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Renoprotective impact of allopurinol in elderly patients with hypertension

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ABSTRACT

Implication for health policy/practice/research/medical education:

Hypertension and hyperuricemia are common problems in elderly patients. These problems could be accelerated decrease in glomerular filtration rate (GFR) with aging. It is suggested that lowering uric acid with allopurinol could be beneficial to prevent chronic insufficiency in the elderly patients with hypertension.

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Introduction

Decrease glomerular filtration rate (GFR) is a prevalent problem in elderly patients. As a consequence of normal aging and specific diseases such as arteriosclerosis, various changes will occur in renal function and structure including interstitial fibrosis and atrophy in the tubules (1). Important contributors to these changes are endothelial dysfunction and vascular oxidative stress (1). Hypertension accelerates this age-related vascular dysfunction, and thus has an impact on progression of vascular damage and decreases GFR in an elderly population (2). On the other hand some drugs such as angiotensin inhibitors or angiotensin blockers also may adversely affect renal perfusion and GFR in the elderly individuals.

Excessive oxidative stress, an imbalance between reactive oxygen species (ROS), and nitric oxide (NO), due to xanthine oxidase activity and vascular dysfunction have been reported in hypertension, diabetes, and atherosclerosis (2). Dysfunction of endothelial cells caused by ROS implicated in the pathogenesis of vascular diseases. Evidences for excessive ROS formation precedes onset of hypertension and is accompanied by excessive production of oxidative stress and consequently elevated high blood pressure, suggesting that ROS has a role in

the development of hypertension (2). ROS are generated from purines hydroxylation by xanthine oxidase. This enzyme also catalyzes the oxidation of hypoxanthine and produced xanthine. Further oxidation of xanthine by xanthine oxidase can produce uric acid. Serum levels of this enzyme are increased in various pathological states, such as inflammatory diseases, carcinogenesis, chronic renal disease and aging (3).

Furthermore, increased extracellular concentration of hypoxanthine, by the activity of xanthine oxidase also induced endothelial dysfunction and cell death (4).

Recent studies suggested that endothelial dysfunction could develop due to excessive uric acid production by impairing nitric oxide production, inducing anti-proliferative effects on endothelial cells, and induction of the renin-angiotensin system (5). These evidences suggested that uric acid also has a causal role in pathogenesis of hypertension. Thus ROS, hypoxanthine and uric acid are involved in damage to endothelial cells and acceleration of end-organ complications.

In aging process, decline of endothelial function, vascular remodeling, and increased arterial stiffness, causes progression of high blood pressure and facilitate end-organ damage (6). Strategies to prevent age related vascular endothelial changes could prevent vascular and

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end-organ damages associated with hypertension in elderly patients.

Allopurinol as a xanthine oxidase inhibitor can decrease ROS production and inhibit production of hypoxanthine and uric acid, thus may have beneficial effects on endothelial cell function. In fact administration of allopurinol, as an adjective antihypertensive agent, produced small but significant beneficial changes in both systolic and diastolic blood pressure (7). Other studies also detected the improvement of GFR, endothelial function and systolic blood pressure by administration of allopurinol. In these studies, the effects of allopurinol were mild but its beneficial effect involved the inhibition of xanthine oxidase-associated oxidants rather than uric acid per se (8).

In a recent case-control study, administration of allopurinol to decrease serum uric acid lower than 6 mg/dL caused minimal but significant improvement in GFR and blood pressure after 3 months. This study showed that hyperuricemia could adversely affect blood pressure and GFR (9). Hence, lowering uric acid may prevent renal disease progression, even in patients with normal blood pressure. This study suggests that lowering uric acid with allopurinol could be an important role in prevention of chronic renal insufficiency in hypertensive patients.

Conclusion

Based on these evidences and high prevalence of hyperuricemia in elderly patient with hypertension, inhibition of xanthine oxidase pathway by allopurinol might be beneficial for patients with essential hypertension and aging kidney even in patients with mild hyperuricemia.

Author's contribution

PM is the single author of the paper.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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