Can Cran-Max® Be Used To Treat Current Urinary Tract Infections?

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Study Summary

• Pilot Study To Determine Effectiveness of Cran-Max as a prescribed method of treatment for current Urinary Tract Infections.
• Study site: McMaster University, Hamilton, Ontario, Canada; Dr. Anil Kapoor, Urologist
• 30 Women, 3 Groups:
  - Norfloxacin BID for five days
  - 500mg Cran-Max once daily for five days
  - 500mg of Cran-Max twice a day for five days

Preliminary Findings

• 6 women with uncomplicated UTI given Cran-Max 500mg twice daily for 3 days
• 4 women required antibiotic therapy after 2-3 days
• 2 women improved with Cran-Max alone and did not require antibiotics
• Preliminary results suggest Cran-Max may have utility in treating select patients with uncomplicated UTI

CIHR Research Proposal:

Treatment of Uncomplicated Urinary Tract Infections with Cranberry Extract

Urinary tract infections (UTIs) are a prevalent and disruptive disease. North American data of the prevalence of UTIs was estimated at approximately 3.5% of the population.[i] They account for 1.2% of all office visits by women and 0.6% of all office visits by men.[ii] In present day medical practice, antibiotic therapy is the treatment of choice for UTIs. Our better understanding of urinary tract pathogens and our development of new antibiotics have made this treatment modality effective. Unfortunately, decades of antibiotic use has given rise to antibiotic resistance. Canadian data shows that E. Coli, the most common pathogen causing UTIs, has resistance rates of 41.1% to ampicillin, 18.9% to trimethoprim-sulfamethoxazole, 7.4% to mecillinam, and 1.2% ciprofloxacin.[iii] [iv] There are limitations to even our best antibiotic family, the fluoroquinolones, which include ciprofloxacin and norfloxacin. “Administration of the fluoroquinolones to immature animals has caused damage to the developing cartilage, and, therefore, these agents are currently contraindicated in children, adolescents, and pregnant or nursing women.”[v] Therefore, it would be a prudent course of action to investigate alternative treatments for UTIs. The first documented use of Cranberry as a medicine was in the 17th century, by the European settlers who observed these medical practices in the Native Indian community. Recent studies have shown prophylactic usefulness of Cranberry Extract
against UTIs. It was once believed that this was a direct result of increased urinary acidity, but now there is evidence that Cranberry Extract inhibits the binding of the bacterial pathogens to the urothelium. Decreased binding ability has been demonstrated in E. coli, Proteus, Klebsiella, Enterobacter and Pseudomonas.[vi] [vii]

To date there is no useful evidence regarding Cranberry Extract's effectiveness as a treatment for UTIs. A meta-analysis looking for such data was performed for the Cochrane Database of Systematic Reviews and in its conclusion it stated that, “After a thorough search, no randomized trials which assessed the effectiveness of cranberry juice for the treatment of urinary tract infections were found. Therefore, at the present time, there is no good quality evidence to suggest that it is effective for the treatment of urinary tract infections.”[viii]

Therefore, I propose to investigate and generate data regarding Cranberry Extract as a treatment for uncomplicated UTIs. Uncomplicated UTIs, for the purposes of our investigation, will be defined as an afebrile, local infection in a patient with a structurally and functionally normal urinary tract. This will be a comparative study between norfloxacin and two different doses of Cranberry Extract working under the null-hypothesis that norfloxacin is more effective than Cranberry Extract in the treatment of UTIs. In the initial study, we propose to randomize 30 patients, which meet our criteria, into 3 branches.

**UTI Pilot Protocol**

*3 arms of the study, 10 patients each*

5 days norfloxacin 400mg PO BID  
(control group)

5 days Cran Maxä 500mg PO OD

5 days Cran Maxä 500mg PO BID

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**Initial Visit (Day 1)**

Data: Urinalysis, Culture and Sensitivity, CBC, History and Physical (including patient data: age, sex, etc.) Symptom score (Validated O’leary-Sant questionnaire)

**Day 2**

Data: Urinalysis, Culture and Sensitivity, Symptom score (if patient is on Cran-Max® and symptoms worsen or there is development of a fever then treatment is changed to antibiotics.) (otherwise continue course)

**Day 5**

Data: Urinalysis, Culture and Sensitivity (if previous Culture positive for growth then change to antibiotics), Symptom score

Optional day 5 extension if Urinalysis positive, but the patient feels much better (physician's decision)

The results will be entered into an Excel database and a subsequent analysis using SPSS statistics program will be performed with the completed data. Appropriate parametric and non-parametric statistical tests will be run to compare between group data, i.e. control versus treatment arms, and within group data. Examples of analytical tests include a Chi-Squared test looking for differences in positive/negative cultures between control and treatment arms, an ANOVA analysis for comparison of between group symptom scores, and a repeated measures ANOVA to see if there are day to day improvements within each treatment regimen. After the analysis, we will have data that will let us draw conclusions, on how effective, if at all, Cranberry Extract is in treatment of uncomplicated UTIs. We will also have data on the time course of each treatment arm, including information on when bacterial levels drop in the urine and when patients start to feel better. The study will produce data by which evidence-based decisions, regarding the usage of Cranberry Extract as a treatment for UTIs, can be made.
Cystitis Symptoms Index

*Please circle the number that best describes your answer to the following questions:*

During the past few days, how often have you felt the strong need to urinate with little or no warning?

<table>
<thead>
<tr>
<th></th>
<th>0. not at all</th>
<th>1. less than 1 time in 5</th>
<th>2. less than half the time</th>
<th>3. about half the time</th>
<th>4. more than half the time</th>
<th>5. almost always</th>
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During the past few days, have you had to urinate less than 2 hours after you finished urinating?

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<th>1. less than 1 time in 5</th>
<th>2. less than half the time</th>
<th>3. about half the time</th>
<th>4. more than half the time</th>
<th>5. almost always</th>
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During the past few days, how often did you most typically get up at night to urinate?

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<th>3. about half the time</th>
<th>4. more than half the time</th>
<th>5. almost always</th>
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During the past few days, have you experienced pain or burning in your bladder?

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<th>4. more than half the time</th>
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Interstitial Cystitis Problem Index:

During the past few days, how much has each of the following been a problem for you?

**Frequent urination during the day?**

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<tr>
<th></th>
<th>0. no problem</th>
<th>1. very small problem</th>
<th>2. small problem</th>
<th>3. medium problem</th>
<th>4. big problem</th>
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**Getting up at night to urinate?**

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<th>2. small problem</th>
<th>3. medium problem</th>
<th>4. big problem</th>
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**Need to urinate with little warning?**

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<th>2. small problem</th>
<th>3. medium problem</th>
<th>4. big problem</th>
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**Burning, pain, discomfort, or pressure in your bladder?**

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<th>3. medium problem</th>
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