

ORIGINAL RESEARCH

Cranberries for Preventing Recurrent Urinary Tract Infections in Uncircumcised Boys

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ABSTRACT

Background • Highly concentrated cranberry juice has long been considered to have protective properties against urinary tract infections (UTIs), on the basis of its content of cranberry proanthocyanidins, with A-type interflavan bonds.

Objective • This study intended to evaluate the benefits of a highly concentrated cranberry juice for the prevention of repeated episodes of UTI in uncircumcised boys.

Design • The study was a randomized, controlled trial.

Setting • The study took place at Taipei City Hospital, Renai and Zhongxing Branches (Taipei City, Taiwan).

Participants • Participants were 55 uncircumcised boys and 12 circumcised boys, aged 6 to 18 y, with histories of uncomplicated UTI, who were patients at the hospital.

Intervention • The uncircumcised boys were randomly divided into 2 groups: (1) group 1 (n = 28) took 4 oz (120 mL) daily of cranberry juice for 6 mo; and (2) group 2 (n = 27), the negative control group, drank a placebo juice for 6 months. The circumcised boys in group 3, a positive control group, also drank a placebo juice for 6 mo.

Outcome Measures • The time to UTI (ie, to the appearance of symptoms plus pyuria) was the main outcome. Asymptomatic bacteriuria, adherence to the treatment, and adverse effects were assessed at monthly visits.

Results • After 6 mo of a prophylactic treatment with cranberry juice, the incidence of bacteriuria, mainly *Escherichia coli*, as shown in urine cultures at $\geq 1 \times 10^5$, were 25% (7/28), 37% (10/27), and 33.3% (4/12) in groups 1, 2 and 3, respectively. The comparisons of the rate of prevention of a recurrence of UTI between group 1 and group 2 and between group 1 and group 3 showed that group 1 had fewer recurrent episodes of UTI. No children withdrew from the study. No adverse events or side effects were recorded.

Conclusions • Cranberry juice may reduce the number of repeated episodes of UTI in uncircumcised boys and may have beneficial effects against the growth of Gram-negative bacterial pathogens. Its preventive benefits against UTI in the uncircumcised boys were even higher than those of circumcision for the circumcised boys. (*Altern Ther Health Med.* 2016;22(6):20-23.)

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The risk of urinary tract infection (UTI) for a normal boy is 1%,¹ and approximately 20% of the children who experience one infection will have a another episode. Previous studies have reported that the rates of UTI were 10 to 20 times higher in uncircumcised than in circumcised boys.² Thus, circumcision in boys may reduce the risk of UTI, and that practice could be considered to be a part of UTI therapy.³

Retrospective studies have suggested that circumcision of newborn boys could reduce the frequency of male, early infantile UTIs by approximately 90%.⁴ In a study by Schoen et al,⁵ the incidence of UTI in the first year of life was 2.15% in uncircumcised males and 0.22% in circumcised males. Newborn circumcision resulted in a 9.1-fold decrease in the incidence of UTI during the first year of life as well as markedly lower UTI-related medical costs and rates of hospital admissions.⁵

Although treatment with long-term, low-dose antibiotics has the strongest evidence base as a treatment for UTI, its benefits are small, with growing antibiotic failure due to the emerging resistance of the bacteria.^{6,7} Also, for children with or without primary nonsevere reflux, antibiotic prophylaxis has not been shown to reduce the rate of recurrent febrile UTIs after the first episode.⁸ Therefore, given the lack of evidence on a positive benefit for using prophylactic antibiotics for children at risk of developing UTI, the routine use of antibiotics for those children is not recommended.⁹

Recurrent UTI is defined as ≥ 3 UTIs per year or ≥ 2 UTIs per half year and is frequently found in female and male patients with complicating urological factors.¹⁰ With the growing antibiotic failure due to the emerging resistance of bacteria, nonsurgical management of pediatric UTIs has begun to play a more important role because of its noninvasive characteristics and few adverse effects. Current evidence supports the use of cranberry juice for prevention of UTIs in adult women.¹¹ Therefore, the current research team evaluated whether cranberry juice could be effective in preventing UTI recurrence in uncircumcised boys.

METHODS

Participants

The current study took place at Taipei City Hospital, Renai and Zhongxing Branches (Taipei City, Taiwan). The participants in the current study were 55 uncircumcised boys and 12 circumcised boys, aged 6 to 18 years, with uncomplicated UTI, who were patients at the hospital. The patients were selected in the pediatrics and urology outpatient clinic of the Renai and Zhongxing branches. Their patients who visited the clinic in the study period were not all boys. The number of children in the study and placebo groups was limited due to limitations of the study grant. Some families declined to participate because Western medicine was more popular in the country. This study was approved by the institutional review board of our hospital, and all of the participants' parents or guardians provided written informed consent.

