Management of Recurrent Urinary Tract Infections with Patient-Administered Single-Dose Therapy

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In a randomized crossover trial, 38 women with recurrent urinary tract infections were assigned to use either continuous prophylaxis with trimethoprim-sulfamethoxazole or intermittent self-administered therapy (single-dose trimethoprim-sulfamethoxazole taken for acute urinary symptoms). The infection rate for patients on prophylaxis was 0.2 episodes/patient-year compared with 2.2 infections/patient-year for patients on self-administered therapy ($p < 0.001$). Thirty-five of thirty-eight symptomatic episodes diagnosed by patients as infection were confirmed microbiologically, and 30 of the 35 infections responded clinically and microbiologically to patient-administered therapy with single-dose trimethoprim-sulfamethoxazole. No complications were seen in the 5 patients in whom therapy failed. The annual costs of prophylaxis and self-therapy were similar ($256 and $239, respectively) and both were less expensive than conventional therapy in women having 2 or more infections per year. In selected women, self-therapy is efficacious and economical compared with conventional therapy or prophylaxis.

MOST PHYSICIANS prescribe a short course of antimicrobial therapy for women with sporadic urinary tract infections (1), and many use antimicrobial prophylaxis in patients having several recurrent infections each year. Despite its efficacy and cost-effectiveness (2, 3), however, chemoprophylaxis carries attendant disadvantages, including adverse drug reactions, selection of antibiotic-resistant strains, and uncertainty as to how long to continue therapy (2-4). An alternative strategy for managing recurrent infections has been to prescribe antimicrobials for susceptible women to keep at home and self-administer when symptoms arise. This strategy becomes particularly attractive if single-dose antimicrobial regimens can be used and if women can accurately self-diagnose their infections. If effective, intermittent self-therapy would have several advantages over chemoprophylaxis, including use of less drug, fewer adverse reactions, decreased selective pressure for antibiotic resistance, improved convenience and compliance, and perhaps less cost. We compared the effectiveness and cost of patient-initiated single-dose antimicrobial therapy with those of antimicrobial prophylaxis for women with frequent recurrent infections.

Methods

PATIENT POPULATION

Women seen at the University of Washington student health center or the outpatient clinic at the Seattle Public Health Hospital were eligible for study if they were aged 18 years or older, had two or more culture-documented urinary tract infections in the 12 months preceding enrollment, had not taken antibiotics within 4 weeks, were not pregnant, and were willing to provide informed consent. We excluded women with a history of allergy to trimethoprim or sulfonamides, previous urologic surgery, renal stones, or renal impairment. Patients were enrolled 4 weeks after treatment of their most recent infection if they had negative urine cultures at that time. Ten women who were on antimicrobial prophylaxis before study entry were enrolled 4 weeks after their antibiotic prophylaxis was discontinued.

STUDY DESIGN

Thirty-eight patients satisfying the study requirements were randomly assigned to receive either 6 months of continuous antimicrobial prophylaxis with trimethoprim-sulfamethoxazole (40 mg of trimethoprim per 200 mg of sulfamethoxazole by mouth daily at bedtime) or 6 months of intermittent therapy with single-dose trimethoprim-sulfamethoxazole (4 tablets of 80 mg/400 mg) administered by the patient at the onset of urinary symptoms. At the end of 6 months, all patients were crossed over and received the alternate regimen for a second 6 months. Twenty-eight patients completed both arms of the study, and ten did not, because of infections with trimethoprim-resistant organisms (two patients), severe adverse drug reactions (two patients), relapsing infections unresponsive to single-dose therapy and to one subsequent 10-day course of antibiotics (two patients), or noncompliance (four patients). Four patients were on the intermittent self-therapy regimen and six were on prophylaxis when they were dropped from the study.

Patients were seen at enrollment and every 2 months thereafter. At each follow-up visit, they were questioned about urinary symptoms, adverse drug reactions, use of other antibiotics, and intercurrent medical problems. We assessed compliance by questioning the patient and by counting the remaining pills at each clinic visit. When patients on prophylaxis developed urinary symptoms, they were instructed to stop their medication and report to the clinic for evaluation. If found to be infected, patients received a 10-day course of antimicrobial therapy and then resumed prophylaxis only after successful treatment was documented.

