Clinical evaluation of herbal coded formulation CranAdvantage to Urixin in the treatment of Urinary tract infection

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Abstract: Urinary Tract Infections are the largest group of infections after the respiratory tract infections. In 85% of the cases the causative organism is *E. Coli*. A clinical trial was conducted to evaluate the efficacy of coded herbal formulation "CranAdvantage" (Test drug) for the treatment of Urinary tract infection comparing with Urixin (Control). One hundred and thirty patients suffering from Urinary tract infection from both groups (Males: 45, mean age: 34±14 and females: 85, mean age: 33±13 year, range: 15-55) were enrolled in the trial and divided in to two groups according to treatment regimens. CranAdvantage (Test drug) 500mg two capsules and Urixin (*Pipemidic Acid* Trihydrate JP15) (Control) 400mg capsules twice daily were prescribed for 2-3 weeks. Urinary tract infection was improved in 23 (35.38%) patients out of 65 patients by the use of CranAdvantage (Test drug), and in 15 (23.07%) patients out of 65 by the use of Urixin (Control drug). Furthermore, there was a significant improvement in Urinary tract infection associated clinical features as compared to Urixin. It is concluded that CranAdvantage possesses a therapeutic value for the improvement of urinary tract infection and its associated symptoms as compared to Urixin.

Keywords: Urinary tract infection, CranAdvantage, Urixin.

INTRODUCTION

Urinary Tract Infection is defined as the growth of a known bacterial pathogen more than 10000cfu/ml in association with a positive dipstick or urinalysis and *Escherichia (E. coli*) (Zorc *et al*., 2005) is the causative organism in most of the uncomplicated urinary tract infections in women, especially in younger women (Foster Sr. 2008). The epidemiology and prevalence rates of urinary tract infection depend upon age, sex and race, of the patient (Tessema *et al.,* 2007). According to Cohort and case controlled studies conducted by Hooton *et al* the risk factors which are associated with recurrent UTI in sexually active premenopausal women are, sexual intercourse, use of spermicides and the age of first urinary tract infection (less than 15 years of age indicates a greater risk of recurrent urinary tract infection) and history of urinary tract infection in the mother is suggesting that genetic/long term environmental exposures might predispose to this condition (Santen and Altieri, 2001).

It is diagnosed by urine analysis and urine culture. The common approach in the treatment of UTI is antibiotic but now a day's antibiotic resistance is increasing. Resistance was observed in multiplegenera including Escherichia, Enterobacter, Klebsiella, Proteus, Salmonella, Serratia and Pseudomonas (Cohen, 1992). Due to the increased rate of development of antibiotic resistant organisms, experiments on the plant materials to investigate the alternative sources of anti-microbials have become more common over the past few years. Hundreds of plants worldwide are used in traditional system of medicine for the treatment of bacterial infections. Many of these have also been evaluated *in vitro* screening but the efficacy of such herbal medicines has not been evaluated in clinical trials. Natural products are usually safer than synthetic antibiotics and many physicians and patients prefer to use herbal medicines. Thus healthcare professionals should be aware of the available evidence for herbal antibiotics. In a recent study, antibiotic activity of commonly used Unani (traditional) medicine plants are evaluated that are commonly used in urinary ailments to explore the natural source for pilot compounds against urinary tract infection (Hakim Ajmal Khan, 1983) Thus, this study was planned to evaluate the efficacy of herbal coded formulation in the management of Urinary tract infection on scientific parameters.

PATIENTS AND METHODS

A randomized controlled, two-arm parallel group clinical trial was conducted to evaluate the efficacy of CranAdvantage (Test drug) as compared to Urixin (control). The therapeutic evaluations of these medicines were conducted on 130 clinically and microscopically diagnosed cases from both groups (Males: 45, mean age: 34±14 and females: 85, mean age: 33±13 year, range: 15-55) at Hakim Saeed Shaheed memorial Hospital, Bahawalpur. All the patients selected for the study were thoroughly examined and clinical history was recorded in the prescribed proforma. The therapeutic evaluation of the drug was made on the basic improvement in the urine D/R and other associated clinical features at periodic intervals

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during the course of treatment. Patients (n=130) were randomly assigned to receive CranAdvantage 500mg two capsules in comparison with Urixin 400mg capsules twice daily for 2-3 weeks.

Ethical issues and clinical trial approval

Study was conducted according the rules of Ethical Committee (EC) of Faculty of Eastern Medicine, Hamdard University Karachi, Pakistan. Study design and protocols were presented to the board members of ethical Committee (EC) and Board of Advance Studies and Research (BASR) for their clearance and permission before the start of clinical trial.

Test drugs formulation

Plant material for test drug CranAdvantage Cranberry (*Vaccinium macrocarpon*) powder was provided by YAAX International, Inc. (USA). Than capsules were made from the powder by the Allegro Pharmaceuticals (Pvt.), Lahore, Pakistan. Each capsule contains *Vaccinium macrocarpon* powder 500mg.

STATISTICAL ANALYSIS

Statistical analyses were performed by using SPSS and various tests were applied. All differences were considered statistically significant by generating a '*p*-value' from test statistics. The significant result with '*p*-value' less than 0.05 was considered as statistically significant.

