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COCHRANE COMMENTARIES

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Cranberries for the prevention of urinary tract infections

What is this review about?

The effectiveness of cranberry products (juice, tablets, capsules and syrup) in preventing urinary tract infections compared with placebo or any other treatment.

What are the findings?

Data included in the meta-analyses (Fig. 1) showed that, compared with placebo, water or no treatment, cranberry products did not significantly reduce the occurrence of symptomatic urinary tract infection (UTI) overall (RR 0.86, 95% CI 0.71-1.04) or for any of the subgroups: women with recurrent UTI (RR 0.74, 95% CI 0.42-1.31); older people (RR 0.75, 95% CI 0.39-1.44); pregnant women (RR 1.04, 95% CI 0.97-1.17); children with recurrent UTI (RR 0.48, 95% CI 0.19-1.22); cancer patients (RR 1.15 95% CI 0.75-1.77); or people with neuropathic bladder or spinal injury (RR 0.95, 95% CI: 0.75-1.20). Overall, there were moderate differences in findings across trials (measured by heterogeneity $I^2 = 55\%$). Gastrointestinal side effects were no more or less likely from cranberry products compared with placebo/no treatment (RR 0.83, 95% CI 0.31-2.27). Many studies reported low compliance and high withdrawal/dropout problems which they attributed to palatability/acceptability of the products, primarily the cranberry juice. Most studies of other cranberry products (tablets and capsules) did not report how much of the 'active' ingredient the product contained, and therefore the products may not have had enough potency to be effective.

What are the findings based on?

This updated review included a total of 24 studies (six crossover studies, 11 parallel group studies with two arms; five with three arms, and two studies with a factorial design) with a total of 4473 participants. Overall, the quality of the studies was good, but only five studies undertook power calculations which may mean that the others were too small to detect a difference. Ten studies were included in the 2008 update, and 14 studies have been added to this update. Thirteen studies (2380 participants) evaluated only cranberry juice/ concentrate; nine studies (1032 participants) evaluated only cranberry tablets/capsules; one study compared cranberry juice and tablets; and one study compared cranberry capsules and tablets. The comparison/control arms were placebo, no treatment, water, methenamine hippurate, antibiotics, or lactobacillus. Eleven studies were not included in the metaanalyses because either the design was a cross-over study and data were not reported separately for the first phase, or there was a lack of relevant data for the outcomes we were interested in. Prior to the current update it appeared there was some evidence that cranberry juice may decrease the number of symptomatic UTI over a 12-month period, particularly for women with recurrent UTI. The addition of 14 further studies suggests that cranberry juice is less effective than previously indicated. Although some of small studies demonstrated a small benefit for women with recurrent UTI, there were no statistically significant differences when the results of a much larger study were included.

Implications for practice

• The current body of evidence suggest that cranberry products (either in juice or as capsules/tablets) compared with placebo provides no benefit in most populations groups, and the benefit in some subgroups is likely to be very small.

• The large number of dropouts/withdrawals from some of the studies indicates that cranberry products, particularly in juice form, may not be acceptable over long periods of time.

• Cranberry capsules or tablets may overcome some issues with treatment adherence, but from current evidence they do not appear to be any more effective that the juice.

• One of the drawbacks of the studies of non-juice products such as capsules is that few of the triallists reported how much 'active' ingredients (if any) were in the tablets or capsules they used. Until there are more studies of products containing enough of the active ingredient, measured in a standardized way, cranberry products cannot be recommended for preventing UTI.

Clinical perspective

No definitive mechanism of action has been established for cranberry in the prevention or treatment of UTI. However, research suggests that cranberries prevent bacteria (particularly *Escherichia coli*) from adhering to uroepithelial cells that line the wall of the bladder. Without adhesion, *E. coli* cannot cause infection. One of the potential problems in demonstrating effectiveness is that the active 'ingredient' in cranberry products (Proanthocyanidin – PAC) is only effective for around 10–12 h. For cranberry juice to be effective, a patient would need to consume two glasses a day for an indefinite