Patients on intermittent self-therapy were apprised of the signs and symptoms commonly associated with urinary tract infections, but specific criteria for drug administration were not established. Rather, patients were encouraged to base their diagnosis of infection on symptoms experienced in previous episodes. Each patient received a packet of four single-strength tablets of trimethoprim-sulfamethoxazole that they were instructed to take as a single dose whenever they suspected infection. Each patient also received an infection report form on which to record the onset and duration of urinary signs and symptoms, date of self-medication, date and time of urine collection, and adverse effects of medication.

To assess the accuracy of self-diagnosis, patients were instructed to collect and refrigerate a clean-catch, midstream urine sample before treating themselves. Urine samples were not accepted if they had been left unrefrigerated for more than 1 hour after collection or if more than 24 hours had elapsed between collection and receipt in the laboratory. Patients were

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seen in the clinic at 1 week and 4 to 6 weeks after self-administered single-dose therapy to assess cure. Women on intermittent self-therapy who had a relapse after single-dose therapy were treated with a 10-day course of an appropriate antibiotic. When follow-up urine cultures showed eradication of infection, they returned to the intermittent self-therapy regimen.

We considered 10^2 or more aerobic, gram-negative bacilli or *Staphylococcus saprophyticus* per millilitre of urine in a woman with acute symptoms as evidence of infection (5). After therapy, infections were considered cured if the presenting signs and symptoms had been alleviated or resolved and if the test-of-cure urine culture obtained 1 week and 4 to 6 weeks later had less than 10^2 colonies/mL of the infecting organism. Recurrent infections were categorized as relapses (last infection less than 6 weeks ago with an organism of the same antibiotic-susceptibility pattern and serotype) or reinfections (infection with an organism of a different species, susceptibility pattern, or serotype).

MICROBIOLOGIC STUDIES

Clean-void, midstream urine specimens were collected for urinalysis and culture, and cultures were made of rectal, urethral, and vaginal specimens obtained with sterile cotton-tipped applicators premoistened with trypticase-soy broth. All specimens were refrigerated until transport to the laboratory.

Quantitative urine cultures were done by pipetting 0.1 mL of undiluted urine and a 0.1-mL aliquot of urine diluted (1:100) in trypticase-soy broth onto MacConkey and blood agar plates. Rectal, urethral, and vaginal specimens were cultured semiquantitatively by inoculating swabs onto the corner of MacConkey and blood agar plates and then streaking the plates. We evaluated all plates at 24, 48, and 72 hours, identified each morphologically distinct colony type using standard methods (6), and determined their quantity.

Antimicrobial susceptibility testing of all urinary isolates was done by standard disk-diffusion techniques (7). We screened rectal, urethral, and vaginal swabs for the presence of trimethoprim-resistant organisms by streaking them onto Mueller-Hinton agar plates containing 10 μg/mL of trimethoprim. Trimethoprim resistance in isolates from these selective plates was confirmed by an agar dilution method using an inoculum of 10^5 colony-forming units and incorporating thymidine kinase at a 0.25-μg/mL concentration into the medium. *Escherichia coli* isolates were serotyped as previously described (8). We used a modification of the method of Jones and colleagues (9) to assess antibody coating of urinary bacteria. Specimens were collected at study entry and at each clinic visit with calcium alginate swabs and were cultured for *chlamydia trachomatis* as previously described (10).

COST ANALYSIS

We determined the direct costs of managing patients on each regimen by using the actual outcomes observed during the study. We calculated the cost of each outcome by summing the charges for clinic visits, laboratory and diagnostic evaluations, and antibiotics, as shown in the Appendix. Patients were assessed the following charges: clinic visit (including physician fee), $50.00; urinalysis, $9.35; urine culture, $20.00; antibiotic sensitivity testing, $20.00 for each organism; and wet-mount microscopic examination of vaginal fluid, $5.00. Drug charges included a pharmacy handling fee of $3.60 and the following charge per tablet: trimethoprim-sulfamethoxazole 80-mg/400-mg tablet, 10 cents; nitrofurantoin, 100-mg tablet, 52 cents; and nystatin vaginal tablets, 25 cents. We made no attempt to estimate the indirect costs (time lost from work, travel, child care) associated with each infection.

