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The effect of *Cornus mas* in preventing recurrent urinary tract infections in women

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ABSTRACT

Background and aims: Urinary tract infections(UTIs)are one of the most common and the second leading infections, after respiratory tract infections, in women. Currently,various chemical drugs are used to prevent the UTIs.Chemical drugs may cause antibiotic resistance and resistant strains are likely to grow in the long-term treatment with antibiotics.The aim of this study is to investigate the effect of *Cornus mas* in preventing recurrent UTIs in women aged15-45 years referring to Ayatollah Kashani Hospital Clinic Shahrekord.

Methods: This experimental study (Parallel Design and Triple-blind) was conducted on42women aged15-45 years referring to Ayatollah Kashani Hospital Clinic of Shahrekord and diagnosed with chronic cystitis. The exclusion criteria were neurogenic bladder, genitourinary system anatomical abnormalities (hydronephrosis, ureterocele stone,etc),and bacterial resistance. The women were randomly assigned to2groups.At baseline, the women were examined for any functional and anatomical disorders and, if necessary, underwent ultrasound. After the current UTIs were treated and the women clinically recovered, one group was administered with *Cornus mas* tablet 500mg and another group administered with placebo for6months.All the women were followed up for6 months. Every2 months, the patients were clinically examined and their urine cultures were investigated for the clinical signs of cystitis. As the symptoms of the UTIs occur, the patients were recommended to refer for repeated urine culture. All patients (42 women)completed the study.

Results: In our study, nosignificant difference was observed between the groups in terms of recurrent UTI recurrence, although there were differences(P>0.005).Positive urine culture in *Cornusmas* group was19% and in placebo was33.4%. In terms of dysuria in6 months and the second time there was significant difference between placebo and *Cornus mas* (P=0.004) Dysuria in *Cornusmas* group was14.2% and in placebo was56.2%.

Conclusion: *Cornusmas can decrease dysuria and frequent urination in patients with recurrent UTIs, So it can be used in the treatment of these patients.*

Keywords: Cornusmas, Urinary tract infections, Treatment

Original article

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INTRODUCTION

Each year, over 250 million people worldwide develop urinary tract infection (UTI) (2). The UTIs are the second leading infection, after respiratory diseases, in women, older people, and infants (1). These infections are caused due to urinary tract microorganisms, and can be symptomatic or asymptomatic. *Escherichia coli*, followed by *Proteosolgaris*, is the leading bacterial cause of the UTIs. *Klebsiella pneumoniae*, *Staphylococcus epidermidis*, Enterobacter, Citrobacter, and *Pseudomonas aeruginosa* can be other bacterial causes of the UTIs (3). In symptomatic UTIs, certain symptoms may be seen, including frequent urination, dysuria, urinary incontinence, forcing urine out, strong-smelling urine, and in some cases, fever (4). According to the available evidence, the incidence of ampicillin and amoxicillin resistance is 100% in the gram-negative bacilli from Enterobacteriaceae.

Moreover, the resistance of different Staphylococcal strains has been reported to be 70%-90% (1). The side effects due to antibiotics and increasing antibiotic resistance have led to increased attention to herbal drugs and nature-based antimicrobial agents.

Cornus mas (*C. mas*) is from family Valerian. The US Indians used it as both a food and a drug for bladder and kidney diseases. Later, physicians prescribed it for bladder infections, small bladder stones, and the toxins in the blood (5). *C. mas* is rich in anthocyanins, which can be the cause of its pharmacological properties, including antioxidant, anti-allergy, antibacterial, and anti-inflammatory (6).

Uropathogenic adhesion to urinary tract cells is the first step of the UTI pathogenesis (7). The anti-adhesion property of *C. mas* can contribute to the prevention of the UTIs either directly through *Escherichia coli* adhesion to urothelial cells or through decreased bacterial adhesion in stool. Recent studies have demonstrated that regular use of *C. mas* is helpful for the patients with UTIs who have antibiotic resistance (8).