Study or subgroup	Cranberry product n/N	Placebo/control n/N	Risk Ratio M-H,Random,95% Cl	Weight	Risk Ratio M-H,Random,95% Cl	
1 Women with recurrent Barbosa-Cesnik 2011	JTIs 31/155	23/164		8.7%	1.43 [0.87, 2.33]	
Kontiokari 2001	12/46	19/45		7.0%	0.62 [0.34, 1.12]	
Sengupta 2011	2/21	4/13		1.5%	0.31 [0.07, 1.46]	
Stothers 2002	19/100	16/50		7.3%	0.59 [0.34, 1.05]	
Subtotal (95% Cl) Total events: 64 (Cranber Heterogeneity: Tau ² = 0.1 Test for overall effect: Z =	322 rry product), 62 (Place 20; Chi ² = 8.50, df = = 1.03 (P = 0.30)	272 ebo/control) 3 (P = 0.04); I ² =65%	•	24.5 %	0.74 [0.42, 131]	
2 Elderly men and women McMurdo 2005	7/187	14/189	_ . _	3.9%	0.51 [0.21, 1.22]	
PACS Study 2008	13/20	12/17	+	9.8%	0.92 [0.59, 1.44]	
Subtotal (95% Cl) Total events: 20 (Cranber Heterogeneity: Tau ² = 0.) Test for overall effect: Z =	207 ry product), 26 (Place 12; Chi ² = 1.92, df = = 0.87 (P = 0.38)	206 ebo/control) 1 (P = 0.17); ² =48%	•	13.7 %	0.75 [0.39, 1.44]	
3 People with neuropathi Lee 2007	c bladder/spinal inju 67/153	ries 71/152	-	15.1%	0.94 [0.73, 1.20]	
Waites 2004	10/26	8/22		5.2%	1.06 [0.51, 2.21]	
Subtotal (95% Cl) Total events: 77 (Cranber Heterogeneity: Tau ² = 0.1 Test for overall effect: Z =	179 rry product), 79 (Place 0; Chi ² = 0.09, df = 1 = 0.44 (P = 0.66)	174 ebo/control) (P = 0.76); I ² =0.0%	•	20.2%	0.95 [0.75, 1.20]	
4 Pregnant women Essadi 2010	182/258	194/286	-	18.7%	1.04 [0.93, 1.16]	
Wing 2008	2/67	0/63		0.4%	4.71 [0.23, 96.15]	
Subtotal (95% Cl) Total events: 184 (Cranb Heterogeneity: Tau ² = 0.1 Test for overall effect: Z =	325 erry product), 194 (Pl); Chi ² = 0.98, df = 1 = 0.72 (P = 0.47)	349 lacebo/control) . (P = 0.32); I ² =0.0%	t	19.1%	104 [0.93, 117]	
5 Children Ferrara 2009	5/27	18/27		4.3%	0.28 [0.12, 0.64]	
Salo 2010	20/126	28/129		8.2%	0.73 [0.44, 1.23]	
Subtotal (95% Cl) Total events: 25 (Cranber Heterogeneity: Tau ² = 0.1 Test for overall effect: Z =	153 ry product), 46 (Place 34; Chi ² = 3.73, df = = 1.54 (P = 0.12)	156 ebo/control) 1 (P = 0.05); I ² =73%	•	12.5%	0.48 [0.19, 1.22]	
6 Radiotherapy patients Cowan 2012	26/59	23/60	-	10.1%	1.15 [0.75, 1.77]	
Subtotal (95% Cl) Total events: 26 (Cranber Heterogeneity: not applic Test for overall effect: Z =	59 ry product), 23 (Place able = 0.63 (P = 0.53)	60 ebo/control)	•	10.1%	115 [0.75, 177]	
Total (95% Cl) Total events: 396 (Cranb. Heterogeneity: Tau ² = 0. Test for overall effect: Z = Test for subgroup differe	1245 erry product), 430 (Pl 05; Chi ² = 25.64, df : : 1.53 (P = 0.13) nces: Chi ² = 5.27, df	1217 lacebo/control) = 12 (P = 0.01); I ² =53% f = 5 (P = 0.38), I ² =5%	•	100.0%	0.86 [0.71, 1.04]	
		0.01 Less with cranberry	0.1 1 10 Less with placebo/co	100 ontrol		

Fig. 1 Risk of one or more UTI during follow up, for trial participants taking cranberry products versus placebo/control.

period of time. Furthermore, cranberry juice is calorific, some people find it unpalatable (and incur side effects such as gastrointestinal upset), and is likely to cost a not insubstantial sum. For cranberry juice to be most effective, a patient would need to be committed to the regimen and not have any other contra-indications (e.g. diabetes). At this time, tablets and capsules should not be recommended unless they clearly contain the recommended amount of PAC (at least 36 mg/day).

Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections. *Cochrane Database of Systematic Reviews* 2012, Issue 10. Art. No.: CD001321. DOI: 10.1002/14651858.CD001321.pub5.

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