Patients on prophylaxis who had no infections were charged only the cost of the initial evaluation and for a 6-month supply of trimethoprim-sulfamethoxazole. Patients who were infected during prophylaxis were charged for a return clinic visit, urinalysis, urine culture, antibiotic sensitivity testing, and a 10-day course of antibiotics. Patients managed without infection on intermittent self-therapy were charged for the initial evaluation and the cost of the single-dose trimethoprim-sulfamethoxazole. Infected patients were charged additionally for each single-dose supply of antibiotics used. For purposes of the study, follow-up urine cultures were routinely obtained to assess the efficacy of single-dose therapy, but for purposes of cost comparison, patients were not charged for these cultures unless they had a relapse. If a relapse occurred, patients were charged for a second clinic visit, urinalysis, urine culture, sensitivity testing, a 10-day course of antibiotics, and a post-therapy urinalysis and culture. If the second follow-up urine culture showed persistent infection, patients were charged for a third clinic visit, a second 10-day course of antibiotics, and a follow-up urinalysis and culture. Adverse effects of medication resulted in charges only if intervention was required. For example, minor reactions such as nausea or mild abdominal pain resulted in no costs, but more severe reactions such as a rash or yeast vaginitis required appropriate diagnostic procedures and treatment, for which patients were charged accordingly.

STATISTICAL ANALYSIS

The McNemar test was used to compare infection rates in the two arms of the crossover trial. All other statistical comparisons were done with Fisher's two-tailed exact test or the Student's *t*-test.

Results

INFECTIONS ON PROPHYLAXIS

Thirty-one of thirty-three patients who were followed for 165 months on prophylaxis remained infection free. Two patients had three infections, and thus the overall infection rate was 0.22/year of prophylaxis. Two of the three infections were caused by trimethoprim-sulfamethoxazole-resistant *Escherichia coli* with minimal inhibitory concentrations to trimethoprim of 1024 μg/mL or more. All three breakthrough infections responded to treatment with a 10-day course of nitrofurantoin.

INFECTIONS ON INTERMITTENT SELF-THERAPY

Twenty-three of thirty-four women followed for 193 months on intermittent self-therapy had 42 symptomatic episodes. Four episodes could not be assessed microbiologically because either the specimen was improperly refrigerated or it was collected after single-dose therapy. In 35 of the 38 evaluable episodes, infections were confirmed microbiologically, with the pathogens being *E. coli* in 24, *Staphylococcus saprophyticus* in 3, *E. coli* and *Klebsiella pneumoniae* in 3, enterococci in 2, *E. coli* and enterococci in 1, *Citrobacter freundii* in 1, and *Pseudomonas aeruginosa* in 1. Eighteen of the thirty-nine infecting pathogens were present in colony counts of 10^5 or more per millilitre of urine, whereas 21 episodes had 10^2 or more but less than 10^5 colonies/mL: 10^4/mL in 13 episodes, 10^3/mL in 6 , and 10^2/mL in 2. Testing for antibody-coated bacteria was done in 29 of the 30 infections with 10^4 colonies/mL or more, and 3 were positive.

Patients on intermittent self-therapy had symptomatic episodes at a rate of 2.6/patient-year. The microbiologically confirmed infection rate was 2.2/patient-year, significantly higher than the rate during prophylaxis ($p < 0.001$). Fifteen patients had only 1 infection whereas eight had multiple episodes. The greatest risk of infection occurred in the first 2 months of intermittent self-therapy, when approximately 20% of remaining susceptible patients developed an infection each month (Figure 1). Twelve of the twenty-three patients who eventually became infected were infected by week 6. We saw no effect of randomization (whether patients received inter-

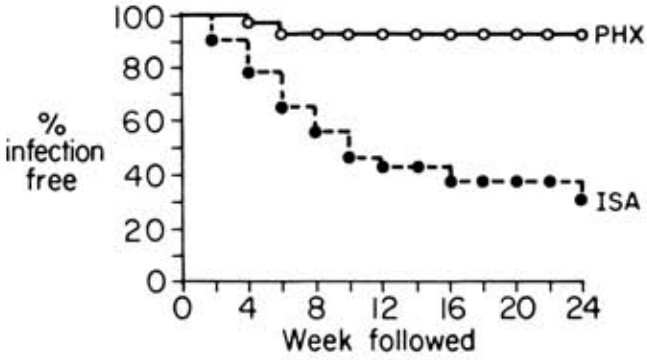

Figure 1. Percent of study patients on prophylaxis (*PHX; n* = 33) and intermittent self-therapy (*ISA; n* = 34) remaining infection-free by week of study.

mittent self-therapy first or prophylaxis first) on the rate of infection or the time to first infection while on intermittent self-therapy.

