ORIGINAL ARTICLE

ROLE OF SYMPTOMATIC TREATMENT IN COMPARISON TO ANTIBIOTICS IN UNCOMPLICATED URINARY TRACT INFECTIONS

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Background: Uncomplicated urinary tract infections (UTIs) are the most common bacterial infections among women presenting to primary care causing rapidly increasing strains of resistant bacteria to the growing antibiotic industry. Restricting antibiotics to necessary indications is the only solution. The objectives of the study were to **c**ompare the efficacy of symptomatic treatment vs antibiotic in patients with uncomplicated UTI, in terms of individual symptom score, i.e., frequency, urgency, dysuria, supra pubic pain scores and total symptoms scores. **Methods:** A randomized control trial (RCT) in 100 women (15–50 years) with symptoms of urinary frequency, urgency, dysuria and pain supra pubic region, associated with uncomplicated UTI, at Urology department, AMI, Abbottabad. Two treatment strategies were compared in uncomplicated UTI patient). Patients were randomized to antibiotic or symptomatic treatment groups on consecutive non-probability basis (50 in each group) given for 05 days. Efficacy of medications was assessed by comparing pre and post treatment symptom scores along with the post treatment scores of both groups compared to see statistical significance of difference by independent samples t-test. **Results:** There was a statistically significant difference in symptoms improvement in both treatment arms of all scores, i.e., *p*-value=0.000. Whereas only dysuria score was able to show a statistically significance of difference in post Rx scores comparison of both groups, *p*-value=0.004. **Conclusions:** Symptomatic treatment is not inferior to antibiotic treatment when proper patient selection is undertaken, resulting in decreased need for unnecessary antibiotics use.

Keywords: Uncomplicated; Urinary tract infections; Symptom score; Antibiotics; Symptomatic treatment

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INTRODUCTION

Urinary tract infections (UTIs) are responsible for over 7.5 million health care provider visits each year.[1,2] Uncomplicated UTI is one of the most common bacterial infections among women presenting to primary care, with an annual incidence of about 7% for all ages of women peaking at 15–24 years,[1,2] and the most common reason for which antibiotics are usually prescribed.[1,2]For this purpose lot of different broad spectrum antibiotics have been introduced for its effective treatment, thereby exposing the general population to the inherent disadvantages of antibiotics prescription.[3]

The increasing use of antibiotics has been associated with emerging resistance of these drugs in different parts of the world. E.coli, the major causative bacteria in UTIs, 80%,[4] is now known to be resistant to first line recommended therapy for UTI, i.e., Trimethoprim-Sulphamethoxazole 40%, amoxicillin-clavulonate 32%.[5,6] Similarly, resistance against other recently developed antibiotics, i.e., Flouroquinolones 25% (efficacy 75%) has also been reported in some parts of world.[5,6] This devastating effect of antibiotics overuse and since less antibiotic prescription is associated with less resistance,[7] efforts should be made to encourage the reduction of unnecessary antibiotics prescription.[7] There is only little evidence available, either for the natural course of untreated uncomplicated UTI or for alternative therapeutic options.[8]

Up to now, only a few RCTs compared antibiotic therapy to placebo for uncomplicated UTI.[9–11] These trials suggested that in most of the cases uncomplicated UTI is a self-limiting condition. Therefore, it was preferred to perform a study to make an estimate of the comparison of Flurbiprofen plus Citrosoda and ciprofloxacin in women with symptoms of uncomplicated UTI. Flurbiprofen was chosen as an alternative treatment option to antibiotics, considering it's inflammatory and analgesia activity as the basis for symptomatic improvement as the important factor for patients to cope with UTI. Also non inferiority of Ibuprofen in comparison to ciprofloxacin has been demonstrated regarding relief of symptoms caused by uncomplicated UTI.[9] Although ciprofloxacin is not recommended as a first line treatment for uncomplicated UTI,[1] it was selected as a reference due to its lower resistance rates, proven efficacy, and high prescription attitude in Pakistan.[12,13]

Potassium citrate has been found useful for the prevention of recurrence as well as for the relief of UTI symptoms in combination with different antibiotics.[8] The aim of this study is to compare Potassium citrate plus Flurbiprofen Vs Ciprofloxacin in patients with uncomplicated UTI. This may then become the basis for decreasing the unnecessary rely on different antibiotics, thereby decreasing the resistance rates and national cost burden of unnecessary antibiotics use.

