# Commentary on: The effect of allopurinol on lowering blood pressure in hemodialysis patients with hyperuricemia

Sir,

We read with great interest the article by Jalalzadeh *et al*., entitled "The effect of allopurinol on lowering blood pressure in hemodialysis patients with hyperuricemia", published recently in your esteemed journal[1]. They conducted a single-blind, randomized cross-over clinical study involving 55 hemodialysis patients with serum uric acid level >6.5 (men) and >5.5 mg/dL (women).[1] They found that allopurinol treatment reduced blood pressure. The results of the study indicates that allopurinol may act as a new potential therapeutic approach for controlling blood pressure in hemodialysis patients.[1]

While less data is published regarding serum uric acid and blood pressure in patients with end-stage renal disease,[2,3] the present study could firstly emphasize on the association of uric acid level and hypertension (HTN) in hemodialysis patients and secondly describe a positive effect of allopurinol on lowering of blood pressure in these patients. We congratulate the authors for their findings, however, we would like to clarify a few points HTN in hemodialysis patients. The majority of end-stage renal failure patients have hypertension. HTN is associated with an increased risk for left ventricular hypertrophy, coronary artery disease, congestive heart failure, cerebrovascular disease, and mortality.[4,5] HTN in hemodialysis patients is multifactorial and antihypertensive drugs alone do not adequately control blood pressure in hemodialysis patients.[4-8] HTN in chronic hemodialysis patients is also very common, with a reported prevalence as high as 72% and is associated with an annual mortality of 23%.[4,7,9] Data on the proportion of treated patients who achieve adequate blood pressure control and the treatment modalities on the control of HTN is limited.[4,7-9] Uncontrolled HTN is a major cause of left ventricular hypertrophy and cardiovascular morbidity and mortality in these patients.[7-10] There is a widely held belief that hypervolemia due to excess intake or inadequate removal of salt and water is the principal cause of HTN in dialysis patients.[3,7,9,10] The risk of failing to consider additional pathophysiological elements is that inadequate or inappropriate therapeutic strategies may be adopted.[7,9-11] Thus, among maintenance hemodialysis patients having HTN, blood pressure should be controlled. Indeed, control of HTN with antihypertensive drugs does not increase mortality, in contrast, studies suggest that treatment of HTN in this high-risk population may in fact improve cardiovascular outcomes.[4,7,9-11] Lowering blood pressure among hypertensive patients should primarily be done by sodium restriction and reaching to dry-weight, and then using antihypertensive drugs. Hyperuricemia is a predictor for the development of HTN and is commonly present in new-onset essential HTN.[12] Also, hyperuricemia is associated with coronary artery disease and chronic kidney disease.[12-14] Uric acid, as the final oxidation product of purine catabolism, has been associated with various clinical conditions such as diabetes and atherosclerotic disease too.[12] Recent studies suggest that uric acid is a relevant and independent risk factor for renal disease, particularly in patients with HTN.[12-17] It was found that hyperuricemia, when induced by an uricase inhibitor, triggers HTN and impairs nitric oxide generation in the macula densa, while both HTN and renal injury are reduced by inducing of nitric oxide.[12,15,17] The mechanism by which uric acid may cause organ damage is not fully understood, however, there is increasing evidence that dysfunction of endothelial cells is a mechanism whereby this substance may affect renal function and structure.[12,15-18] HTN is consistently associated with endothelial dysfunction,[9,12-15] and hyperuricemia is a strong predictor of HTN and blood pressure progression.[11,13,17] However, irrespective of renal involvement, elevated serum uric acid is associated with kidney development of HTN.[12,15-18]

It was also shown that in the adolescents with newly diagnosed HTN, treatment with allopurinol resulted in lowering of blood pressure.[12,18-21] The results represent a new potential therapeutic approach. However, these preliminary findings need confirmation in larger clinical trials.

There are less specific data on the relationship of serum uric acid and HTN in the maintenance hemodialysis setting. In a cross-sectional study, the relationship of uric acid and endothelial dysfunction was investigated in 189 stable peritoneal dialysis patients by Tang *et al*. They found an independent correlation between uric acid and flow-mediated dilatation of the brachial artery as an indicator of endothelial dysfunction. They concluded that worse endothelial function may contribute to HTN.[2] Accordingly, in the study of Silverstein *et al*., the relationship between serum uric acid and blood

pressure in 63 pediatric dialysis patients was assessed. They found that pretreatment systolic blood pressure percentile was associated with a high serum uric acid level. They concluded that serum uric acid impacts blood pressure in pediatric hemodialysis patients, independent of volume, nutritional, and weight status.[3]

Hence finding of Jalalzadeh *et al*. explains a new therapeutic modality in the treatment of hypertensive hemodialysis patients. However, larger control studies need to better found this aspect of hemodialysis patients.

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