We found no significant differences between the 23 patients who did and the 11 patients who did not develop infection on intermittent self-therapy in terms of age, age of first urinary infection, history of pyelonephritis, history of prophylaxis before enrollment into the study, or baseline rate of infection in the 12 months preceding enrollment. However, only 1 or 4 patients with two infections in the 12 months before study enrollment became infected while on intermittent self-therapy compared with 22 of 30 patients who had three or more infections in this period ($p = 0.08$).

RESPONSE TO SELF-ADMINISTERED TRIMETHOPRIM-SULFAMETHOXAZOLE

Thirty of the thirty-five symptomatic infections that occurred during intermittent self-therapy responded clinically and microbiologically to single-dose trimethoprim-sulfamethoxazole treatment. In three of the five women who did not respond, urinary symptoms persisted and post-treatment urine cultures grew the original infecting organism (identical by serotype for two *E. coli* infections and by susceptibility pattern for one *P. aeruginosa* infection). The other two patients became symptom-free and culture-negative immediately after therapy but had a relapse shown clinically and microbiologically 20 and 35 days later. None of the five patients who did not respond or had a relapse after single-dose therapy developed signs or symptoms of pyelonephritis or bacteremia, and all were cured with a 10- to 20-day course of antibiotic. Assays for antibody coating in all five patients were negative.

EFFECT ON RECTAL, URETHRAL, AND VAGINAL ENTEROBACTERIA

Compared with the number in the prestudy period, the proportion of patients who had rectal and urethral carriage of enterobacteria was decreased after 2, 4, and 6 months of prophylaxis with trimethoprim-sulfamethoxazole (Figure 2; $p < 0.05$). Vaginal carriage was reduced at 4 months ($p < 0.05$) but not at 2 or 6 months of prophylaxis. In contrast, intermittent self-therapy had no apparent effect on rectal, urethral, and vaginal carriage of enterobacteria (Figure 2).

ADVERSE REACTIONS

Eight adverse reactions, five in patients on prophylaxis and three in patients on intermittent self-therapy, were seen. One patient on prophylaxis developed transient nausea and mild abdominal pain and a second had two episodes of yeast vulvovaginitis. Both continued to take prophylaxis. Two patients developed skin reactions—a morbilliform rash and oral ulcers—in the third month and second week of prophylaxis, respectively. Both rashes resolved spontaneously when trimethoprim-sulfamethoxazole therapy was discontinued. All three reactions occurring in patients on intermittent self-therapy were transient nausea.

COST COMPARISON

The average direct cost of successful prophylaxis with trimethoprim-sulfamethoxazole for 6 months in a patient without adverse reaction or urinary tract infection was $104.37. The additional cost for managing a breakthrough infection, consisting of the cost of a return clinic visit ($50.00), initial laboratory evaluation ($49.35), 10-day course of nitrofurantoin ($24.00), and follow-up urinalysis and culture ($29.35), was $153.10. The total cost of managing 33 women for 6 months on prophylaxis, including the cost of evaluation and treatment of adverse reactions and episodes of infections, in our study was $4227.90 or $128.12 per person (annual cost, $256).

In contrast, the average cost of 6 months of intermittent self-therapy uncomplicated by infection was $83.34 per patient. Of the 42 symptomatic episodes, 38 resolved after single-dose therapy and did not require follow-up. Management of these episodes therefore amounted only to the cost of medication ($151.62). Treatment of the five relapses that failed to respond to single-dose therapy amounted to $1325.47. The total cost of managing 34 patients for 6 months on intermittent self-therapy with complications was $4056.64, or $119.31 per patient (annual cost, $239).

