Efficacy of prophylaxis in women with sex induced cystitis

C. Stamatiou[1], *M.D.*; **G. Petrakos**[2], *M.D.*; **C. Bovis**[1], *Ph.D.*; **P. Panagopoulos**[2], *Ph.D.*; **A. Economou**[2], *M.D.*; **C. Karkanis**[1]

[1]*Urology Department, "Tzaneion" General Hospital Piraeus;*
[2]*Gynecology Department, "Tzaneion" General Hospital Piraeus (Greece)*

Summary

Sexual intercourse has been established as one of the most important risk factors for both isolated and recurrent uncomplicated infections of the urinary tract [1]. Prophylactic therapy requires only a small dose of an antimicrobial agent, which is generally given at bedtime for 6 to 12 months. An alternative method is to give an antimicrobial agent for six months post-intercourse. It is still unknown which of the two methods is most effective.

A total of 123 women with suspected sexually induced recurrent cystitis (mean age 28 years, range 15 to 65) and a history of recurrent urinary tract infection (UTI) (the last one within the last six months) were subjected to prophylactic therapy for six months. Half of them were treated with low-dose trimethoprim-cotrimoxazole (TMP-SMX) and cefaclor given orally post-intercourse (spontaneous usage), while the other half were treated with low-dose TMP-SMX and cefaclor given at bedtime. The response to the prophylactic therapy was classified as *continued cure* in 106 cases (86.17%), *failure* in 13 cases (10.56%), and *unknown* in four cases (3.25%).

TMP-SMX administered in continuous nightly prophylaxis showed similar efficacy and tolerability as cefaclor post-intercourse.

Objective: To determine the efficacy of prophylaxis in women with recurrent sex induced cystitis and compare the post-intercourse versus the conventional bedtime given long-term, low-dose use of prophylactic antimicrobials.

Key words: Prophylaxis; Women; Sex-induced cystitis; Lower urinary tract infections.

Patients and Methods

The patients in this study included 123 women who had a history of recurrent urinary tract infection (UTI) selected among 2,882 women with symptoms of lower urinary tract infections between August 2002 and August 2004. All were aged between 18 and 65 years. All were from Piraeus and suburban locations. There was discretion differences in profession, social class or place of birth.

Each of 2,882 women had to have a positive urinalysis suggestive of pyuria or more than two signs or symptoms suggestive of an acute uncomplicated UTI (i.e., dysuria, frequency, urgency, suprapubic pain), with an onset of symptoms within 72 hours of enrollment.

Women were eligible for enrollment if they had a history of recent cystitis diagnosed clinically within six months and absence of bacterial growth in the urine culture on the third day of therapy (of the current infection).

At enrollment, a clean-catch midstream urine specimen was obtained from each patient. A positive culture was defined as isolation of an uropathogen in quantities > 10^5 colony-forming units (CFU)/ml urine, and pyuria was defined as > 10 leukocytes/mm^3 in unspun urine examined in a counting chamber. Women eligible for enrollment were subjected to an ultrasound evaluation of their urinary tract. Cases with abnormalities on ultrasound (dilatation of ureteropelvic junction, renal calculi, etc.) were excluded. Cases of neurogenic bladder dysfunction, fistula, and/or severe diseases such as diabetes mellitus were also excluded. Other exclusion criteria were neutrophil count < 1000 cells/mm^3, CD4+ count < 200 cells/mm^3, or other conditions associated with significant immunosuppression; use of a systemic antimicrobial agent within 48 hours before enrollment serum creatinine level > 3.0 mg/dl or creatinine clearance < 30 ml per min/1.73 m^2; and liver impairment (i.e., baseline aspartate amino-transferase, alanine aminotransferase, and/or total bilirubin > 3 times the upper limit of normal).

All patients received the appropriate antimicrobial therapy proportionally to the spectrum of aetiological agents. Approximately half of the patients were prescribed ampicillin. Five patients received fluoroquinolone (because of history of hypersensivity to penicillin) and the remaining patients of those surveyed were treated with trimethoprim-cotrimoxazole (TMP-SMX).

The remaining cases were subjected to urinalysis on the third and seventh day of the management. Women with samples containing bacteria were excluded from further analysis.

Women with absence of bacterial growth in the urine culture had to complete a questionnaire on behavioral risk factors. Women with a history of at least two episodes of recurrent cystitis who had an active sexual life and reported sexual intercourse 24 to 72 hours before the onset of symptoms were evaluated as possible cases of sex-induced cystitis (SIC).

E. coli was the causative pathogen in 84% of sex-induced reinfections. Other enterobacteria responsible for the remaining infections were Proteus, Klebsiella and Staphylococcus saprophyticus.

Urinalysis was obtained six to ten days after initial therapy (test-of-cure visit). At the test-of-cure visit, the clinical response was categorized as *cure* (disappearance of or improvement in signs and symptoms of the infection such that additional antimicrobial therapy was not required), *failure* (no apparent response to therapy, persistence of signs and symptoms of infection and reappearance of signs and symptoms at or before the test-of-cure visit), or *indeterminate* (could not be evaluated).