The anti-adhesion property of *C. mas* has been reported to persist for 2-10 hours after use (9). Anticianidine, a compound found in *C. mas*, can prevent the pathogens adhesion to urothelial cells. Some studies have reported that *C. mas* can decrease the incidence of recurrent UTIs and some others have found no (predictable) effects of *C. mas* in the incidence of the recurrent UTIs (10). Moreover, inconsistent findings have been obtained on *C. mas* effects on the UTIs. Regarding the high prevalence of the UTIs in the community and because the people of Chaharmahal and Bakhtiari province have long been using plants to treat diseases, especially the UTIs, we conducted this study to investigate the effects of *C. mas* on the recurrent UTIs in women aged 15-45 years.

METHODS

This randomized clinical trial was done on two groups (each group: 21) of 15-45 year's old women with different weight and recurrent cystitis that were referred to clinic of shahrekord kashani hospital at 2013 that sample size using the software Stata and was determined according to available studies. The

subjects were matched in view of the year's old, length of disease, level of education, social category, place of life and quality of individual health. Then using SPSS 16 the subjects were allocated to groups randomly, Patients, sampling and Analyzer of data were blinded. This study was approved by ethical committee of Shahrekord University of medical sciences and was done with ethical code (4-3-93) and code of Iranian randomized clinical trial center (IRCT2015111625072N1). Written informed consent was obtained from all subjects and other ethical principals were achieved. Before the subjects were enrolled in the study, their anatomical and functional problems were examined and sonography and intra venous pyelography were done if necessary. The subjects with anatomical problems of urinary system (kidney stone, urethrocel, hydronephrosis) and dysfunction of urinary system (neurogenic bladder) were excluded from study. Because of differences in the number of subjects' intercorsing and to prevention of study error, we applied a long time and low dose of consuming the drug in this study. After treatment of primary urinary infection and promoting clinical status, we gave the C. mas tablet (500mg, Based on existing studies) to the first group for 6 month nightly and the placebo to the second group for 6 months nightly. For extraction, 30 kg of C. mas prepared by the city of Qazvin, Iran was dried in shadow gradually and converted to powder by mechanical milling, and then the powder was mixed with ethanol 70% (1 vs. 5) by maceration method for 4 days. The extraction was passed from filter paper and was concentrated under vacuum by rotary operator machine. Then, concentrate extract was knead with calcium triphosphate and dried in granulation form. After the standardization by assessing the anthocyanin content, we were filled the tablets with C. mas granule. For making the placebo, we provided dough from starch and starch paste and converted to dried granule, and then the same tablets were filled by the dried herb extract (14). The patients were followed for 6 months and stayed on clinical examination, urine analyzing, urine culturing and assessing for cystitis clinical sign (dysuria, incontinency and suprapubic pain). The patients with positive test were excluded from the study and treated for their recurrent infection and recommended them for repeating urine culture whenever if infection sign was seen. During the months 2, 4, 6, after urine culturing, urine incontinency, dysuria, abdominal pain were assessed and signed in the checklist by the researcher. The data were calculated and analyzed with chi-square test using SPSS software.

Table 1. The frequency distribution of the urine culture in the groups of the study

P value	*Cornus mas*		Placebo		Groups	
	Negative urine culture	Positive urine culture	Negative urine culture	Positive urine culture		Variables
0.159	17	4	14	7	No.	During six months
	81	19	66.6	33.4	%	
0.463	17	4	16	5	No.	The first two months
	81	19	76.2	23.2	%	
0.362	21	0	20	1	No.	The second two months
	100	0	95.2	4.8	%	
0.362	21	0	20	1	No.	The third two months
	100	0	95.2	4.8	%	

P<0.005 was considered the level of significance.

RESULTS

In the *C. mas*-treated group, four (19%) people developed recurrent UTI and in the placebo group, 7 (33.4%) did. Although there were some differences in the mean incidence of the recurrent UTIs during the six months, chi-square test indicated no significant difference in the incidence of the recurrent UTIs between the two groups (P>0.005).