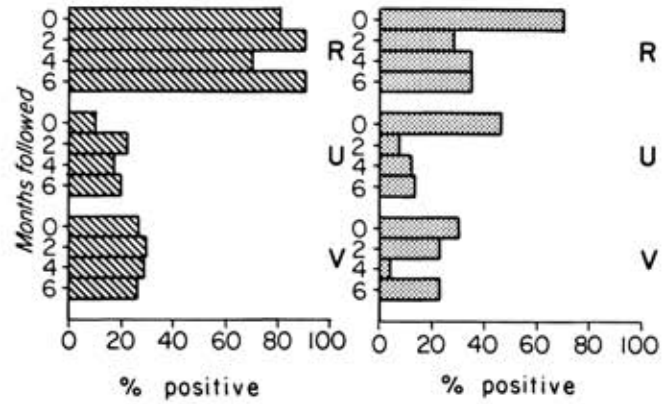

Figure 2. Percent of study patients on intermittent self-therapy (*left*) and prophylaxis (*right*) colonized with enterobacteria in the rectum (*R*), urethra (*U*), and vagina (*V*) by month of study.

Discussion

The rationale for use of intermittent self-therapy rests on two assumptions: that patients can accurately self-diagnose infection, and that the infections, once acquired, can be treated effectively with self-administered single-dose antimicrobials. Our results suggest that patients can indeed accurately self-diagnose infection, because 35 of 38 suspected episodes were confirmed microbiologically. However, we studied a select population of women, many of whom had attended a special clinic on urinary tract infection and all of whom were sufficiently motivated to enroll in a long-term clinical study. In addition, they had extensive personal experience with these infections, being selected on the basis of having had at least 2 demonstrated bacterial infections in the preceding year. Because of this preselection, the likelihood of a symptomatic episode being due to acute cystitis, rather than other causes of dysuria such as urethritis or vaginitis (11), was high. In an unselected population, the accuracy of self-diagnosis would, no doubt, be less than in this group of women.

All symptomatic infections that occured during intermittent self-therapy presented clinically as acute uncomplicated cystitis. In addition, 90% of the infecting strains were sensitive in vitro to trimethoprim-sulfamethoxazole, and the proportion characterized by a positive antibody-coated bacteria assay was low (10%). These three factors would predict a high rate of success with single-dose therapy (1, 12) and, indeed, 30 of 35 infections responded clinically to single-dose trimethoprim-sulfamethoxazole therapy. It might be expected that women using intermittent self-therapy would, on average, receive therapy earlier in the course of their disease than patients who must visit a physician to obtain a prescription. Because early treatment probably prevents ascending renal infection from developing, early intervention may be an advantage of intermittent self-therapy. The two patients in our study in whom treatment failed and the three who had relapses after therapy all responded to 10-day courses of antibiotics, and we encountered no cases of pyelonephritis or bacteremia.

Our results confirm those of previous studies (2, 13) showing the effectiveness of continuous low-dose trimethoprim-sulfamethoxazole therapy in preventing recurrent infections: Only three breakthrough episodes occurred during 165 patient-months of observation (0.22 infections/patient-year). In contrast, the same women averaged 2.2 confirmed infections per year on intermittent self-therapy. This difference was not unexpected, however, because patients on self-therapy have no intervention until they become infected. In addition, intermittent self-therapy did not alter urethral and vaginal colonization with gram-negative bacilli as prophylaxis did. Stamey and colleagues (14) and others (15) have considered persistent introital colonization to be an important factor predisposing women to repeated urinary infections. Because intermittent self-therapy did not influence vaginal or urethral colonization, one might expect little change in the frequency of recurrent infections during intermittent self-therapy.

In a 1977-1978 study of continuous antibiotic prophylaxis (2), we saw no infections caused by trimethoprim-resistant or trimethoprim-sulfamethoxazole-resistant gram-negative rods, and only 1 of 316 *E. coli* isolates from rectal, urethral, and vaginal cultures taken from patients given 6 months of prophylaxis and followed for 6 months after prophylaxis showed resistance to 15 μg/mL or more of trimethoprim. In contrast, in this study, we saw 13 instances of rectal, urethral, and vaginal colonization with trimethoprim-resistant *E. coli,* and 2 patients developed infections with trimethoprim-sulfamethoxazole-resistant *E. coli.* Thus, although the reported proportion of trimethoprim resistance in *E. coli* urinary isolates obtained from outpatients in this country has generally been less than 5% (16, 17), trimethoprim resistance among women on trimethoprim-sulfamethoxazole prophylaxis has increased since our earlier study. The degree to which prophylaxis directly contributed to this increase is unclear, but continuous antimicrobial use no doubt provides a selective advantage to resistant strains present in the gastrointestinal tract. Unlike prophylaxis, single-dose antibiotic therapies do not appear to greatly influence rectal, urethral, or vaginal carriage of aerobic gram-negative rods, but whether this will result in lesser antimicrobial resistance needs further evaluation.