Patient characteristics

Baseline characteristics of all patients are given in table 1.

Urine D/R

It was noted that 23 patients (35.38%) out of 65 patients by the use of CranAdvantage (Test drug) showed improvement in Urine D/R whereas it was in 15 patients (23.07%) out of 65 by the use of Urixin (Control drug). Chi-Square Test was applied and *p*-value was calculated as 0.0235 indicating that there is significant difference between these two drugs (table 2 and fig. 1).

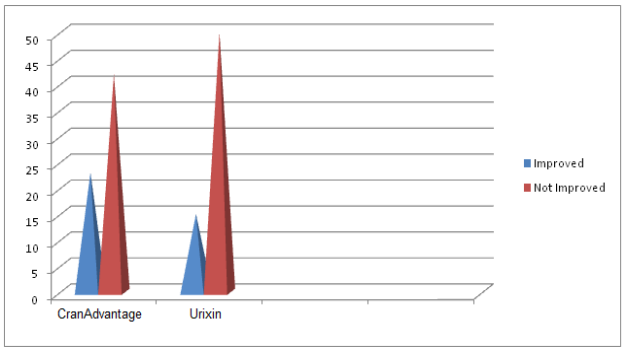

Fig. 1: Improvement in Urine D/R by the use of CranAdvantage and Urixin.

Furthermore, improvement in clinical features associated with urinary tract infection such as burning micturation, dysuria, frequency of micturation, lower abdominal pain and fever was especially noted when treated with CranAdvantage as compared to Urixin (fig. 2).

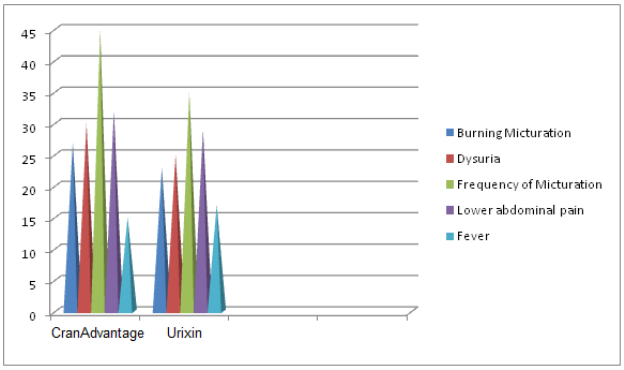

Fig. 2: Improvement in clinical features by both test and control groups.

DISCUSSION

Urinary tract infection is most common infection in women. The use of allopathic drugs has been considered as one of the effective treatment. But this is not feasible as besides being most cost prohibitive, they are not without side effects. Frequent antibiotic use can result in vaginal and intestinal dysbiosis as well as antibiotic resistance. Thus, it is desirable to seek alternative methods of prevention and treatment of simple UTIs. For this purpose a coded herbal formulation *CranAdvantage* has been formulated. It contains the Cranberry powder, which is known for its wide range of clinical use in indigenous medicine. Cranberry possesses significant antibacterial activity (McMurdo, 2005). Results of our present study showed that cranberry products are useful in the treatment of Urinary Tract Infection. It was once thought to benefit UTIs because hippuric acid in cranberries has the potential to acidify the urine. However, a more complete understanding of the pathogenesis of UTIs has led to a greater understanding of the mechanisms of action of cranberry in prevention and treatment as an anti-adhesion agent. Cranberries have been found effective in the form of pure juice, sugared cocktail, and capsules and extract. Following respiratory tract infections, urinary tract infections (UTIs) are the second most frequent infections in human body (Kass *et al.*, 2002). UTIs occurring in an ascending pattern are mostly caused by Gram-negative bacteria such as *Escherichia coli* and *Staphylococcus saprophyticus*, whereas the much less frequent descending UTIs are mostly caused by Gram-positive bacteria such as group B *Streptococcus* (Hooton 2000). The results of our study showed that *Vaccinium macrocarpon* is highly active against *Escherichia coli* and show mild activity *Staphylococcus saprophyticus* and *Proteus mirabilis*.

Table 1: Baseline characteristics of all patients in both test and control groups

Characteristics	CranAdvantage	Urixin	P value
Male	22	23	NS
Female	42	43	NS
Mean ± SD	34±14 33±13	34±14 33±13	NS
Range	15-55	15-55	NS
Married	45	50	NS
Un Married	20	15	NS

Table 2: Improvement in Urine D/R after treatment

Urine D/R	CranAdvantage (Test)	Urixin (control)	Total (n)	P Value
Improved	23 (35.38%)	15 (23.07%)	38	
Not Improved	42 (64.61)	50 (76.92)	92	
Total	65	65	130	0.0235

CONCLUSION

The finding from this clinical trial demonstrated there was statistically significant difference when comparing the effectiveness of herbal medicine CranAdvantage to Urixin (control) for the treatment of urinary tract infections. Hence, CranAdvantage possesses a therapeutic value for the treatment of urinary tract infections and its associated symptoms. However, further clinical trials on larger scale and studies pertaining to mechanism of action of CranAdvantage are required

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