

Original Research Article

Role of Cranberry Juice in Improving Symptoms of Recurrent UTI in Women of Reproductive Age Group

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ABSTRACT

Objective: To evaluate the efficacy of cranberry juice in improving urinary symptoms in women presenting with recurrent Urinary Tract Infection (UTI).

Methods: This was an open label single arm study eligible study, participants satisfying the inclusion and exclusion criteria were enrolled in Department of Gynaecology, Muhammad Medical College (MMCH), Mirpurkhas, Sindh, Pakistan from March, 2011 to February, 2015. After satisfying the inclusion and exclusion criteria, the eligible participants were recruited in this prospective clinical trial. The clinical trial has two study periods; for a period of one year the recruited study participants were treated as usual (a Pre Cranberry juice period) and after a washout period of two weeks the study participants were prescribed cranberry juice and followed for a period of one year. The recurrence of UTI and organisms causing UTI was recorded for each episode of infection. For the present study ethical approval was granted by the institutional ethical review committee of Muhammad Medical College Hospital (MMCH), Pakistan. Written informed consent was obtained from all participants prior to recruitment. The data was analysed using SPSS version 21 (IBM, Chicago, IL).

Results: One hundred eligible women satisfying the inclusion and exclusion criteria were prescribed cranberry juice to use. There was significant difference in overall recurrence for Urinary Tract Infection during one year of follow up in the study population intervened with the Cranberry Juice was 30% compared to 50% when no Cranberry Juice was prescribed (p -value < 0.05). Thirty cultures confirmed recurrent UTI episodes were observed. Escherichia Coli was the most common causative organism for infection at enrolment (74%) and recurrence (83.5%). No serious adverse events occurred in the study participants during the course of the trial.

Conclusion: Among healthy sexually active women intake of Cranberry Juice has been found effective in reducing the incidence of recurrent UTI at 1 year follow up.

Keywords: Cranberry Juice, Escherichia Coli, Recurrence, Urinary Tract Infection

INTRODUCTION

The prevalence of Urinary Tract Infection (UTI) among women has been reported as around 60%.^[1] Thus, UTI has a significant burden of disease as commonly affecting young healthy women of reproductive age group.^[2] Among risk factors, sexual activity has been reported as one of the most important risk factor for UTI.^[3] The recurrence of UTI is quite common, with one third women in age group 25-29 years or greater than 55 years showed recurrence in the following year.^[4]

Considering the high recurrence rate, antimicrobial prophylaxis are prescribed, but considering the increased emerging resistance of antimicrobial agents an alternative is desirable for improved clinical outcomes.^[5]

Considering the increased cost of care on account of repeated infections and antibiotic resistance, the treatment of UTI is much of concern for clinicians.^[6-7] An efficacious, safe with limited adverse events and increased compliant treatment modality is required. Ingestion of Cranberry products

have used as a preventive approach since decades. [8-9] An in vitro study has reported efficacy of cranberry, having inhibiting P-fimbriated uropathogen stains of *Escherichia coli*, being a critical step for UTI. [10-12]

The efficacy of cranberry juice having reducing the recurrence of UTI has been reported in clinical trials. [13-17] Thereby, there has been a role of cranberry juice or product in decreasing the incidence of recurrent UTI. However, in some clinical trials the results did not demonstrated statistically significant difference in UTI recurrence between cranberry products and placebo. [18-19] Thereby, controversies still existed in prescribing cranberry juice for prevention against recurrent UTI. Furthermore, there is no evidence available from Pakistan with clinical trial being conducted to evaluate the efficacy of cranberry juice, a product which is gaining popularity among physicians for prescription. Considering, this a clinical study was conducted with an objective to evaluate the efficacy of cranberry juice in reducing the recurrence of UTI among women of reproductive age group, a population more commonly being affected. The findings of the study will provide useful guidelines to clinicians related to prescription of cranberry juice among women of reproductive age group with history recurrent UTI.

METHODS

The open label single arm prospective study was conducted at the Department of Gynaecology, Muhammad Medical College (MMCH), Mirpurkhas, Sindh, Pakistan from March, 2011 to February, 2015. Muhammad Medical College Hospital having established in 1999, located 6 km just outside Mirpurkhas, Sindh. The hospital has a well established Gynaecological department and women residing in both rural and urban areas nearby visits for routine ante natal checkups, deliveries and gynaecological problems.

The eligible study participants satisfying the inclusion and exclusion criteria were enrolled in this trial after written informed consent. The inclusion criteria were as follows; premenopausal women with age in the range of 19 to 45 years, history of episodes of three or more clinically confirmed diagnosis of UTI in the past year agree to avoid other cranberry related product for the duration of one year of the trial. Pregnant or lactating women or those having psychiatric illness were excluded. Moreover, women with pre-diagnosed anatomical abnormalities, urolithiasis, diabetes, malignancy, vaginitis or cystitis, having used antibiotics in the last two weeks and intolerance to cranberry products were excluded.