MATERIAL AND METHDS

In this randomised control trial efficacy of symptomatic treatment **(**Potassium citrate (1xb.i.d.) plus flurbiprofen (100mg, 1xb.i.d.)**)** was compared with antibiotic **(**Ciprofloxacin (250 mg 1xb.i.d.)**)** in patients with uncomplicated UTI presenting with symptoms of urinary frequency, urgency, dysuria and pain supra pubic region.

The trial was conducted at Urology department Ayub Teaching Hospital Abbottabad from June–December 2014 comprising of 100 women (15–50 years) with symptoms of urinary frequency, urgency, dysuria and pain supra pubic region, associated with uncomplicated UTI. Two treatment strategies were compared in uncomplicated UTI patients (antibiotics for group A and symptomatic treatment for group B). Patients were randomized to groups on consecutive non probability basis (50 in each group) given for 5 days. Efficacy of medications was assessed by comparing pre and post treatment symptom scores along with the post treatment scores of both groups compared to see statistical significance of difference by independent samples *t*-test. Sample size was calculated by WHO sample size calculator using 58.3% efficacy of symptomatic treatment and 51.5% of antibiotic, confidence level 95%, power of test 90%, as shown by Bleidorn *et al*.[9] Data was collected using a written structured proforma and analysed in SPSS version 18.

RESULTS

Baseline urinary frequency, urgency, dysuria, suprapubic pain and total symptoms score were found statistically not significantly different among the two groups. After administering treatments in both groups, mean post treatment symptom scores in both treatment groups were noted and statistical significance of any difference calculated between pre and post treatment scores by independent samples *t*-test. These results show that both the treatments, antibiotics as well as symptomatic, resulted in statistically significant improvement in all the symptom scores (p=0.000). Interestingly when post Rx scores of individual symptoms were compared (Independent sample *t*-test), only dysuria score showed a statistically significant difference with symptomatic treatment in comparison to antibiotics. This study shows relief of symptoms due to uncomplicated UTI treated with symptomatic medications almost as much as with antibiotics.

Mean age of the patients among the two groups

	Group A (antibiotic treatment)	Group B (symptomatic treatment)
Age	26.40 (SD 6.698)	27.06 (SD 6.843)
Total Patients	50	50

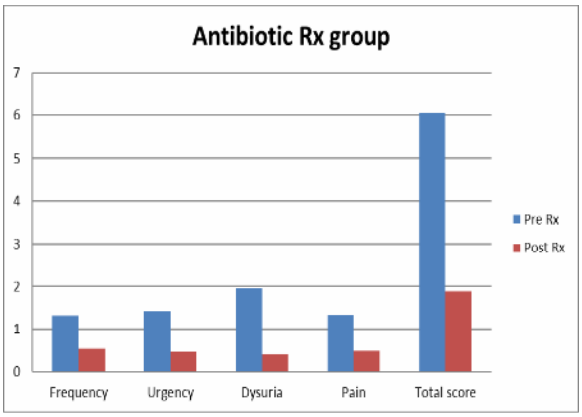

Figure-1: Graphical comparison of means of pre-treatment and post treatment symptom score for urinary frequency, urgency, dysuria, pain and total scores in antibiotic Rx group.

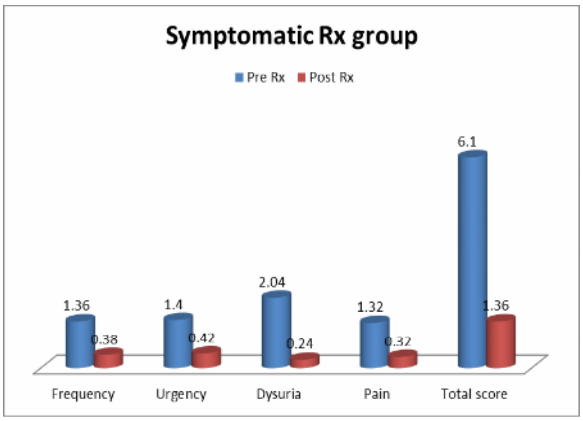

Figure-2: Graphical representation of means of pre-treatment and post treatment symptom score for urinary frequency, urgency, dysuria, pain and total scores in symptomatic Rx group

Table-1: Comparison of means of pre-treatment symptoms scores of urinary frequency, urgency, dysuria, pain and total symptom score with *p*-values