Chi-square test indicated no significant difference in the urine culture in the first, the second, and the third two-month periods between the two groups (P>0.005). Moreover, there were some differences in the frequent urination between the two groups, but chi-square test indicated no significant difference in the frequent urination during the six months between the two groups (P>0.005). During the six months, in the placebo group, 38% developed frequent urination and in the *C. mas*-treated group, 22.4% did. In other words, the frequent urination decreased in the *C. mas*-treated group by 15.6% compared to the placebo group. In addition, there were some differences in abdominal pain between the two groups of the study, but chi-square test indicated no significant difference in abdominal pain between the two groups during the six-month period (P>0.005). During the six months, in the placebo group, 19% of

Table 2. The frequency distribution of the frequent urination in the groups of the study

Groups / Variables		Placebo		Cornus mas		P value
		Negative frequent urination	Positive frequent urination	Negative frequent urination	Positive frequent urination	
During six months	No.	16	5	13	8	351.0
	%	76.2	22.4	62	38	
The first two months	No.	19	2	18	3	0.852
	%	90.4	9.6	85.8	14.2	
The second two months	No.	19	2	18	3	0.852
	%	90.4	9.6	85.8	14.2	
The third two months	No.	19	2	17	4	0.325
	%	90.4	9.6	81	19	

P<0.005 was considered the level of significance.

Table 3. The frequency distribution of dysuria in the groups of the study

Groups / Variables		Placebo		Cornus mas		P value
		Negative dysuria	Positive dysuria	Negative dysuria	Positive dysuria	
During six months	No.	18	3	9	12	0.004
	%	85.8	14.2	42.8	57.2	
The first two months	No.	19	2	15	6	0.116
	%	90.4	9.6	71.4	28.6	
The second two months	No.	20	1	15	6	0.038
	%	95.2	4.8	71.4	28.6	
The third two months	No.	20	1	16	5	0.078
	%	95.2	4.8	76.2	22.4	

P<0.005 was considered the level of significance.

the women developed abdominal pain and in the *C. mas*-treated group, 4.8% did.

There were some differences in dysuria between the first and the second two months, but chi-square test indicated no significant difference in dysuria between the first and the second two months (P>0.005). Chi-square test indicated a significant difference in dysuria in the second two months (the fourth month) and during the six-month months between the placebo group and the *C. mas*-treated group (P<0.005). Within the six months, in the placebo group, 57.2% of the women developed dysuria and in the *C. mas*-treated group, 14.2% did. More clearly, dysuria decreased in the *C. mas*-treated group by 43% compared to the placebo group.

DISCUSSION

This study was conducted to compare the effects of *C. mas* tablet and placebo in preventing the recurrent UTIs in the women aged 15-45 years referring to Ayatollah Kashani Hospital Clinic of Shahrekord. The UTIs are one of the most common reasons for referring of the outpatients to health care centers. These infections may lead to hospital stay due to critical conditions or an underlying debilitating disease in the patient. In the present study on 42 women with recurrent UTIs during six months, there were some differences in the recurrent UTIs between the two groups yet statistically non significant. The urinary tract symptoms also were studied, and there was a statistically significant difference in dysuria between the placebo and the *C. mas*-treated groups. In Kontiokari et al study on 150 women with recurrent UTIs, the incidence of the UTIs decreased after six months of using concentrated *C. mas*. In this study, the overall incidence of the recurrent UTIs during 12 months was statistically significantly different between the case and the control groups (P=0.048). In the case group, treated with *C. mas* extract for six months, 16% of the patients developed recurrent UTI at least once, while in the control group, 36% did. The incidence of the recurrent UTIs decreased in the case group by 20% compared to the control group (15), which is inconsistent with our study. This may be due to conducting a study during a longer period of time compared to our study. Moreover, Takahashi et al investigated the effects of *C. mas* juice in preventing the recurrent UTIs in a small number of women who used *C. mas* juice for 24 weeks, and found the *C. mas* juice to be effective in preventing these infections (6). However, in the present study, the tablets of *C. mas* were used and no significant difference was seen in the incidence of the recurrent UTIs between the two groups. This inconsistency may be due to the differences in the concentrations of effective compounds between the *C. mas* tablet and pure juice. of *C. mas* tablet in preventing the UTIs in spinal cord lesion (SCL) patients with neurogenic bladder.

