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## The significance of compliance for the success of antimicrobial prophylaxis in recurrent lower urinary tract infections: the Greek experience

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#### Abstract

In an attempt to define the most important driver responsible for recurrence of cystitis in women, 181 records were retrospectively analysed among 1010 consecutive references in a tertiary centre for lower urinary tract infections (UTIs). All 181 women had more than three episodes of cystitis per year; 129 were under continuous prophylaxis and 52 were under postcoital prophylaxis. Analysis revealed that the most important factor affecting successful outcome of chemoprophylaxis was the compliance of patients (odds ratio 0.074; P<0.0001). Among women treated for ≥6 months, the most effective regimen was nitrofurantoin, with a success rate of 96.8% compared with 82.8% for trimethoprim/sulphamethoxazole and 72.3% for norfloxacin (P = 0.046 between agents). Failure of chemoprophylaxis was observed in 51 women in total; in 26 of them resistance to the administered agent had developed. Results of this retrospective study revealed that the most important driver leading to failure of prophylaxis for recurrent lower UTIs was the lack of compliance of women with their medication. Nitrofurantoin was the most potent among the administered agents.

Keywords: Cystitis; Recurrence; Chemoprophylaxis; Compliance; Nitrofurantoin

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#### 1. Introduction

Approximately 2–10% of women experience recurrent episodes of lower urinary tract infections (UTIs) [1]. The main strategy applied for management of these infections comprises daily administration of oral antimicrobials for a period of 3-12 months [2]. However, this strategy is not always successful and more than 50% of women

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relapse either during therapy or after discontinuation of therapy.

The present study is a retrospective analysis of the characteristics of these strategies for the management of recurrent cystitis in a tertiary university centre in Greece. The study was required because of the need to provide answers to two crucial questions: (a) what is the driving force leading to recurrence of cystitis in women; and (b) what might be the impact of antimicrobial resistance for the advent of these recurrences. The latter question is of major importance based on the high resistance rates reported for the Greek community of up to 22% for co-trimoxazole and 6% for the second-generation fluoroquinolones for the urinary pathogen Escherichia coli [3].

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#### 2. Patients and methods

#### 2.1. Study design

This retrospective study enrolled all adult women >18 years of age who were followed-up over the period September 1998 to September 2000 for lower UTIs at the outpatient clinic of Infectious Diseases of the 4th Department of Internal Medicine. During that period, the 4th Department of Internal Medicine was situated at the 'Sismanoglion' General Hospital of Athens. A total of 1010 patient records were reviewed and those with the following characteristics were selected for analysis:

- Recurrent episodes of cystitis at a frequency of three or more per year by the same pathogen as assessed by repeat urine cultures. Criteria for recurrence were based on those applied by other authors [4].
- Diagnosis of cystitis based on (a) the presence of pyuria defined as >10 white blood cells per high-power field; and (b) isolation of one pathogen at ≥10<sup>5</sup> colony-forming units (CFU)/mL of urine [4].

Following diagnosis of recurrent cystitis, all women received antimicrobial prophylaxis as standard therapy. Young women with a history connecting episodes of infection to sex were given postcoital prophylaxis; the remaining women were administered continuous prophylaxis with a single dose of antimicrobial each night. The following characteristics of the women were recorded: age, sexual habits, type, dose and duration of administered antimicrobial, results of urine cultures, underlying predisposing factors and compliance with prophylaxis.

All patients were subjected to regular follow-up with urine cultures every 3 months. If a woman experienced symptoms of cystitis she was advised to come back for consultation. Success of chemoprophylaxis was considered as any lack of recurrence of cystitis during treatment and for 3 months after the end of treatment. Urine cultures were performed in the research laboratory of the 4th Department of Internal Medicine. Quantitative urine cultures were performed after serial dilution of an aliquot of 0.1 mL in Mueller-Hinton broth (Oxoid Ltd., London, UK) and by plating another aliquot of 0.1 mL onto MacConkey agar (Becton Dickinson, Cockeysville, MD). Samples yielding a pathogen at a concentration >10<sup>5</sup> CFU/mL were considered positive. Identification of Gram-negative pathogens was performed by the API20E and the API20NE systems (bioMérieux, Paris, France). For Gram-positive cocci, identification was based on catalase and coagulase tests. For all pathogens, susceptibility testing was done with the Kirby-Bauer disk diffusion technique with interpretation according to Clinical and Laboratory Standards Institute criteria [5].

#### 2.2. Statistical analysis

Patients were divided into the following subgroups: (a) those who received prophylaxis for <6 months and  $\geq$ 6 months; (b) those who received postcoital prophylaxis and those who received daily prophylaxis; and (c) those who admitted absolute compliance with the instructions of the attending physician and those who did not. Each of the above subgroups was further subdivided according to the type of administered antimicrobial for prophylaxis. The most common risk factor related to failure of antimicrobial prophylaxis was determined after estimation of the Maentel–Haenszel's common odds ratio (OR) and its 95% confidence interval (CI). Comparisons were performed by  $\chi^2$  test. Any P-value <0.05 was considered significant.

#### 3. Results

From the files reviewed, 181 met the inclusion criteria and were analysed. Their demographic characteristics are shown in Table 1. From these women, 129 were under continuous prophylaxis and 52 were under postcoital prophylaxis, with mean ( $\pm$  standard deviation) ages of 49.82  $\pm$  17.64 and 31.58  $\pm$  11.48 years, respectively (P<0.0001).

Among these women, definite answers to the question of compliance were given by 117 women. Analysis of these patients revealed that the most important factor affecting suc-

Table 1
Characteristics of 181 women with recurrent episodes of cystitis analysed for the study

Characteristic	No. (%)
Predisposing factors	
Nephrolithiasis	23 (12.7)
Diabetes mellitus	6 (3.3)
Isolated pathogens	
Escherichia coli	144 (79.6)
Proteus mirabilis	14 (7.7)
Klebsiella pneumoniae	6 (3.3)
Pseudomonas aeruginosa	4 (2.2)
Others	13 (7.2)
Antimicrobial susceptibilities of the	isolated pathogens (%)
E. coli	Ampicillin 70.1%
	Cefalothin 82.6%
	TMP/SMX 82.6%
	Norfloxacin 91.7%
	Nitrofurantoin 92.1%
P. mirabilis	Ampicillin 78.6%
	Cefalothin 100%
	TMP/SMX 100%
	Norfloxacin 100%
K. pneumoniae	Ampicillin 50.0%
	Cefalothin 50.0%
	TMP/SMX 50.0%
	Norfloxacin 100%
	Nitrofurantoin 100%

TMP/SMX, trimethoprim/sulphamethoxazole.

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