Given the frequency of urinary infections, the cost of any management strategy becomes an important consideration. In our study, the annual costs of prophylaxis and intermittent self-therapy were $256 and $239, respectively. Both are less costly than treatment of two episodes of infection by the conventional method of 10 days of antibiotics with follow-up urinalysis and culture ($273 using the same charges). Therefore, from an economic point of view, both prophylaxis and intermittent self-therapy appear to be equally suitable alternatives for managing women who have two or more infections per year. However, charges for treating an acute infection vary considerably in different settings, and the least expensive management strategy will depend on individual practices and charges. It should be noted that the per annum charges calculated were based on the first year any of these strategies were used in a given patient, and they therefore include an initial visit, culture, and urinalysis. Subsequent annual charges would be less if routine follow-up evaluations were not judged necessary in individual patients. In addition, we made no attempt to estimate the indirect benefits of prophylaxis and intermittent self-therapy, such as the reduction in time lost from work, patient discomfort, or anxiety associated with infection. Putting any value on these indirect benefits would clearly increase the advantage of prophylaxis and intermittent self-therapy over conventional treatment and may even enhance the relative value of prophylaxis over self-therapy, because in the former, infections are largely avoided.

We previously found that a patient's baseline rate of urinary infection over 2 to 4 years usually predicts the likelihood of continued infection without prophylaxis (2, 18). In this study, we observed a similar relationship between the baseline infection rate and the risk of infection on intermittent self-therapy. Logically, a higher infection rate may also be predictive of multiple infections or re-

lapses while a patient is on self-therapy, although the numbers of patients in our study with multiple infections (five patients) or relapses (five cases) were too small to draw any conclusions. Nevertheless, it may be reasonable to use the baseline infection rate as one practical guideline in choosing between prophylaxis and intermittent self-therapy. Prophylaxis would be most useful for women with baseline rates of three or more infections per year, with intermittent self-therapy reserved for women who average one to two each year.

In view of our data, intermittent self-therapy can be added to the strategies available for management of women with recurrent infections, which include thrice-weekly antibiotic prophylaxis (19), postcoital prophylaxis (20, 21), and continuous (daily) low-dose prophylaxis. As we have stressed, the choice among these modes hinges primarily on assessment of efficacy, cost, and risk of adverse effects, but individual patient characteristics must also be considered. Patients who are noncompliant would not be good candidates for daily or thrice-weekly prophylaxis. Because our study was done with healthy, well-motivated women with previous uncomplicated infections, our results may not be applicable to other groups. Thus, patients who show a poor capacity for accurate self-diagnosis or who are unlikely to seek follow-up care if single-dose antibiotics should fail would be poor candidates for self-diagnosis and therapy. Nicolle and coworkers (22), have shown that urinary infections may be precipitated by sexual intercourse. Therefore, premenopausal women whose infections are associated with sexual intercourse may do best on postcoital antibiotic prophylaxis. The optimal management strategy for each patient can be ascertained after weighing these considerations and tailoring therapy to each woman's pattern of infection.

Appendix: Calculation of Cost

SUCCESSFUL PROPHYLAXIS (29 PATIENTS)

Initial clinic visit ($50.00 + urinalysis ($9.35) + urine culture ($20.00) + trimethoprim-sulfamethoxazole prophylaxis for 6 months ($25.02) = $104.37 × 29 patients = $3026.73.

SEVERE ADVERSE REACTION ON TRIMETHOPRIM-SULFAMETHOXAZOLE PROPHYLAXIS (1 PATIENT)

Initial clinic visit ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + return clinic visit for adverse reaction ($50.00) + trimethoprim-sulfamethoxazole prophylaxis for 1 month ($6.57) + nitrofurantoin prophylaxis for 5 months ($66.00) = $201.92.

