Grape Seed for Prevention of Reperfusion Injury

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Ischemia and reperfusion in the kidney increase free radicals and activate inflammatory pathways. Reactive oxygen species (ROS) are generated in high concentration after reperfusion. In normal condition, antioxidant enzymes reduce the cellular effect of ROS. However, the cell cannot resist when there is a high concentration of ROS.[1] Reduction of ROS with antioxidative drugs or dietary products is the basis of approaches towards slowing progressive kidney injury. Grape seed extract (GSE) contains pro-anthocyanidin, which has been introduced as an effective antioxidant drug. In an original article published in the current issue of the *Iranian Journal of Kidney disease*, Ashtianti and colleagues[2] investigated in a well-designed animal study the antioxidant effect of GSE after reperfusion injury in the kidney. In a randomized controlled study, they used malondialdehyde, the final product of lipid peroxidation, as a marker of increase production of free radicals. Plasma total antioxidant capacity was measured by ferric-reducing ability of plasma. The level of serum creatinine, urine and plasma osmolarity, and finally kidney histology were markers of kidney damage. They clearly demonstrated the antioxidant and anti-injury effect of GSE on a small group of rats.

However, the authors could not use the standard effective component of GSE. In a recent study, by Wei and coworkers[3] with a similar design in rat model of reperfusion injury, the authors measured superoxide dismutase, catalase, and glutathione peroxidase as antioxidant enzymes. Grape seed extract was used with a dose of 2.5 g/kg 1 week before reperfusion injury and contained 96% proanthocyanidin content. This study also clearly showed better antioxidant, biochemical, and histologic markers in pretreated rat group. The protective effect of GSE has extensively been studied in the use of nephrotoxic drugs such as cisplatin,[4] methotrexate,[5] aminoglycosides,[6,7] and cyclosporine[8] in rats. These studies showed anti-oxidant effect of GSE in prevention of toxic nephropathies. Li and colleagues[9] studied the GSE effect in diabetic Wistar rats and showed that treated animals had a reduction in serum advanced glycosylation end product, proteinuria, and systolic blood pressure. Although there are several studies in support of antioxidative effect of GSE, but the standardized component has not been described yet. Rodents were the animal targets in majority of studies. There is no randomized controlled trial in human to support its effect.

CONFLICT OF INTEREST

None declared.

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Serum Magnesium Level and Cardiovascular Disease in Dialysis Patients

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Magnesium is the second major intracellular divalent cation which is involved in maintaining normal cellular function.[1] Approximately, 50% of the total body magnesium is found in the bone. The other half is present predominantly inside cells and only 1% is in blood. The serum concentration of magnesium is closely monitored within normal range (1.5 mEq/L to 2.3 mEq/L or 1.8 mg/dL to 2.8 mg/dL).[1] In chronic kidney disease (CKD) patients, fractional excretion of magnesium increases with diminution of glomerular filtration rate in order to maintain serum magnesium within normal ranges; however, when glomerular filtration rate goes down to 30 mL/min, hypermagnesaemia occurs.[1,2] Although, the severity of hypermagnesaemia is variable, hypermagnesaemia is generally mild and asymptomatic. In CKD stage 5 dialysis patients, dialysis solution magnesium concentration and oral magnesium intake are the main factors controlling serum magnesium levels.[2,3] In fact, there is a wide variability in magnesium balance in dialysis patients and it is not surprising that magnesium balance to be normal or even low in dialysis patients, because of low dietary intake or impaired intestinal absorption.[3,4]

Cardiovascular disease (CVD) is the most important cause of morbidity and mortality in both CKD and dialysis patients.[3-5] Recently, there is increasing evidence suggesting an association between low serum magnesium levels and CVD in CKD as well as in general population.[3-5] It seems that magnesium depletion may be the missing link between cardiovascular risk factors and atherosclerosis. Vascular calcification is an important factor for increased morbidity and mortality in CKD and dialysis patients.[4-6] Although, the mechanism of vascular calcification is multifactorial, it is now evident that magnesium depletion is involved in the pathogenesis of vascular calcification.[6-8] On the other hand, low serum magnesium level is associated with the other CVD risk factors including hypertension, dyslipidemia, coronary vasospasm, atherosclerosis, and ischemic heart disease. Moreover, at least in animal model, the association between hypomagnesemia and the presence of pro-inflammatory state has been shown.[7] This pro-inflammatory state can disrupt the arterial endothelium and promote thrombosis and atheroma formation, hypertension, arteriosclerosis, and vascular calcification.[7,8]

There are unanswered questions about magnesium balance and its effects in both CKD and dialysis patients. Further studies, especially randomized trials, are required to confirm the