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Systematic review with meta-analysis: Cranberry-containing products are associated with a protective effect against urinary tract infections

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Context

Urinary tract infection (UTI) is a common clinical problem that often recurs, leading to the institution of preventive measures for recurrent UTI (rUTI) (1, 2). Antimicrobial prophylaxis is highly effective, but risks adverse effects and induction of resistance (1, 2). These considerations and widespread increases in antimicrobial resistance have intensified interest in alternative means of preventing UTIs, such as cranberry products. However, few well-designed clinical trials were available for analysis in the last Cochrane review of cranberry for the prevention of rUTI in 2008 (3). Wang and colleagues have re-evaluated this issue, adding several trials and an analysis of factors influencing efficacy of cranberry in preventing UTI: subject characteristics, type of cranberry product, amounts of proanthocyanidin (PACs; putative active ingredient), dose and dosing interval.

Methods

This systematic review followed PRISMA guidelines. Two authors Medline- and manually-searched randomized controlled trials comparing cranberry products vs placebo or nonplacebo control for prevention of UTI reporting outcomes as incidence of UTI. Four authors conducted data extraction and quality assessment of type of study and design, study population characteristics, interventions and controls, UTI definition, outcomes, and subject loss to follow-up. Analysis tools were Cochrane risk of bias tool, R2.11.1 statistical software, Galbraith and funnel plots; risk-ratios, heterogeneity, random effects summary estimates, sensitivity analyses, and subgroup analyses with meta-regression were performed.

Findings

Thirteen trials involving 1616 subjects were qualitatively evaluable. Five subgroups were defined: women with rUTI, elderly patients, patients with neurogenic bladder, pregnant women, and children. The form, dose, dosing interval, and PAC content of cranberry products varied considerably. Cranberry juice was used in 9/13 trials. Ten trials comprising 1494 subjects reported cumulative incidence of UTI and were quantitatively analyzed. One trial (4) with unusually low control UTI rates was an outlier. Excluding this trial, cranberry products were effective in preventing rUTI (RR 0.62, 95% CI 0.49–0.80), especially in

Competing interests: none

women with rUTI, female populations, children, people using cranberry juice and dosing more than twice daily.

Commentary

Increasing resistance to traditional first line antimicrobials for UTI and new understanding of how rapidly and persistently resistance develops after treatment of UTI (5) have narrowed options for treatment of acute UTI in women (6, 7). This has important downstream implications for prevention of rUTI. In the absence of guidelines, most experts recommend offering antimicrobial prophylaxis to patients experiencing 3 or more UTIs annually, based on individual and community antimicrobial resistance data (1).

Cranberry products are a potentially attractive non-pharmacological prophylaxis, and their putative mechanism, inhibition of bacterial attachment (2), is unlikely to induce antimicrobial resistance. However, in 2008, only 4/10 trials were sufficiently well designed for inclusion in a Cochrane meta-analysis (3), also precluding examining factors affecting efficacy.

Four years later, Wang and colleagues re-evaluated cranberry in preventing UTI, analyzing five additional trials and key clinical parameters influencing efficacy: dose, frequency of administration, form of cranberry, and subject characteristics. Their findings of protective effects and particular efficacy in women with rUTI confirm the 2008 Cochrane findings (3). Subgroup analyses showed better efficacy with cranberry juice than cranberry tablets or capsules, or with dosing more than twice daily. These findings are biologically logical and most relevant for clinical practice. The active ingredient(s) in cranberry remains unclear, and bioavailability and pharmacokinetics of non-food cranberry products are generally unknown. Pending more information about mechanism of action of cranberry in preventing UTI, additional studies of efficacy, and dose response studies, it may be prudent to suggest cranberry juice or foods, dosed as frequently as tolerated, for patients interested in trying cranberry products for prevention of rUTI.

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