	Group A(antibiotic)			Group B (symptomatic)		
Mean	**Pre Rx (SD)**	**Post Rx (SD)**	***p*-value**	**Pre Rx (SD)**	**Post Rx (SD)**	***p*-value**
Urinary frequency	1.32 (0.471)	0.54 (0.57)	0.001*	1.36 (0.485)	0.38 (0.490)	0.001*
Urgency score	1.42 (0.499)	0.46 (0.646)	0.000*	1.40 (0.495)	0.42 (0.575)	0.000*
Dysuria score	1.96 (0.755)	0.42 (0.499)	0.000*	2.04 (0.781)	0.24 (0.431)	0.000*
Pain s/p score	1.34 (0.519)	0.48 (0.580)	0.000*	1.32 (0.513)	0.32 (0.513)	0.000*
Total score	6.06 (0.978)	1.88 (1.923)	0.000*	6.10 (0.995)	1.36 (1.411)	0.000*

Table-2: Means of pre-treatment symptoms scores of urinary frequency, urgency, dysuria, pain and total symptom score with *p*-values

	Group A (Antibiotic)	Group B (Symptomatic)	
Pre Rx		**Pre Rx**	***p*-value**
Urinary frequency	1.32	1.36	0.677
Urgency score	1.42	1.40	0.841
Dysuria score	1.96	2.04	0.604
Pain supra pubic region score	1.34	1.32	0.847
Total score	6.06	6.10	0.840

Table-3: Means of Post-treatment symptoms scores of urinary frequency, urgency, dysuria, pain and total symptom score with *p*-values

	Group A (antibiotic) Post Rx	Group B (symptomatic) Post Rx	*p*-value
Urinary frequency	0.54	0.38	0.139
Urgency score	0.46	0.42	0.744
Dysuria score	0.42	0.24	0.004*
Pain supra pubic region score	0.48	0.32	0.147
Total score	1.88	1.36	0.126

DISCUSSION

The results of this study suggest a tendency towards equivalence or non-inferiority of symptomatic treatment as compared to ciprofloxacin for the treatment of uncomplicated UTI with respect to symptom resolution. These results suggest the assumption that uncomplicated UTI is a self-limiting disorder in most of the patients. Even without antibiotic treatment, symptomatic infection seems to heal in a substantial number of women. Therefore, only symptom control may be sufficient in a majority of cases. Christiaens *et al* compared the antibiotic nitrofurantoin to placebo in 78 patients with UTI and reported symptoms improvement or at least resolution rates of about 50% after three and seven days.[14] In contrast, Ferry *et al* compared various antibiotic regimens and a placebo in a large UTI trial with slightly hopeless results for the placebo administered group (26% symptom resolution after 7 days).[15] However, none of these studies involved a symptomatic treatment arm for comparison. Administering symptomatic medications to group B yielded the mean urinary frequency score as 0.38, as compared to the mean urinary frequency score of 0.54 among the antibiotic treated group A. Although this shows a slightly more improvement in the urinary frequency among the group B than group A, but the difference was statistically not significant, i.e., *p*-value=0.139 (>0.05). Similarly, the mean urgency score was also found more improved, i.e., 0.42 among the symptomatic treated group than the antibiotic treatment, i.e., 0.46. But this difference was also noted to be statistically not significant, i.e., *p*-value= 0.744.

Mean dysuria score was also found to have improved in the group given only symptomatic treatment, i.e., 0.24 as compared to the group administered with antibiotics, i.e., 0.42. This difference was noted to be statistically significant, i.e., *p*-value=0.004 (<0.05). Pain in suprapubic region associated with UTI was found to have improved more among the symptomatically treated group of patients (mean score 0.32 vs 0.48). But this difference was also not statistically significant, i.e., *p*-value=0.147.

Total symptom score calculated as sum of all individual symptoms scores was also compared between the two treatment groups. Mean total symptoms score was found lower in the group given symptomatic treatment, i.e., 1.36 in comparison to the antibiotic group, i.e., 1.88 and again this difference was found statistically not significant, i.e., *p*-value=0.126.

Among the individual symptoms scores only dysuria score showed statistically significant improvement with symptomatic treatment. All of the symptoms as well as total symptom scores were found to have improved in the symptomatic treatment arm, but the differences are not statistically significant except that of dysuria.