The absence of bacterial growth in the urine upon completion of ten days of therapy was a prerequisite for the next phase of the study.

Approximately half of the patients (60 women) received prophylactic therapy with a low dose of TMP-SMX while the remaining (63 women) received prophylactic therapy with a low

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dose of cefaclor. Half of each group received an antimicrobial agent for six months post-intercourse while the other half also received an antimicrobial agent at bedtime for six months.

Urinalysis was obtained upon completion of six months (test-of-prophylaxis visit). The clinical outcome was evaluated based on serial assessments of the effect of therapy on the signs and symptoms of UTI (dysuria, frequency, urgency, and suprapubic pain). At the late follow-up visit, the clinical response was classified as *continued cure* (continued absence of or improvement in all signs and symptoms of infection such that additional antimicrobial therapy was not needed), and *failure* (reappearance of signs and symptoms of infection requiring antimicrobial therapy in a patient with a response of *cure* at the test-of-cure visit), or *unknown* (not evaluated if patient interrupted the prophylaxis trial for any reason).

No other discretions were to the patient selection but the history of allergy or of previous adverse reaction in a certain antimicrobial agent.

Results

The initial clinical response was categorized as cure in 100% of the cases since all responded to antimicrobial therapy.

The response to the prophylactic therapy was classified as *continued cure* in 106 cases (86.17%), *failure* in 13 cases (10.56%), and *unknown* in four cases (3.25%).

Twenty of 30 patients who received TMP-SMX and 30 of 32 patients who received cefaclor post-intercourse were classified as *continued cure.* Twenty-eight of 30 patients who received TMP-SMX and 16 of 31 patients who received cefaclor at bedtime were classified as *continued cure* as well.

Two patients who received TMP-SMX and three patients who received cefaclor post-intercourse were classified as *failure*. Four patients who received TMP-SMX and four patients who received cefaclor at bedtime were classified as *failure* as well.

One patient who received TMP-SMX but 0 patients who received cefaclor post-intercourse were classified as *unknown outcome*. No patients who received TMP-SMX but three patients who received cefaclor at bedtime were classified as *unknown outcome* as well.

Trimethoprim-cotrimoxazole administered in continuous nightly prophylaxis showed similar efficacy and tolerability as cefaclor post-intercourse.

Two patients received cefaclor nightly interrupted the trial because of vulvovaginal overgrowth with Candida.

Discussion

One effective approach for the management of recurrent uncomplicated UTI is the prevention of infection through the use of long-term, low-dose prophylactic antimicrobials: reinfection and recurrences decreased by 95% when compared with a placebo or with the patients' prior experiences as controls [1-3].

There is a vast array of antibacterial agents but some currently available have emerged as the preferred treatment choices for UTI [4, 5]. Since vaginal colonization with urinary tract pathogens is thought to be an etiological factor for recurrent sex-induced cystitis, drugs that achieve good concentrations in vaginal secretions may be more effective than drugs that do not [6]. TMP-SMX has been considered a powerful prophylactic agent for the prevention of reinfections in females [7]. Indeed, TMP-SMX eradicates gram-negative aerobic flora that may colonize the periurethral area and subsequently cause episodes of sex-induced cystitis in women from the gut and vaginal fluid. These important biologic effects occur in addition to antimicrobial concentrations of TMP-SMX in the urine during nightly prophylaxis [8]. Nevertheless, both need a stable bactericidal level in the urine and this may explain why according our findings continuous nightly prophylaxis with TMP-SMX is more effective than spontaneous post-intercourse use.

Oral first generation cephalosporins have not been found to be particularly successful in the treatment of UTI [2]. In addition cephalosporins show an increasing trend for producing resistance to fecal bacteria. Nevertheless, prophylactic efficacy of cephalexin in low doses is well documented [9]. This occurs since minimal doses show minimal adverse effects on the fecal and vaginal flora: cephalexin (250 mg) given nightly for an interval of six months did not change the rectal and vaginal carriage of Enterobacteriaceae [10].

Although the prophylactic efficacy of second generation oral cephalosporins is less known, it seems that they may perform better, particularly because of their greater activity against gram-negative bacilli. Low dosage and spontaneous (post-intercourse) use is the key for effective profylaxis with cefaclor. Indeed, oral cefaclor 500 mg post-intercourse showed better efficacy and tolerance than oral cefaclor 500 mg once daily.

Cephaclor represents an alternative antimicrobial agent when history of allergy or previous adverse reaction to TMP/SMX occurs [11], since fluoroquinolones are expensive for *such* long-term use [12] and throughout therapy with nitrofurantoin, colonization of the vaginal introitus with enterobacteriaceae continues.

Conclusions

In this study prophylactic therapy was effective in the management of women with recurrent sex-induced cystitis. Since the efficacy and tolerability of TMP-SMX administered nightly for six months to women were comparable to those of cephalexin 500 mg administered post-intercourse for six months, we consider cephaclor to be an effective option for empiric prophylaxis when TMP-SMX is contraindicated.

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Address reprint requests to:
P. PANAGOPOULOS, Ph.D.
69 Lasithiou Str.
16674 Glyfada (Greece)