

## Conflicts of interest

None declared.

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# Recurrent urinary tract infections in older people: the role of cranberry products

Urinary tract infections (UTI) are the commonest bacterial infection in older people. Half of all women experience at least one UTI and the risk increases with age [1]. The present management of recurrent urinary tract infection is prophylaxis with low-dose, long-term antibiotics. However, there is a growing reluctance to prescribe antibiotics unless absolutely essential because of fears about antimicrobial resistance. So the recent resurgence in interest in the potential role of cranberry products is timely.

Cranberries contain tannins called proanthocyanidins which are stable phenolic compounds exhibiting potent *in vitro* anti-adhesion activity against both antibiotic-sensitive and -resistant strains of P-fimbriated *Escherichia coli* [2]. While preventing bacterial adherence to uroepithelial cells is believed to be the primary mechanism, a direct mild antimicrobial activity against other bacteria causing UTI has been reported. There is no evidence to support the use of cranberry products as treatment of a symptomatic UTI [3].

However, the renewed interest in cranberry has been prompted by a recent (2008) Cochrane review *Cranberries for preventing urinary tract infections* which assessed the evidence in different susceptible subpopulations including infants, pregnant women, older people and patients with diabetes and long-term catheters [4]. The review concluded that cranberry products might decrease the number of symptomatic UTIs in younger women with recurrent UTI, but found insufficient evidence in other subpopulations. This conclusion was mainly based on two good quality randomised trials in younger women (mean ages 32 and 43 years) with recurrent UTI which found that 6–12 months of treatment with cranberry significantly reduced symptomatic UTI compared to placebo [5, 6]. The Scottish Intercollegiate Guideline (number 88, 2006) recommends that ‘women with recurrent UTI should be advised to take cranberry products to reduce the frequency of recurrence’. The number needed to treat (NNT) with cranberry products to prevent one symptomatic UTI in 6 months was estimated at 6.4.

Only three randomised trials or quasi-randomised trials have been done in older people comparing four or more weeks of cranberry against placebo and have found no reduction in the incidence of symptomatic UTI. A study of 192 women (mean age 78 years) from a long-term care facility and 9 housing complexes found no significant differences between groups for symptomatic UTI over 6 months but a significant reduction in asymptomatic bacteriuria with pyuria in the cranberry group [7]. This commercially funded trial was criticised for its randomisation and blinding procedure because of a significant baseline imbalance in group characteristics in which UTI was considerably more frequent in the placebo group at baseline. An 8-week crossover study of 38 participants (mean age 81 years) reported fewer occurrences of bacteriuria when taking cranberry juice, but only 7 participants were included in final analysis [8]. Even if the suggested reduction in asymptomatic bacteriuria is genuine, it seems of little value as treating asymptomatic bacteriuria in older people is not recommended because doing so neither reduces future symptomatic UTI nor mortality [9]. In fact, asymptomatic bacteriuria is common in older people and is found in almost 25% of those in institutional care [1]. The only trial in older people to use symptomatic UTI as the primary outcome randomised 376 hospital patients (mean age 81.4 years, 32% male) to either cranberry juice or placebo for 35 days or until hospital discharge. This study was insufficiently powered to detect a reduction in symptomatic UTI with cranberry juice as the incidence of UTI in the placebo group was lower than that reported in longer term studies [10].

A 2004 Cochrane review *Antibiotics for preventing recurrent urinary tract infection in non-pregnant women* found that prophylactic antibiotics were highly effective in non-pregnant women with a NNT of 1.85 to prevent one recurrence during 6- to 12-months treatment. Unfortunately, however there was a high relative risk of severe side-effects (1.58; 95% CI 0.47–5.28) [11]. Only one head-to-head trial has compared the effectiveness of a low-dose antibiotic (100 mg trimethoprim) directly against cranberry. In a 6-month double blind study of

older women (mean age 63 years) with recurrent UTI, there was a modest but non-significant advantage of antibiotics over cranberry. The relative risk of a symptomatic UTI during treatment was 1.62 in the cranberry group but the relative risk of withdrawals due to side-effects tended to be lower than that in the trimethoprim group [12]. The median time to recurrence of UTI was not significantly different between the groups. Although less effective than low-dose antibiotics, cranberry products may still have a role in older people with recurrent UTI.

Cranberry products are well tolerated in short-term studies; however, their tolerability in longer term studies particularly in older people may be poor with studies reporting withdrawal rates as high as 30–40% [7, 8, 10]. A further restriction in older people, who are potentially more likely to require anticoagulation, is the probable interaction between cranberry and warfarin leading to elevated international standardised ratios [13]. There is little consensus on which product and what dose of cranberry products should be used. There appears to be a dose-related effect on the virulence of *E. coli* in urine [14] and cranberry products may be more effective in people with glomerular filtration rates (GFR) >75 ml/h [15]. Many older people have lower GFRs potentially requiring higher doses of cranberry product to achieve sufficient urinary concentrations. Tablets or capsules (1:30 parts concentrated juice) may be more acceptable in the longer term as they are cheaper, have equivalent efficacy to juice and are more convenient to deliver adequate doses [6].

The superior efficacy of antibiotics in preventing recurrent UTI comes at the cost of adverse effects on gut microflora which increases the risk of infection with *Clostridium difficile* and antimicrobial-resistant bacteria. Prophylaxis with low-dose antibiotics has only a modest advantage over cranberry tablets in recurrent UTI. Cranberry products are natural, affordable and available without prescription. Advice regarding potential benefits of cranberry products, especially in older women, will enable people to make informed choices. Future research should look at longer studies and compare the acceptability and efficacy of cranberry tablets to different prophylactic antibiotics in older people.

## Conflicts of interest

None.

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