Variability of commercial cranberry dietary supplements for the prevention of uropathogenic bacterial adhesion

OBJECTIVE: In the United States, urinary tract infections are one of the most common bacterial infections, affecting 8 million people per year.[1] Approximately 50% of women will develop a urinary tract infection during their lifetime.[1] In 2000, the United States spent $2.14 billion toward UTI treatment.[1] Urinary tract infections are generally considered easily treatable, with the majority of patients prescribed a regimen of antibiotics. Overuse of antibiotic therapy has burdened the clinical management of urinary tract infections, which has led to the increasing prevalence of antibiotic resistance.[1] An alternative prophylactic is needed to combat the emergence of ineffective treatments. Cranberry may be beneficial in preventing recurrent urinary tract infections in certain at-risk populations.[2]

The mechanism of action of cranberry was initially thought to be due to the fruit's acidity, producing a bacteriostatic effect in the urine.[2] More recently it was found that components in cranberry called proanthocyanidins, condensed tannin molecules with A-type linkages, exhibit potent bacterial antiadhesion activity.[3] Herbals, such as cranberry, are not required to undergo the same rigorous testing to establish efficacy, dosage and safety as pharmaceutical agents regulated by the Food and Drug Administration.[4] We sought to measure the bacterial anti-adhesion activity and proanthocyanidin levels in 7 commercially available cranberry supplements.

STUDY DESIGN: The bioactivity of the 7 cranberry supplements in preventing adhesion of uropathogenic P-fimbriated *Escherichia coli* was tested by measuring the ability of the supplements to suppress agglutination of human red blood cells (A1, Rh+) following incubation with the bacteria.[5] Endpoint concentrations were compared among the cranberry products, with the lowest concentration representing the highest bacterial antiadhesion activity. Wells containing bacteria plus phosphate-buffered saline, human red blood cells plus phosphate-buffered saline, bacteria plus test fraction, and human red blood cells plus test fraction served as negative controls for agglutination, and wells containing bacteria plus human red blood cells served as a positive control for agglutination.

RESULTS: Antiadhesion activity of the supplements ranged from 0.47 to 60 mg/mL, with 4 products yielding negative results (Table). Typically, cranberry products that result in production of antiadhesion activity in urine when consumed have whole-product activities of 0.47–7.5 mg/mL. Proanthocyanidin levels ranged from 0.56 to 175 mg/g. In clinical trials, consumption of cranberry products containing about 36 mg of proanthocyanidin have resulted in significant reductions in recurrent urinary tract infections.

CONCLUSION: Despite clinical trials showing the efficacy of cranberry in preventing urinary tract infections, the actual antiadhesion activity and concentration of active proanthocyanidins in commercially available supplements is highly variable. In this study, several products contained virtually no active cranberry compounds. The clinical significance of this suggests that, although some are very potent, not all cranberry supplements have sufficient active compound to potentially achieve biologically relevant outcomes for urinary tract infection prevention. Although the benefits of utilizing cranberry for the maintenance of urinary tract health are

TABLE

Comparison of cranberry products with PAC level, antiadhesion activity of the whole product, and antiadhesion of the isolated PACs

Product	PAC level, mg/g	Antiadhesion (MIC) whole product, mg/mL	Antiadhesion (MIC) of PACs, μg/mL
1	25.4	3.5-7.5	156
2	4	Negative	5000
3	4	0.60	312
4	175	0.47	78
5	1.2	Negative	2496
6	1.4	Negative	2496
7	0.56	Negative	312–624

MIC, minimal inhibitory concentrations; *PAC*, proanthocyanidin.

Chughtai. Commercial cranberry dietary supplements. Am J Obstet Gynecol 2016.

definitely warranted because of resistance issues associated with antibiotic use, both physicians and patients alike need to be aware of the variability in quality of supplements available to consumers. Additionally, there needs to be stricter guidelines on the labeling and claims of these herbal medications. ■

Bilal Chughtai, MD
Dominique Thomas, BS
Department of Urology
Weill Cornell Medical College/New York Presbyterian Hospital
New York, NY
bic9008@med.cornell.edu

Amy Howell, PhD
Marucci Center for Blueberry Cranberry Research
Rutgers University
Chatsworth, NJ

The authors report no conflict of interest.