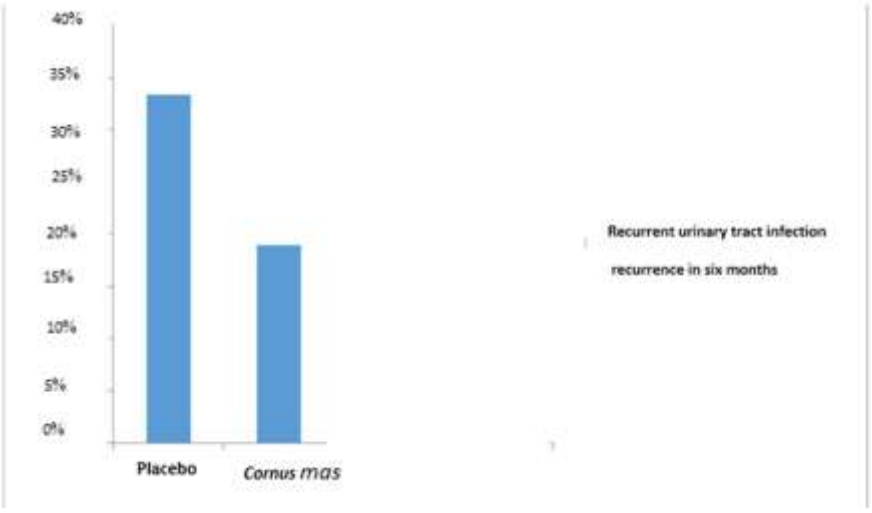

Figure 1. The frequency distribution of the urine culture in the groups of the study

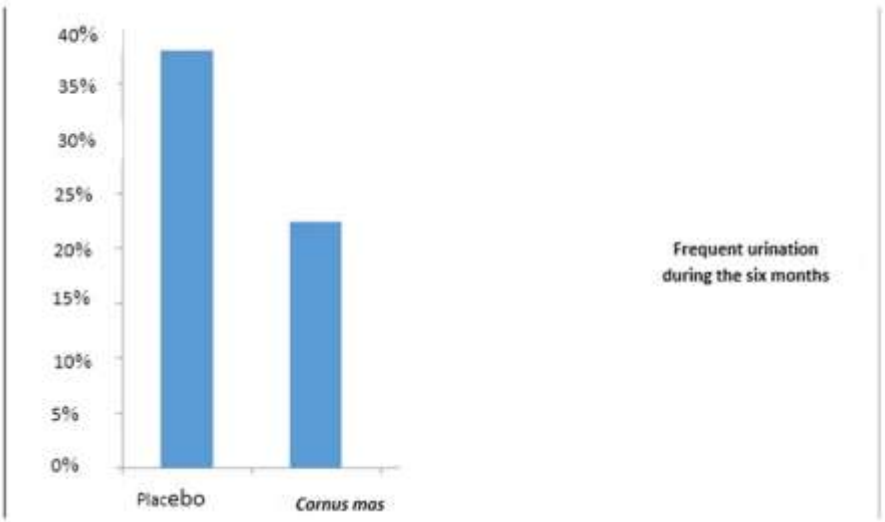

Figure 2. The frequency distribution of the frequent urination in the groups of the study