The eligible participants were recruited in this prospective clinical trial. The clinical trial has two study periods; for a period of one year the recruited study participants were treated as usual (a Pre Cranberry juice period) and after a washout period of two weeks the study participants were prescribed cranberry juice and followed for a period of one year. Thereby, each study participant was followed for the duration of two year in this prospective clinical study. Thereby, in this study each participant was their own control. The intervention (cranberry juice) was prescribed as extracts 250 mg in sachets with each sachet containing 40% of cranberry juice extracts.

The data was recorded on a pre-designed proforma. The socio demographic information (i.e. age, marital status, ethnicity, education and occupation) were recorded. The recurrence of UTI and organisms causing UTI was recorded for each episode of infection. For the confirmation of infection, a clean voided midstream urine sample was obtained for culture whenever the study participants in this trial complaint of symptoms of UTI (i.e. urgency or increased frequency of urination, dysuria, haematuria, pyrexia, and flank or back pain) and culture greater than 10^5 cfu/ml were considered as infection (event).

UTI is considered as a separate event, if urine culture reported no bacterial growth between two cultures with positive infection. Moreover, the adverse events reported during the course of cranberry juice intake were also recorded.

For the present study ethical approval was granted by the institutional ethical review committee of Muhammad Medical College Hospital (MMCH), Pakistan. Written informed consent was obtained from all participants prior to recruitment having explained comprehensively the process involved, intervention given (Cranberry juice) and benefits/ risks of being the part this research. It was ensured that anonymity and confidentiality of recruited participant's data was maintained throughout the research and no unauthorized person had an access to the data. The participants had a right to withdraw at any point of this prospective study.

Data Analysis

The data was analysed using SPSS version 21 (IBM, Chicago, IL). Descriptive statistics were performed. The qualitative variables were presented as frequency/ percentage whereas the quantitative variables were presented as mean and standard deviation. A paired analysis was performed and mean episodes of UTI were compared between the two periods using Paired T test. The McNemar test was used to compare the proportion between the two periods.

RESULTS

A total of 335 women were screened for participation; 40 were unwilling to participate, and 150 were not eligible. Of the 145 enrolled women, 45 were lost to follow-up. Thus, remaining 100 eligible participating women having recruited in this prospective trial and followed for the study duration were analysed.

The demographic characteristics of the study participants were shown in *table 1*. Majority (48%) in age group (20-30 years), followed by 31-40 years (41%), 41-45 year

category (7%) and least in less than 20 years age group (4%). Majority (80%) of women were married and belonged to poor socio economic status (45%). Moreover, the highest proportion of participants enrolled has education of eight years or less (48%) followed by 9-12 years (28%). Furthermore, majority (78%) were house wives and non working status. Majority of the women enrolled in the study belong to the ethnic category Sindhi (75%), followed by Urdu speaking (10%), Punjabi (8%), Balochi (5%) and Pakhtun (2%).

Table 1: Characteristics of the Study Participants

Characteristics of Study Participants	n (%)
Age categories (Years)	
< 20 years	4 (4)
20-30 years	48 (48)
31-40 years	41 (41)
41-45 years	7 (7)
Marital Status	
Single	20 (20)
Married	80 (80)
Socioeconomic	
Poor	45 (45)
Middle	35 (35)
Upper	20 (20)
Education	
≤ 8 years	48 (48)
9 -12 years	28 (28)
> 12 years	24 (24)
Occupation	
House Wife	78 (78)
Working women	22 (22)
Residence	
Urban	78 (78)
Rural	22 (22)
Race	
Urdu Speaking	10 (10)
Sindhi	75 (75)
Punjabi	8 (8)
Pakhtun	2 (2)
Balochi	5 (5)

The *table 2* gives details of recurrence of UTI and causative organisms during the two trial period. The overall recurrence for UTI during one year of follow up when the study population intervened with the Cranberry Juice was 30% compared to 50% recurrence of UTI when no Cranberry juice was prescribed. There was significant reduction in the UTI infections a result of cranberry juice (p-value < 0.05). Moreover, there was also a significant reduction in the mean number of episodes of UTI between the two periods (4.1 ± 1.7 vs. 2.5 ± 1.3; p-value < 0.01). No

significant difference was observed in causative organism with E coli as a most common isolate for UTI in both treatment periods.

The figure 1 give details of the most common causative organism for infection at enrolment was Escherichia Coli (74%), followed by Staphylococcus saprophyticus

(6%), Enterococcus species (6%), Klebsiella species (5%), and Proteus mirabilis (3%). Moreover, the commonest organism for recurrent infection isolated was E coli (83.5%), followed by Staphylococcus saprophyticus (3.3%), Enterococcus species (3.3%), Klebsiella species (3.3%), and Proteus mirabilis (3.3%).

Table 2:Recurrence and bacterial strains causing UTI

Recurrence of Urinary Tract Infection	Pre Cranberry Juice (n = 100)	During Cranberry Juice (n = 100)	P-value
Overall Recurrence (%) at 1 Year Follow up	50 (50)	30 (30)	0.005
Mean Number of Episodes of UTI	4.1 ± 1.7	2.5 ± 1.3	0.001
Causative Organism			
E. Coli	44 (88)	25 (83.5)	0.74
Other bacteria	6 (12)	5 (16.5)	

Data presented as n (%) or Mean ± SD.