Procedures

The children were drank the cranberry juice or placebo juice at home under the parent supervision. The cranberry juice (North American cranberry, Ocean Spray Cranberries, Inc), which contained A-type proanthocyanidins, was bought from the supermarket. The placebo juice is a diluted tomato juice with sugar added. Postintervention urine culture every month for 1 year was performed after completion of 6 months of the cranberry juice intervention. Voiding urine culture collection was assisted by the nurse and performed by the hospital lab. Antibiotic was only given for patients with culture-positive symptoms.

Using computer-generated random numbers, the uncircumcised participants were randomly assigned to 1 of 2 groups, either group 1, the intervention group, or group 2,

Table 1. Preintervention Characteristics of the Study's Male Participants

	Group 1: (Noncircumcised) Cranberry Juice for 6 Mo Daily	Group 2: (Noncircumcised) Placebo Juice 6 for Mo Daily	Group 3: (Circumcised) Placebo Juice for 6 Mo Daily
No. of patients	28	27	12
Mean age, y	9.6	9.7	8.7
First time UTI	Yes	Yes	Yes
Results of clean-catch urine culture	<i>E coli</i> $\geq 1 \times 10^5$	<i>E coli</i> $\geq 1 \times 10^5$	<i>E coli</i> $\geq 1 \times 10^5$
Results of VUR	Negative	Negative	Negative
Complete course of antibiotic treatment	Yes	Yes	Yes

Note: Participants in groups 1 and 2 were uncircumcised boys. Group 1 drank cranberry juice daily for 6 mo, and group 2 drank a placebo juice daily for the same period. Participants in group 3 were circumcised boys who drank a placebo juice daily for 6 mo.

Abbreviations: UTI, urinary tract infection; VUR, vesicoureteral reflux.

the negative control group. The circumcised participants were assigned to group 3, the positive control group. Table 1 shows the preintervention characteristics of the boys in the 3 groups.

The participants, physicians, outcome assessor, and statistician were all blinded to the treatment allocation. The physicians only participated for case collection and communication with the parents. The outcome assessor was a method blind physician. The statistician was a hospital staff member.

Intervention

Group 1 (n = 28) drank approximately 4 oz (120 mL) daily of cranberry juice for 6 months, and group 2 (n = 27) drank approximately 4 oz of placebo juice for 6 months. Group 3 also drank 4 oz of placebo juice for 6 months.

Outcome Measures

The primary measure was a urine culture that could confirm any symptomatic UTI. *Culture positive* was defined as bacteria count $\geq 1 \times 10^5$.

Statistical Analysis

SPSS, version 21 (IBM, Armonk, NY, USA) for Microsoft Windows (Redmond, WA, USA) for the Mann-Whitney U test processed the resulting data. $P < .05$ was considered statistically significant.

RESULTS

All of the participants, including the positive control group, completed the study. No adverse reactions were observed.

Table 2. Comparison of the Prevention of Recurrent Episodes of UTI in Group 1 and Group 2

	Boys With Recurrent Episodes n (%)	Pathogen Growth in Urine Cultures	P Value
Group 1 (n = 28)	7 (25%)	<i>E coli</i> $\geq 1 \times 10^5$	<.05
Group 2 (n = 27)	10 (37%)	<i>E coli</i> $\geq 1 \times 10^5$	

Note: Group 1 included uncircumcised boys who drank cranberry juice daily for 6 mo. Group 2 included uncircumcised boys who drank placebo juice for 6 mo.

Abbreviation: UTI, urinary tract infection.

Table 3. Comparison of the Prevention of Recurrent Episodes of UTI in Group 1 and Group 3

	Boys With Recurrent Episodes n (%)	Pathogen Growth in Urine Cultures	P Value
Group 1 (n = 28)	7 (25%)	<i>E coli</i> $\geq 1 \times 10^5$	<.05
Group 3 (n = 12)	4 (33.3%)	<i>E coli</i> $\geq 1 \times 10^5$	

Note: Group 1 included uncircumcised boys who drank cranberry juice daily for 6 mo. Group 3 included circumcised boys who drank placebo juice for 6 mo.

Abbreviation: UTI, urinary tract infection.

After 6 months of a prophylactic treatment with a highly concentrated cranberry juice for group 1 or the placebo juice for groups 2 and 3, urine cultures measured the growth of bacteriuria, mainly *Escherichia coli*, at $\geq 1 \times 10^5$. The rates of recurrence were 25%, or 7 of 28 participants, in group 1; 37%, or 10 of 27 participants, in group 2; and 33.3%, or 4 of 12 participants, for group 3 (Table 2 and Table 3).

The results showed that cranberry juice significantly reduced the number of repeated episodes of UTI in uncircumcised boys, and its preventive benefit was higher than that of the circumcisions in group 3 ($P < .05$).