REFERENCES

1. Barber AE, Norton JP, Spivak AM, Mulvey MA. Urinary tract infections: current and emerging management strategies. Clin Infect Dis 2013;57:719-24.
2. Dieter AA. Cranberry capsules (2 taken twice daily for an average 38 days) reduce the risk of postoperative urinary tract infection in women undergoing benign gynaecological surgery involving intraoperative catheterisation. Evid Based Med 2015;20:137.
3. Sanchez-Patan F, Bartolome B, Martin-Alvarez PJ, Anderson M, Howell A, Monagas M. Comprehensive assessment of the quality of commercial cranberry products. Phenolic characterization and in vitro bioactivity. J Agric Food Chem 2012;60:3396-408.
4. Feifer AH, Fleshner NE, Klotz L. Analytical accuracy and reliability of commonly used nutritional supplements in prostate disease. J Urol 2002;168:150-4; discussion 154.
5. Foo LY, Lu Y, Howell AB, Vorsa N. A-type proanthocyanidin trimers from cranberry that inhibit adherence of uropathogenic P-fimbriated *Escherichia coli*. J Nat Prod 2000;63:1225-8.

 http://dx.doi.org/10.1016/j.ajog.2016.03.046

Self-reported human papillomavirus vaccination does not have an impact on the risk for high-grade cervical intraepithelial neoplasia among women referred for colposcopy

OBJECTIVE: Human papillomavirus (HPV) vaccination should reduce the risk for high-grade cervical intraepithelial neoplasia (CIN2+) among women with abnormal Papanicolau tests by reducing the proportion with HPV16/18, provided vaccination was prior to HPV exposure.[1-4] Limited data support this concept.[5] We aimed to estimate the prevalence of self-reported vaccination among women referred for colposcopy and to assess the vaccine impact on the prevalence of CIN2+ on final pathology.

STUDY DESIGN: We reviewed a retrospective cohort of women who were age eligible for the HPV vaccine (26 years old or younger in 2006 when the vaccine was approved by the Food and Drug Administration) and were undergoing colposcopy at Barnes-Jewish Hospital (St Louis, MO) between 2008 and 2013. Vaccine history was obtained by self-report. Vaccine trends were compared using the Cochran-Armitage trend test. Stepwise logistic regression was used to evaluate correlates of HPV vaccination and the association between HPV vaccine and high-grade CIN2+.

RESULTS: Among 701 patients with recorded vaccine histories, 102 (15%) reported HPV vaccination, although the median number of doses received was 1. Over 6 years, vaccination rates increased from 13% to 26% ($P = .0063$). Sociodemographic and clinical characteristics by self-reported HPV vaccination status are listed in the Table. Among vaccinated women, 54% were white, median number of lifetime sexual partners was 7, 45% were cigarette smokers, and 6% were human immunodeficiency virus positive. Most were referred for cytology read as low-grade squamous intraepithelial lesion (47%), followed by atypical squamous cells of undetermined significance and high-risk HPV (25%) and high-grade squamous intraepithelial lesion (18%). Compared with unvaccinated women, vaccinees were younger (mean age 24 years vs 25 years, $P = .037$) and more often white ($P = .02$), with fewer pregnancies (median gravidity 1 vs 2, $P = .001$). A total of 470 biopsies and 430 endocervical curettages were performed. In the vaccinated group, 24% had CIN2+ on colposcopic biopsy compared with 27% in the unvaccinated cohort ($P = .928$). Self-reported vaccination was not associated with a lower risk of CIN2+ (odds ratio [OR], 0.86, 95% confidence interval [CI], 0.53−1.41, $P = .546$]. Compared with women with lesser results, a higher proportion of women with CIN2+ were white (48% vs 37%, OR, 1.57, 95% CI, 1.12−2.20, $P = .008$) and presented with higher-grade abnormal Papanicolau smears (OR, 5.96, 95% CI, 3.92−9.06, $P < .001$). After adjusting for those factors that were significant (race, abnormal Papanicolau) or marginally significant (age and smoking), self-reported vaccination remained not associated with a lower risk of CIN2+ (OR, 0.81, 95% CI, 0.48−1.38, $P = .438$).