Journal View

Is Cranberry Useful in Preventing Recurrent Urinary Tract Infections?

Cranberry capsules aren't as effective as trimethoprim-sulfamethoxazole (TMP-SMX) in preventing recurrent urinary tract infections (UTIs), but TMP-SMX is associated with high rates of emerging antibiotic resistance, concludes a trial published in the *Archives of Internal Medicine*.

The randomized trial included 221 premenopausal women with a history of recurrent UTIs: at least three symptomatic infections in the previous year. In double-blind, double-dummy fashion, patients were assigned to receive prophylactic TMP-SMX 480 mg once daily, or cranberry capsules 500 mg twice daily. Over 1 year of treatment, the rates and numbers of symptomatic UTIs were compared between groups. The development of antibiotic resistance in native *Escherichia coli* was monitored as well.

During the study year, patients taking cranberry capsules had about twice as many infections as those taking antibiotics: 4.0 versus 1.8. At least one infection occurred in 78.2 percent versus 71.1 percent of patients; the median time to initial recurrence was 4 versus 8 months, respectively.

However, prophylactic TMP-SMX was associated with high rates of antibiotic resistance. Fecal *E. coli* isolates resistant to TMP-SMX were found at 1 month in 86.3 percent of the antibiotic group versus 23.7 percent of the cranberry group. Patients taking antibiotics also had higher rates of asymptomatic bacteriuria *E. coli* isolates as well as increased rates of trimethoprim, amoxicillin, and ciprofloxacin resistance. The differences in antibiotic resistance resolved 3 months after discontinuation of TMP-SMX.

Prophylactic antibiotics are widely used for prevention of recurrent UTIs. However, problems with antibiotic resistance have led to renewed interest in the potential for cranberry to reduce recurrent UTI risk.

The new trial found a lower rate of recurrent UTIs with prophylactic TMP-SMX than with cranberry capsules. However, this benefit of TMP-SMX was accompanied by high rates of antibiotic resistance. A formal cost-utility analysis of these two alternatives is planned [Beerepoot MAJ, et al. Cranberries vs. antibiotics to prevent urinary tract infections: a randomized double-blind noninferiority trial in premenopausal women. *Arch Intern Med* 2011; 171:1270–1278].

Desensitization Shows Survival Benefit in Kidney Transplant Candidates

For HLA-sensitized patients awaiting a kidney transplant, desensitization therapy followed by HLA-incompatible kidney transplantation leads to better survival than continued waiting for a compatible organ, reports a study published in the *New England Journal of Medicine*.

The study included a "treatment group" of 211 HLA-sensitized patients who received an HLA-incompatible living donor kidney after undergoing desensitization treatment with plasmapheresis and low-dose intravenous immune globulin from 1998 through 2009. They were carefully matched to patients who continued to receive dialysis or who underwent dialysis or HLA-compatible kidney transplantation.

The Kaplan-Meier estimated survival for patients undergoing desensitization therapy was 90.6 percent at 1 year, 85.7 percent at 3 years, and 80.6 percent at both 5 and 8 years. This was significantly higher than for the "dialysis-only" control individuals, for whom survival was 91.1 percent at 1 year, 67.2 percent at 3 years, 51.5 percent at 5 years, and 30.5 percent at 8 years. It was also superior to the "dialysis-or-transplantation" group: 93.1, 77.0, 65.6, and 49.1 percent, respectively. Desensitization was linked to better survival at all levels of donor-specific anti-HLA antibody.

For HLA-sensitized patients, depletion of donor-specific antibodies may allow timely living donor kidney transplantation as an alternative to remaining on the waiting list. The new study suggests that desensitization therapy provides a significant survival advantage compared with continued dialysis or later HLA-compatible kidney transplantation. "By 8 years, this survival advantage more than doubled," the researchers write [Montgomery RA, et al. Desensitization in HLA-incompatible kidney recipients and survival. *N Engl J Med* 2011; 365:318–326].

As Diabetes Increases, So Does Diabetic Kidney Disease

Over the past two decades, the rates of diabetic kidney disease (DKD) in the United States have increased in proportion to the rising prevalence of diabetes, reports a study published in the *Journal of the American Medical Association*.