MINOR ADVERSE REACTION ON TRIMETHOPRIM-SULFAMETHOXAZOLE PROPHYLAXIS (1 PATIENT)

Initial clinic visit ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + [return clinic visit for vaginitis ($50.00) × 2 visits] + [wet mount examination of vaginal fluid ($5.00 × 2] + [nystatin medication for yeast vaginitis ($6.10) × 2 courses] + trimethoprim-sulfamethoxazole prophylaxis for 6 months ($25.02) = $226.57.

THREE BREAKTHROUGH URINARY TRACT INFECTIONS (2 PATIENTS)

Patient 1: Episode 1: initial clinic evaluation ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + return clinic visit for breakthrough infection ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + sensitivity testing ($20.00) + nitrofurantoin therapy for 10 days ($24.40) + followup urinalysis ($9.35) + urine culture ($20.00) = $232.45. Episode 2: return clinic visit for breakthrough infection ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + sensitivity testing ($20.00) + nitrofurantoin macrocrystal therapy for 10 days ($24.40) + follow-up urinalysis ($9.35) + urine culture ($20.00) + trimethoprim-sulfamethoxazole prophylaxis for 3 months ($12.51) + nitrofurantoin prophylaxis for 3 months ($50.40) = $216.01. Total cost for two episodes = $448.46.

Patient 2: Initial clinic visit ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + return visit for breakthrough infection ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + sensitivity testing ($20.00) + treatment with nitrofurantoin for 10 days ($24.40) + follow-up urinalysis ($9.35) + urine culture ($20.00) + trimethoprim-sulfamethoxazole prophylaxis for 1 month ($6.57) + nitrofurantoin prophylaxis for 5 months ($85.20) = $324.22. Total cost of three episodes = $772.68.

SUCCESSFUL INTERMITTENT SELF-THERAPY (11 PATIENTS)

Initial clinic visit ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + cost of single-dose trimethoprim-sulfamethoxazole ($3.99) = $83.34 × 11 patients = $916.74.

THIRTY INFECTIONS ON INTERMITTENT SELF-THERAPY CURED WITH SINGLE-DOSE TRIMETHOPRIM-SULFAMETHOXAZOLE (20 PATIENTS)

Initial clinic visit ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + cost of single-dose trimethoprim-sulfamethoxazole ($3.99) = $83.34 × 20 patients = $1666.80 + cost of 30 infections cured with single-dose trimethoprim-sulfamethoxazole ($119.70) = $1786.50.

FIVE RELAPSING INFECTIONS ON INTERMITTENT SELF-THERAPY (4 PATIENTS)

Initial clinic visit ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + cost of single-dose trimethoprim-sulfamethoxazole ($3.99) = $83.34 × 3 patients = $250.02 (fourth patient first had a reinfection and is included in cost calculation above).

Cost of single-dose trimethoprim-sulfamethoxazole ($3.99) + return clinic visit for relapse ($50.00) + urinalysis ($9.35) + urine culture ($20.00) + sensitivity testing ($20.00) + treatment with nitrofurantoin for 10 days ($24.40) = $127.74 × 5 relapses = $638.70.

Follow-up urinalysis for 5 relapses ($9.35 × 5) + urine cultures ($20.00 × 5) + sensitivity testing for 2 infections that failed conventional therapy ($20.00 × 2) + return clinic visit for failures ($50.00 × 2) + retreatment with cephradine ($15.00) and carbenicillin indanyl sodium ($50.65) + follow-up urinalysis ($9.35 × 2) + urine culture ($20.00 × 2) + trimethoprim-sulfamethoxazole prophylaxis for 4 months ($19.08) + 1 month ($6.57) for the 2 patients that required second course of conventional antibiotics for cure = $436.75. Total cost = $1325.47.

THREE FALSE-POSITIVE DIAGNOSES AND FOUR SYMPTOMATIC EPISODES MICROBIOLOGICALLY UNCONFIRMED

Cost of single-dose trimethoprim-sulfamethoxazole ($3.99) × 7 = $27.93.

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