Effect of Addition of Silymarin to Renin-Angiotensin System Inhibitors on Proteinuria in Type 2 Diabetic Patients With Overt Nephropathy: A Randomized, Double-Blind, Placebo-Controlled Trial

Abstract: Background: A large proportion of patients with type 2 diabetes mellitus have diabetic nephropathy. Despite current therapies including renin-angiotensin system inhibitors, diabetic nephropathy progresses to end-stage renal disease in most of these patients. Therefore, there is an urgent need to find new treatments for such patients. The aim of this study was to evaluate the efficacy of silymarin, an herbal drug with antioxidant and anti-inflammatory properties, in preventing the progression of diabetic nephropathy.

Study Design: Randomized, double-blind, placebo-controlled, 2-arm parallel trial.

Setting & Participants: 60 patients with type 2 diabetes with macroalbuminuria (urinary albumin excretion > 300 mg/24 h) despite treatment with the maximum dose of a renin-angiotensin system inhibitor for more than 6 months and estimated glomerular filtration rate > 30 mL/min/1.73 m(2).

Intervention: Patients were randomly assigned to 2 equal groups to receive three 140-mg tablets of silymarin or 3 tablets of placebo daily for 3 months.

Outcomes: The primary outcome was absolute change in urinary albumin-creatinine ratio (UACR) from baseline to the end of the treatment phase.

Measurements: UACR and urinary and serum levels of TNF-alpha (tumor necrosis factor alpha; an inflammatory marker), malondialdehyde (MDA; an oxidative stress marker), and TGF beta (transforming growth factor beta; a marker of fibrosis) at baseline and the end of the treatment phase.

Results: Although UACR decreased in both groups, this decrement was significantly higher in the silymarin compared with the placebo group; mean difference in change in UACR between the 2 groups was -347 (95% CI, -690 to -4) mg/g. Urinary levels of TNF-alpha and urinary and serum levels of MDA also decreased significantly in the silymarin compared with the placebo group.
Limitations: Small sample size and short duration of the treatment phase.

Conclusions: Silymarin reduces urinary excretion of albumin, TNF-alpha, and MDA in patients with diabetic nephropathy and may be considered as a novel addition to the anti-diabetic nephropathy armamentarium. Am J Kidney Dis. 60(6): 896-903. (C) 2012 by the National Kidney Foundation, Inc.