The researchers analyzed data from the Third National Health and Nutrition Examination Survey (NHANES III) 1988 to 1994, NHANES 1999–2004, and NHANES 2005–2008. On the basis of hemoglobin A1c level and use of glucose-lowering drugs, diabetes was present in 8.2 percent of individuals in NHANES III, 11.1 percent in NHANES 1999–2004, and 13.4 percent in NHANES 2005–2008.

On the basis of a urine albumin-to-creatinine ratio of 30 mg/g or higher and/or a GFR of less than 60 mL/min per 1.73 m^2, the prevalence of DKD was 2.2 percent in 1988–1994, 2.8 percent in 1999–2004, and 3.3 percent in 2005–2008. This trend reflected the rising prevalence of diabetes; among individuals with diabetes, the proportion with DKD was unchanged.

The use of glucose-lowering drugs by diabetic individuals increased from 56.2 percent in NHANES III to 74.2 percent in NHANES 2005–2008. The use of renin-angiotensin-aldosterone system inhibitors increased from 11.2 percent to 40.6 percent.

The percentage of diabetic individuals with impaired GFR increased significantly, from 14.9 percent to 17.7 percent. The albuminuria rate decreased nonsignificantly, from 27.3 percent to 23.7 percent.

These cross-sectional NHANES data show an increase in DKD in proportion to the rising prevalence of diabetes in the United States. Among people with diabetes, the prevalence of DKD has remained about the same, despite increased use of diabetes therapies. The researchers write, "[A]dditional interventions are needed to prevent the development of diabetes and to target GFR loss once diabetes is diagnosed." [de Boer IH, et al. Temporal trends in the prevalence of diabetic kidney disease in the United States. *JAMA* 2011; 305:2532–2539].

Ambulatory BP Data Predict Renal and Cardiovascular Risks in Chronic Kidney Disease

In patients with chronic kidney disease (CKD) not yet receiving dialysis, ambulatory BP monitoring improves the ability to predict renal and cardiovascular events, according to a study published in the *Archives of Internal Medicine*.

The Italian multicenter cohort study included 436 patients with stage 2–5 CKD who were not receiving dialysis. At baseline, the GFR was 42.9 mL/min per 1.73 m^2; diabetes was present in 36.5 percent of patients and cardiovascular disease in 30.5 percent. Office and ambulatory BP data were compared for their ability to predict time to renal death (ESRD or death) and time to fatal and nonfatal cardiovascular events. The median follow-up time was 4.2 years.

The mean office BP was 146/82 mm Hg. During ambulatory monitoring, the daytime BP was 131/75 mmHg and the nighttime BP 122/66 mmHg. At follow-up, 155 patients had reached the renal endpoint, and 103 had reached the cardiovascular endpoint.

Patients with daytime systolic BP greater than 126 to 135 mmHg had a higher rate of cardiovascular events: adjusted hazard ratios (HR) of 2.23 at a level of 136–146 mmHg and 3.07 at higher than 146 mmHg. The same groups were at increased risk of renal death: HR 1.72 and 1.85, respectively.

Patients with nighttime systolic BP greater than 106–114 mmHg were at increased risk of the cardiovascular endpoint: HR 2.52 at 125–137 mmHg and 4.00 at greater than 137 mmHg. They were also at

increased risk of renal death: HR 1.87 and 2.54, respectively. The rates of both outcomes were higher in patients who were "nondippers" and "reverse dippers" receiving ambulatory BP monitoring. Office BP measurements did not predict either outcome.

Ambulatory BP monitoring provides additional prognostic value in patients with essential hypertension. The new study suggests that ambulatory BP measurement—especially nighttime BP data—allows more accurate assessment of adverse renal and cardiovascular outcomes in patients with CKD who are not receiving dialysis. By contrast, office BP measurements provide little or no useful information about these risks [Minutolo R, et al. Prognostic role of ambulatory blood pressure measurement in patients with nondialysis chronic kidney disease. *Arch Intern Med* 2011; 171;1090–1098].