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Feasibility of Cranberry Capsule Administration and Clean Catch Urine Collection among Long-Term Care Residents

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To the Editor

Urinary tract infection (UTI) is a common bacterial infection in nursing home residents, and there is no accepted prevention strategy. Cranberry products represent a non-antimicrobial method for UTI prevention. Among older adults, cranberry juice has demonstrated reductions in bacteriuria.^{1–3} However, daily ingestion of large volumes of cranberry juice is challenging for long-term care residents making cranberry capsules an appealing alternative. The goal of this pilot study was to determine the feasibility of administering cranberry capsules and non-invasively collecting urine samples.

Four dementia units participated in this study. Exclusion criteria included: 1)chronic indwelling catheter, 2)residence <4 weeks, 3)prednisone therapy, 4)active UTI symptoms, 5)terminal, 6)end stage renal disease, 7)<60 years old, 8)chronic suppressive antibiotic therapy, 9)history of kidney stones, 10)unable to provide baseline urine, and 11)warfarin therapy.⁴ Surrogates of residents were approached for verbal consent. Chart review and clean catch urine specimens were performed at baseline and monthly for 6 months. Participants were assigned to one of three arms by a random number generator: 1)no capsules, 2)one capsule daily, or 3)one capsule twice daily. Each capsule of TheraCran® contained 16.25mg proanthocyanidins. The Yale Human Investigation Committee approved this study. The ClinicalTrials.gov identifier is NCT00596635. The primary outcomes were the rate of successful cranberry capsule administration and the collection of uncontaminated urine specimens. Additional outcomes included the incidence of possible adverse outcomes and preliminary effectiveness. Analyses with the t-test, Fisher's Exact test, and log-rank test were conducted using SAS 9.1.

Of 123 eligible residents, 56 enrolled (45.5% participation rate) and were followed from 9/2007-6/2008. The mean age of participants was 87 years, 82.1% were female, and all were Caucasian. Half (28/56;50%) had a UTI in the past year. Approximately half (31/56;55%)

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were able to provide clean catch urines monthly for five months with 24 (42%) being able to provide urine for all six months. Overall, 207(86%) of 240 scheduled monthly urine collections were successfully completed. Among the 263 urine cultures obtained, 39(15%) were negative (no growth), 85(32%) were contaminated (≥ 3 organisms), and 139(53%) were positive (103—1 organism, 36—2 organisms). Most participants had at least one contaminated urine (40/56;71%). *E. coli* was present at least once from half the participants (28/56;50%). Thirteen participants were treated for UTI during the study which resulted in study termination. Out of a total of 237 scheduled doses, only 7 (3%) were missed or refused. Six participants (10.5%) had an adverse event possibly attributable to cranberry capsules (i.e., nausea, vomiting, and/or diarrhea).

Seventeen participants were randomized to the control arm, 20 to the 1 capsule daily arm, and 19 to the 1 capsule twice daily arm. *E. coli* bacteriuria prior to randomization was similar in the control and treatment arms, 29% and 28%, respectively, and remained similar during the intervention period, 47% and 51%, respectively. Time to first *E.coli* positive culture or to first urine culture $>100,000$ cfu/ml was no different between the three groups and history of UTI did not change this association (see Table 1). The incidence of treated UTI was 4.66 per 100 person-months and was not significantly different between the control and treatment arms.

This study demonstrates that a cranberry UTI prevention study is feasible to conduct in long-term care. Although the incidence of contaminated urine specimens was high, negative or positive clean catch urines were obtained in 68% of attempts. Since maintaining oral hydration is challenging⁵ and many residents dislike the acrid flavor and volume of cranberry juice necessary,^{3, 6} it is not an optimal UTI preventive strategy. Cranberry tablets reduce UTI among spinal cord injured patients with neurogenic bladder.⁷ In this small sample size, efficacy of cranberry capsules was not demonstrated among long-term care residents; however, the primary goal of this study was to determine feasibility.

The results of this pilot study have implications for designing a definitive trial. The inability to follow all participants for the full six months reflects the vulnerability of the population. Future studies will require unique recruitment strategies since loss to follow up is common in this population.⁸ In addition, since there was no trend towards efficacy of cranberry capsules, it is possible that the cranberry capsules were under-dosed. Escalating doses of proanthocyanidins (up to 108mg) were increasingly effective at inhibiting *E.coli* adherence to uroepithelium.^{9–10} Additional clinical studies of higher doses of proanthocyanidins are warranted to identify the optimal dose of cranberry capsules for prevention of bacteriuria and UTI among long-term care residents. Such a preventive strategy could be well tolerated with few side effects and have a major impact on long-term care.

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Table 1

Time to first <i>E. coli</i> event						
	N	N1	Total follow-up time (days)	Rate (100 person-month)	Rate ratio 95% CI	P-value
Overall	Control	17	8	1903	12.78	1.00
	1 capsule	20	8	1817	13.38	1.04 (0.34–3.20)
	2 capsules	19	12	1972	18.49	1.44 (0.54–4.06)
History of UTI	Control	9	3	638	14.29	1.00
	1 capsule	12	3	1088	8.38	0.59 (0.08–4.38)
	2 capsules	12	6	1251	14.58	1.02 (0.22–6.30)
No History of UTI	Control	8	5	1265	12.02	1.00
	1 capsule	8	5	729	20.85	1.74 (0.40–7.54)
	2 capsules	7	6	721	25.30	2.10 (0.54–8.72)
Time to first urine culture with any organism >100,000 cfu/ml						
	N	N1	Total follow-up time (days)	Rate (100 person-month)	Rate ratio 95% CI	P-value
Overall	Control	17	12	1488	24.51	1.00
	1 capsule	20	13	1453	27.20	1.11 (0.47–2.66)
	2 capsules	19	14	1890	22.51	0.92 (0.39–2.17)
History of UTI	Control	9	5	428	35.51	1.00
	1 capsule	12	6	872	20.92	0.59 (0.15–2.44)
	2 capsules	12	8	1169	20.80	0.59 (0.17–2.28)
No History of UTI	Control	8	7	1060	20.07	1.00
	1 capsule	8	7	581	36.63	1.82 (0.55–6.10)
	2 capsules	7	6	721	25.30	1.26 (0.35–4.38)