TREATMENT OF HYPERURICEMIA WITH ALLOPURINOL IN RESISTANT HYPERTENSIVE PREDIALYSIS CHRONIC KIDNEY DISEASE PATIENTS HAVE ADDITIONAL POSITIVE EFFECT ON BLOOD PRESSURE AND RENAL FUNCTION

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INTRODUCTION

Elevated levels of serum uric acid have been associated with an increased risk of cardiovascular disease. Small studies have observed an antihypertensive effect of urate-lowering therapy with allopurinol in hyperuricemic patients and in obese adolescent males with hypertension. Resistant hypertension is defined as high blood pressure that remains uncontrolled despite treatment with at least three antihypertensive agents (one of which is a diuretic) at best tolerated doses. The aim of this study was to investigate effects of allopurinol therapy on blood pressure and renal function parameters in predialysis chronic kidney disease patients with resistant hypertension.

SUBJECTS AND METHODS

A total of 50 patients with resistant hypertension and predialysis chronic kidney disease were divided in two groups: 25 who had blood pressure readings taken before and after being prescribed allopurinol for 6 weeks (Group 1) and 25 who had not taken allopurinol (Group 2). Patients in both groups were 68 7 years old with 12M/13F, duration of resistant hypertension 11 6 years, from Registar of resistant hypertension patients in our Hospital. Resistant hypertension was defined as nlood pressure remaining above goal, despite the use of optimal doses of 3 or more than three medicines of different classes (including a diuretic). Patients with a history of gout were excluded, and levels of serum uric acid were form 333-605 umol/L. No patients received a higher dose than 200 mg allopurinol daily. We investigated the incidence of worsening of chronic kidney disease in Group 1 and 2 using the Modification of Diet in Renal Disease Study (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations in estimating glomerular filtration rate (eGFR). Level of statistical significance was chosen to be $p<0.05$. Statistical analysis was performed by statistical package STATA/IC ver.11.1.

RESULTS

Treatment with allopurinol caused an additional significant reduction in clinic blood pressure: systolic blood pressure fell 9.8 mmHg while diastolic fell 8.0 mm Hg, compared with Group 2. There was a reduction of blood pressure that was not related to the primary uric acid level or to other drugs the patients were taking (number of antihypertensive medication was for 3-8 and most used drug classes were: diuretic in 100% (including thiazides which can raise uric acid levels and indapamide), angiotensin- converting enzyme (ACEI) inhibitors or angiotensin receptor blockers (ARB) in 100%, calcium antagonists in 94%, beta blockers (nebivolol or carvedilol) in 82%, central acting drugs in 64%, alfa-blockers in 26%, vasodilatators in 8%, mineralocorticoid receptor antagonists: spironolactone 50 mg in 24% or eplerenone (50 mg) in 4%). There were not worsening in chronic kidney disease in Group 1: MDRD ≥ 60 mL/min per 1.73 m2 (stages 1 and 2) have 62% in Group 1 and 60% in Group 2 , 38% of pateints in Group 1 have CKD stage 3 (22%), stage 4 (14%) and stage 5 (2%, one man). In Group 2 40% of patients have CKD stage 3 (23%), stage 4 (15%) and stage 5 (2%, one man). There were no significant differences between the eGFR values derived by MDRD and CKD-EPI in both groups ($p>0.05$).

CONLUSION

The results of our study suggest that therapy with allopurinol in dose 200 mg daily lowered blood pressure in patients with resistant hypertension and predialysis chronic kidney disease without worsening of kidney function. Blocking the xanthine oxidase-mediated conversion of molecular oxygen to produce mediators of oxidative stres can partially explane additional blood pressure lowering effect and safety of allopurinol in those patients.

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