Strength of this study is that it is based on symptomatic patients and resulting symptomatic outcomes. This quite well fits in the needs and current recommendations of General practitioners for symptom-oriented, therapeutic management without unnecessary laboratory investigations. The main limitation of this study seems to be that the follow up of the patients was not performed after the duration of study, i.e, 5 days. It may be noted that concerns on patient's safety or fear of complications may incite the GPs to administer antibiotic treatment in uncomplicated UTI despite being aware of the hazard of over treatment. Anyway, no serious complications were observed in either study group, and the incidence of minor adverse events was found similar in both groups.

CONCLUSIONS

Our results clearly support the assumption of non-inferiority of symptomatic treatment uncomplicated UTI. This study suggests the modified treatment recommendations towards symptomatic management of uncomplicated urinary tract infections.

AUTHORS' CONTRIBUTION

All authors contributed equally.

REFERENCES

1. Gupta K, Hooton T, Naber K, Wullt B, Colgan R, Miller LG, *et al*. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011;52(5):e103–20.
2. Schappert SM, Rechtsteiner EA. Ambulatory medical care utilization estimates for 2007. Vital Health Stat 2011;169:1–38.
3. Baldo BA, Zhao Z, Pham NH. Antibiotic allergy: immunochemical and clinical considerations. Curr Allergy Asthma Rep 2008;8(1):49–55.
4. Walters MS, Lane MC, Vigil PD, Smith SN, Walk ST, Mobley HL. Kinetics of Uropathogenic Escherichia coli Metapopulation Movement during Urinary Tract Infection. MBio 2012;3(1):e00303–11.
5. Aypak C, Altunsoy A, Düzgün N. Empiric antibiotic therapy in acute uncomplicated urinary tract infections and fluoroquinolone resistance: a prospective observational study. Ann Clin Microbiol Antimicrob 2009;8:27.
6. Gobernado M, Valdés L, Alós JI, García-Rey C, Dal-Ré R, García-de-Lomas J, *et al*. Antimicrobial susceptibility of clinical Escherichia coli isolates from uncomplicated cystitis in women over a 1-year period in Spain. Rev Esp Quimioter 2007;20(1):68–76.
7. Butler CC, Dunstan F, Heginbothom M, Mason B, Roberts Z, Hillier S, *et al*. Containing antibiotic resistance decreased antibiotic-resistant coliform urinary tract infections with reduction in antibiotic prescribing by general practices. Br J Gen Pract 2007;57(543):785–92.
8. Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, *et al*. Effectiveness of five different approaches in management of urinary tract infection: randomized controlled trial. BMJ 2010;340:c199.
9. Bleidorn J, Gágyor I, Kochen MM, Wegscheider K, Eva Pradier EH. Symptomatic treatment (ibuprofen) or antibiotics (ciprofloxacin) for uncomplicated urinary tract infection? - Results of a randomized controlled pilot trial. BMC Med 2010;8:30.
10. Gágyor I, Hummers-Pradier E, Kochen MM, Schmiemann G, Wegscheider K, Bleidorn J. Immediate versus conditional treatment of uncomplicated urinary tract infection - a randomized-controlled comparative effectiveness study in general practices. BMC Infect Dis 2012;12:146.
11. Head KA. Natural Approaches to Prevention and Treatment of Infections of the Lower Urinary Tract. Altern Med Rev 2008;13(3):227–44.
12. Ullah F, Malik S, Ahmed J. Antibiotic susceptibility pattern and ESBL prevalence in nosocomial Escherichia coli from urinary tract infections in Pakistan. Afr J Biotechnol 2009;8(16):3921–6.
13. Ahmed K, Imran. Prevalence and Antibiogram of Uncomplicated Lower Urinary Tract Infections in Human Population of Gilgit, Northern Areas of Pakistan. Pak J Zool 2008;40(4):295–301.
14. Christiaens TC, De Meyere M, Verschraegen G, Peersman W, Heytens S, De Maeseneer JM. Randomized controlled trial of nitrofurantoin versus placebo in the treatment of uncomplicated urinary tract infection in adult women. Br J Gen Pract 2002,52(482):729–34.
15. Ferry SA, Holm SE, Stenlund H, Lundholm R, Monsen TJ. The natural course of uncomplicated lower urinary tract infection in women illustrated by a randomized placebo controlled study. Scand J Infect Dis 2004;36(4):296–301.

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