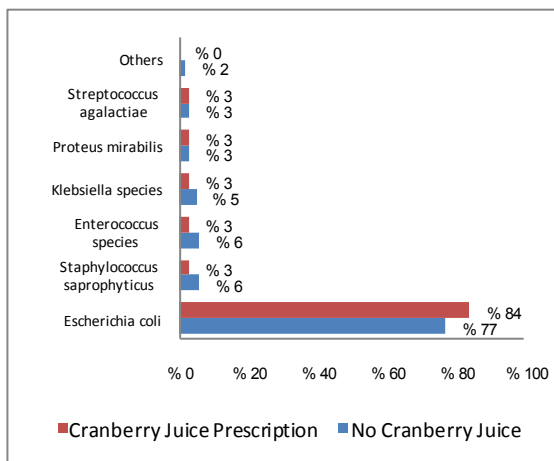


Figure 1: Distribution of bacterial organisms causing recurring UTI among study participants during two study periods

No serious adverse events occurred in the study participants during the period participants were prescribed cranberry juice. Minor adverse effects included primarily gastrointestinal (constipation, heartburn, loose stool), vaginal itching/ dryness, and migraine symptoms were reported. The proportions of women who reported minor adverse effects were 10 of 100 (10%).

DISCUSSION

The result of this open label single arm trial to evaluate the efficacy of cranberry juice in reducing the recurrence of urinary tract infection showed comparable results with other studies. In this study there was significant reduction around 20% in the UTI infections a result of cranberry juice

prescription. Moreover, there was also a significant reduction in the mean number of episodes of UTI between pre Cranberry and post Cranberry juice time periods (4.1 ± 1.7 vs. 2.5 ± 1.3 ; p -value < 0.01). Importantly, the study participants did not report any serious adverse effects and only minor adverse events were reported.

The findings of reduced UTI recurrence as a result of Cranberry juice intake are consistent with findings of the previous research. Clinical trials reported a significant decrease in recurrence of UTI as a result of prescription of Cranberry juice. [13,20] A randomised controlled clinical trial that recruited 150 women of age 21 to 72 years reported lower incidence of UTI recurrence as 20% in Cranberry juice group compared to placebo (32%). [14] A larger clinical trial that recruited slightly less than four hundred women of increased age (greater than 60 years) reported no significant difference in incidence of symptomatic UTI between the two study groups, placebo and Cranberry juice. [21] A meta-analysis has reported a significant risk reduction of 34% in the incidence of UTI at 12 months follow-up for participants having intake of cranberry juice. [9] The improved outcome in the form of reducing recurrent infections can be on account of the fact that Cranberry Juice contains ascorbic acid, which has also been suggested to prevent UTI. [21] It is also of importance that though

some women may find the cranberry taste being bitter but it is important for them to continue the oral intake of cranberry products and do not stop intake as compliance is of great importance in reducing the incidence of recurrent infection. Cranberry products in different forms are being available globally, and it's beneficial for patient to select the most appropriate one which they feel comfortable with.

Though antibiotics are believed to be of more advantage for the prevention of UTI but they are associated with more frequent adverse events and the micro-organism resistance is inevitable. [15] The common and frequent prescription of antibiotic leads to antibiotic resistant strains of micro-organisms. Thus, cranberry juice which never leads to induce antibiotic resistant bacteria or decreased efficacy. Another advantage of cranberry juice is its availability in oral form and ease of intake. However, there are also some issues related to the intake of cranberry juice. The most important and significant one is being the tolerance and compliance with intake for a longer duration of time. A study that recruited the pregnant women to evaluate the efficacy of cranberry juice reported that more than one third of the participating women (38.8%) did not complete the recommended intake of cranberry juice and withdrew from the clinical trial. [22] The most common adverse events reported were gastrointestinal symptoms (i.e. nausea, vomiting and diarrhoea) and dislike of taste. [22] However, the adverse events (i.e. gastrointestinal symptoms) were reported to be lower in other studies. One study reported only slightly more than 1% of gastrointestinal symptoms while another study reported no adverse event. [20,23] No studies have highlighted any serious adverse event with the intake of cranberry juice. The findings were consistent to the present clinical trial where no serious adverse event was reported. However, the present study does report the adverse event as 10% which were minor and did not let the participants

to leave the trial or stop taking the cranberry juice.

This was the first trial in Pakistan to evaluate the efficacy of Cranberry Juice to reduce the recurrence of UTI infections. However, in future a multicentre double blinded randomised controlled trial with adequate sample size in each arm of the trial should be conducted to better evaluate the effectiveness of the Cranberry Juice.

CONCLUSION

In conclusion, among healthy sexually active women intake of Cranberry Juice has been found effective in reducing the incidence of another UTI at 1 year follow up. Importantly, Cranberry Juice prescription was not related with the risk of serious adverse events. Thus, cranberry juice is a suitable and safer option for women with a risk of UTI.

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