transporter is regulated via cyclic adenosine monophosphate pathways with vasopressin amplifying its expression and prostanoid prostaglandin E2 reducing its expression. The change of these factors may aggravate the obvious contraction of renal blood vessels, which lead to reduce the renal blood flow and the urine output. The decreasion of urine output in this patient may be related to the above mechanism [16].

This patient had a history of Diabetic nephropathy (DN). DN, a severe microvascular complication, is a leading cause of renal failure. Previous studies found that the severity of AKI in the mice correlated with their blood glucose levels [17]. In patients with diabetes, high blood glucose level causes the formation of glucose toxic substances in the body and activate a variety of pathways. Then the renal interstitial fibrosis and glomerular sclerosis accured, which cause decreasion of the GFR and even reduction of urine output in some conditions. To Sum up, CHF, hypertension and using of a large dose of diuretic were initiative fators to AKI in diabetic nephropathy patients.

In this case, the patient, presented with CHF and diabetic nephropathy, used benazepril, a large dose of loop diuretics and seroperitoneum to treat CHF. Adverse renal effects could be considerate to be related to these conditions, and the most one is Benazepril.

Conclusion

Physicians and pharmacists should use ACEIs with caution, especially in CHF patients who suffered from diabetic nephropathy and used large dose of diuretics. These patients were generally never be studied until today. In addition, Scr is not the only index to evaluate renal function. The Scr value (< 3.0mg/dl) is not the only precaution to ensure applying ACEIs. Attention to benazepril should be given to the patients accompanied with CHF and diabetic nephropathy, even if who with only mild to moderate CKD. Routine hemodynamic examination and biochemical monitoring was suggested before and during the period of benazepril therapy in such patients. Even, careful dose titration to understand control state of blood pressure and Scr is mandatory in these patients.

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