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File: ■ Grape (*Vitis vinifera*, Vitaceae) Seed Extract ■ Chronic Kidney Disease

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RE: Grape Seed Extract May Slow Progression of Chronic Kidney Disease

Turki K, Charradi K, Boukhalfa H, Belhaj M, Limam F, Aouani E. Grape seed powder improves renal failure of chronic kidney disease patients. *EXCLI J*. June 27, 2016;15:424-433.

Chronic kidney disease (CKD) is a slow, progressive decline of renal function characterized by high creatinine, low glomerular filtration rate (GFR), and proteinuria. Oxidative stress and inflammation are commonly observed in patients with CKD and contribute to disease progress. Grape (*Vitis vinifera*, Vitaceae) seed extract (GSE) is a polyphenolic mixture that has demonstrated antioxidant and anti-inflammatory properties. This randomized, double-blind, placebo-controlled, pilot study tested the effect of GSE on kidney dysfunction in patients with different stages of CKD.

Patients with CKD with renal failure at stages 2, 3, or 4 were recruited at the hemodialysis unit of the Regional Hospital of Menzel Bourguiba, Tunisia. All exhibited diabetic nephropathy and hypertension. The study was conducted from May to October 2011. Patients continued with their current treatment of insulin (2 doses/day), captopril 50 mg (2 doses/day), furosemide 40 mg (2 doses/day), folic acid (2 tablets/day, doses not specified), and iron for anemia (2 tablets/day, doses not specified) through the study period. Patients were excluded if they were smokers or received antioxidant treatment in the past 6 months. Patients in the placebo group (n = 10) consisted of 3 patients in stage 2 (GFR ≤ 90 mL/min/1.73 m^2), 4 patients in stage 3 (GFR ≤ 60 mL/min/1.73 m^2), and 3 patients in stage 4 (GFR ≤ 30 mL/min/1.73 m^2). The GSE group (n = 23) had 6 patients in stage 2, 11 patients in stage 3, and 6 patients in stage 4. Patients in the GSE group were instructed to take 6 capsules of GSE, each containing 350 mg of grape seed powder, daily. The placebo group received capsules containing starch. Blood samples, after overnight fasting, and urine samples were collected at baseline and after 6 months, and panels of markers of kidney function and inflammation, and blood cell counts, were measured. GSE was processed from the grape cultivar Carignan grown in northern Tunisia. Seeds were separated, washed, dried, ground with an electric grinder to a fine powder, and mixed with 3% colloidal silica. The GSE polyphenol composition is described in a previous publication.[1]

Proteinuria was comparable in the GSE and placebo groups at the start of the study. After 6 months of supplementation, proteinuria had increased in both groups but was significantly lower in the GSE group (−32.67%, P = 0.041). At 6 months, the inverse of the plasma creatinine ratio (i.e., units of L/mmol) was significantly higher in the GSE group (+19.42%, P = 0.044), due to a decrease in the placebo group that was not seen in the GSE group. GSE had no significant effect on plasma urea or uric acid. There was a nonsignificant trend toward improvement in GFR (+18.70%, P = 0.604) in the GSE group, versus no mean change in the placebo group. The initial numbers of stage 4 and stage 3 patients in the GSE group decreased from 6 to 2 and from 11 to 10, respectively, resulting in 11 of 23 patients in the GSE group being in stage 2 by the end of the study (+83.33%).

The GSE group showed significant decreases in plasma malondialdehyde (−14.96%, P = 0.0307) and protein carbonylation (−38.82%, P = 0.0319). There was no significant effect on hydrogen peroxide. GSE significantly increased plasma catalase by 95.94% (P = 0.015) and superoxide dismutase by 25.99% (P = 0.049). There was no significant effect on plasma glutathione peroxidase activity. There was a nonsignificant 12.81% reduction in plasma C-reactive protein at 6 months (P = 0.168), which increased during the study period in both groups. The authors state that GSE "totally counteracted [increases in] plasma LDH [lactate dehydrogenase]," but this result was nonsignificant (P = 0.623). There was a slight, nonsignificant decrease in triglyceride levels in the GSE group (−16.44%, P = 0.067), and a significant increase in plasma lipase activity (+29.67%, P = 0.006).

Overall, there was no effect on cholesterol levels. The GSE group showed a slight, nonsignificant increase in white blood cells (+23.48%, P = 0.276), especially granulocytes. GSE also prevented anemia of patients with CKD (GSE increased free iron by 13.26% [P = 0.019] versus placebo). A nonsignificant tendency toward decreasing red blood cells was noticed in the placebo group (4.72 ± 0.14 to 4.37 ± 0.19; P = 0.127), but not in the GSE group (4.22 ± 0.21 to 4.23 ± 0.25; P = 0.692). GSE did not affect hemoglobin or the decrease of hematocrit, which was observed in both groups. Platelet count increased significantly from baseline in the GSE group (+24.63%, P = 0.030) and nonsignificantly in the placebo group (+10.93%, P = 0.327), but the difference between groups was not significant.

While the sample size of this study was too small to create strong statistical significance, the results of this study are hopeful, if preliminary. Future studies should be larger, and perhaps longer. The authors suggest using a far higher GSE dose to obtain more significant outcomes, based on animal studies; however, human patients might find the necessary volume unacceptable.

—Alexis Collins, MA, MS

Reference

[1]Charradi K, Elkahoui S, Karkouch I, et al. Protective effect of grape seed and skin extract against high-fat diet-induced liver steatosis and zinc depletion in rat. *Dig Dis Sci*. 2014;59(8):1768-1778.

Referenced article can be accessed at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5083963/.