DISCUSSION

UTI in children is common at 5% to 10% and recurs in 10% to 30%.¹² Shaikh et al¹³ have shown that UTI can cause abdominal pain, back pain, and dysuria and can increase the frequency or can trigger the onset of urinary incontinence. That study also showed that a lack of circumcision can increase the likelihood of UTI in children. In their study, Craig et al¹⁴ reported that the rate of UTI was 1.4% in circumcised preschool boys compared with 6.3% for those who were uncircumcised. Recently, Morris and Wiswell¹⁵ showed that the single risk factor of lack of circumcision conferred a 23.3% chance of UTI during a man's lifetime. In a study by Gucuk et al,¹⁶ the researchers showed that circumcision decreased the colonization of periurethral pathogenic flora, and in boys with low-grade vesicoureteral reflux, circumcision plus prophylactic antibiotics prevented recurrent and febrile UTIs.

In the opposite vein, previously reported differences in the rate of UTI by circumcision status may have been entirely due to sampling and selection bias. Until the advent of clinical studies that adequately control for sources of bias, circumcision should not be recommended as a preventive for UTI.¹⁷ In addition, in Israel, almost all male infants are circumcised. Nevertheless, a high incidence of UTI occurs following that Jewish ritual as well as a relatively high preponderance of bacteria other than *E coli* in patients with UTI, which may suggest a causal relationship between circumcision and UTI.^{18,19}

Antibiotics are widely administered to children with the intention of preventing UTI. However, concerns are

increasing regarding antimicrobial resistance worldwide, and elective antimicrobial pressure and multiple admissions to hospitals have been found risk factors associated with antimicrobial resistance.²⁰

Febrile UTIs are common and associated with a risk of renal scarring and long-term complications. Antimicrobial prophylaxis has been used to reduce the risk for recurrence. However, antimicrobial use is a major risk factor for resistance. Numerous studies have shown that the single most important risk factor for development of antimicrobial resistance is previous exposure to antimicrobial agents.²¹ Also, numerous reports have documented resistance rates for *E coli* to trimethoprim-sulfamethoxazole and ampicillin at 20% to 31% and 40% to 45%, respectively.^{22,23}

UTIs are preserved in 30% to 50% of children after the first UTI. Of those recurrences, approximately 90% occur within 3 months of the initial episode, and *E coli* accounts for 80% of the urinary tract pathogens.²⁴ Due to an emerging resistance to the antibiotics and to the existence of only a small number of studies in that area, all of which were of poor quality and that have provided no reliable evidence for the effectiveness of antibiotics in preventing recurrent symptomatic UTIs, prophylactic antibiotics for recurrent UTIs should not be considered.

North American cranberries have long been considered to have protective properties against UTIs. A study by McCall et al²⁵ showed that the swimming and swarming motilities of *Proteus mirabilis* and the swarmer-cell differentiation were inhibited by cranberries. The A-type proanthocyanidins in cranberry fruit are bioactive components associated with the prevention of UTIs.²⁶

A study by Jepson RG et al²⁷ showed that some evidence existed that cranberry juice might decrease the number of symptomatic UTIs during a 12-month period, particularly for women with recurrent UTIs. Cranberry juice with high concentrations of proanthocyanidins that were given to children daily for a 1-year period appeared to be effective in the prevention of nonfebrile UTIs.²⁸

A concurrent reduction in urinary P-fimbriated, *E coli* strains supports the biological plausibility of cranberry activity, and some evidence has shown that cranberries can prevent the adhesion of *E coli* to the bladder epithelium.^{11,29}

Another study showed that cranberries may have beneficial effects against the growth and biofilm-producing capability of Gram-positive bacterial pathogens.³⁰

In a study by Salo et al,³¹ the researchers evaluated whether cranberry juice was effective in preventing UTI recurrences in children and demonstrated that the intervention did not significantly reduce the number of children who experienced a recurrence of UTIs, with the cranberry group showing 0.16 fewer episodes. That study did show that cranberries were effective in reducing the actual number of recurrences per participant in the cranberry group, with 12 recurrences, versus the placebo group, with 28 recurrences, as well as reducing the related antimicrobial use (6 d per patient-year).

With growing antibiotic failure due to the emerging resistance of bacteria, nonsurgical management of pediatric UTI has begun to play a more important role because of its noninvasive characteristics and few adverse effects. The current study used North American cranberry juice to assess its preventive effectiveness against recurrent episodes of UTI in uncircumcised boys from 6 to 18 years of age. The study's results showed the benefits of drinking approximately 4 oz (120 mL) daily of cranberry juice for 6 months in reducing the recurrence of UTI: (1) group 1, uncircumcised boys who drank the cranberry juice—a 25% rate of recurrence, or 7 of 28 participants; (2) group 2, uncircumcised boys who drank the placebo juice—a 37% rate of recurrence, or 10 of 27 participants; and (3) group 3, circumcised boys who drank the placebo juice—a 33.3% rate of recurrence, or 4 of 12 participants (Table 2 and Table 3).

CONCLUSIONS

The North American cranberry, with its high concentrations of proanthocyanidins, may be effective in the prevention of recurrent UTI episodes in uncircumcised boys. In addition, the rate of prevention of UTI by the cranberry juice in group 1 was higher than that of the circumcised boys in group 3. Further large-group studies are required in the future.

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AUTHOR DISCLOSURE STATEMENT

The authors declare that there are no conflicts of interest that could affect the current study.

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