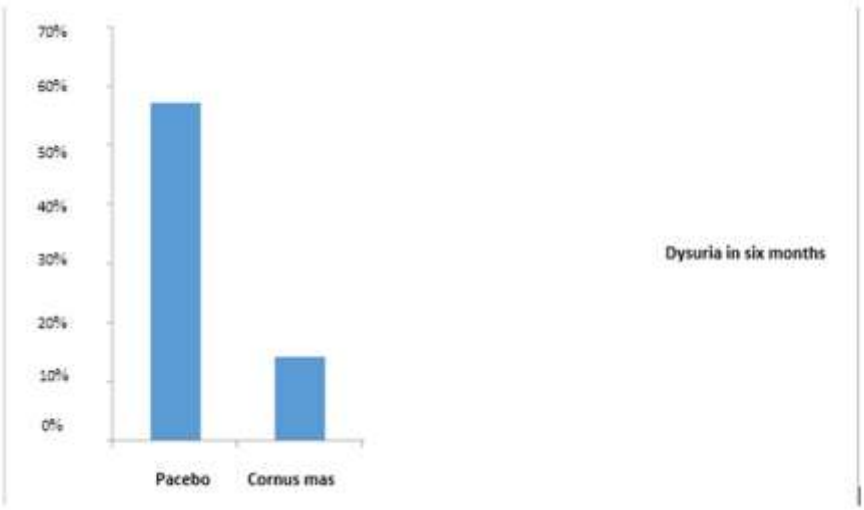

Figure 3. The frequency distribution of dysuria in the groups of the study

Hess et al investigated the effects The patients were randomly assigned to two groups, the controls and the cases, and administered with placebo and the *C. mas* tablet, respectively, for six months. After six months, the clinical symptoms of the UTIs decreased probably due to taking the *C. mas* tablets and even, compared to the controls, the frequency of the UTIs incidence per year decreased (16). Similarly, in our study, the *C. mas* tablet was used and the urinary tract symptoms decreased partly in the case group compared to the controls, but the recurrent UTIs did not decrease significantly. Barbosa- Cesnik et al investigated the effects of *C. mas* juice on the risk of the recurrent UTIs incidence in 319 female university students. In this study, the incidence of the recurrent UTIs did not decrease in the group who used *C. mas* juice twice a day compared to the placebo-receiving group during a period of six months (17). In our study, *C. mas* tablet was used and, consistent with Barbosa-Cesnik et al study, no significant decrease was seen in the recurrent UTIs between the two groups of the study. In a study on 48 SCL patients with neurogenic bladder, 22 patients received placebo and 26 were administered with the *C. mas* tablet. The *C. mas* tablet was found to cause bacteriuria and pyuria in the SCL patients (18).

In another study on SCL patients with neurogenic bladder, *C. mas* tablet had no effect in reducing bacterial colony counts, pyuria, and the incidence of the UTIs in these patients (19). Similarly, the present study demonstrated that use of *C. mas* tablet caused no decrease in the recurrent UTIs. In our study, the incidence of recurrent UTIs was 19% and 33.4% in the *C. mas*-treated and the placebo groups, respectively, with no significant difference. Uropathogenic adhesion to urinary tract cells is considered the first step of the UTIs pathogenesis. The anti-adhesion property of *C. mas* can prevent the UTIs through two mechanisms, directly through *E. coli* adhesion to urothelial cells or through helping to decrease bacterial adhesion in stool. Because the anti-adhesion property of *C. mas* can persist for 2-10 hours after use (11), the incidence of the recurrent UTIs is more likely to decrease if each day two *C. mas* tablets are used. Regarding other studied variables, such as frequent urination and abdominal pain, some differences were seen but they were not statistically significant within the six months according to t chi-square test.

CONCLUSIONS

Regarding the findings of this study on *C. mas* and botanical evidence on use of this plant to treat the UTIs, use of *C. mas* tablet 500 mg a day can decrease dysuria among patients with UTIs. The findings of this study can be an introduction to reducing the incidence of the recurrent UTIs and dysuria in patients with UTIs. Patients, especially those with allergy to chemical drugs, can be recommended to use *C. mas* tablet as it is plant-based

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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