

## The Effect of Antibiotic Prophylaxis on Post-Operative Infection in Patients Undergone Flexible Cystoscopy

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**Purpose:** The aim of this study is to determine whether antibiotic prophylaxis is required in this outpatient procedure.

**Materials and Methods:** A non-randomised, prospective observational study that included 184 patients subjected to flexible cystoscopy divided into three groups: - Group 1:60 patients with prophylaxis of 500 mg of ciprofloxacin; - Group 2:62 patients with prophylaxis of 3 g of phosphomycin; and Group 3:62 without antibiotic prophylaxis. Prior to inclusion in the study, absence of infection was checked by means of a urine culture obtained 7 days before the procedure. An analysis was made of urinary infection after 7 days, the cystoscopy indications and its diagnosis, the presence of comorbidities, and the urinary symptoms during the following 7 days.

**Results:** The mean age of the patients in Group 1 was 65.3 (SD: 12.5) years, 66.7 (10.8) years in Group 2, and 66.9 (10.8) years in Group 3 ( $P = .7$ ). Bacteriuria was present in 15% of the patients in Group 1, compared to 22.6% in Group 2, and 12.9% in Group 3, with the differences not statistically significant. In multivariate analysis, it was observed that there was no association with the appearance of bacteriuria between the groups for age ( $P = .8$ ), diabetes ( $P = .2$ ), smoking ( $P = .4$ ), lower urinary tract symptoms ( $P = .7$ ), or immunosuppression ( $P = .6$ ).

**Conclusion:** The use of ciprofloxacin or phosphomycin as prophylaxis does not appear to be indicated in flexible cystoscopy in our health area.

**Keywords:** ciprofloxacin; flexible cystoscopy; prophylaxis; phosphomycin; urinary infection.

### INTRODUCTION

Antibiotic prophylaxis in urological surgery continues to be a subject of debate years after the first publications that recommended the use of beta-lactams only, or in combination with aminoglycosides, and placing special emphasis on patients of advanced age and with certain comorbidities<sup>(1,2)</sup>. Subsequent studies continue to indicate that more studies are required in order to optimize and establish the correct prophylaxis in urological procedures performed on outpatients, as well as in those that require hospital admission<sup>(3,4)</sup>. The increase in the performing of transurethral procedures has led to the need to find a more suitable plan of action as regards antibiotic prophylaxis, since although some authors recommend its use in high risk procedures, they do not believe it is indicated in low risk procedures, such as flexible cystoscopy<sup>(5)</sup>. As regards the use of antibiotic prophylaxis, two recent reviews recognized that there is low-moderate scientific evidence that lead us to the option of not giving prophylactic antibiotic treatment, although they mention that more well-designed studies are required to compare the use of antibiotic prophylaxis against not using it<sup>(6,7)</sup>. Different types of antibiotics have been used in the prophylaxis of out-

patient procedures such as cystoscopy. These include quinolones that, although some authors defend their use in decreasing bacteriuria and urinary infection<sup>(8,9)</sup>, this point must be clarified, as we have previously seen in recent reviews<sup>(6,7)</sup>. As can be seen from the current scientific evidence and from usual clinical practice, there are no protocols on the use or not of antibiotic prophylaxis in flexible cystoscopy, nor is there a consensus on whether or not it is appropriate. The justification for this study is based mainly on this, in the interest that it contributes to increasing the scientific evidence on whether there is a need or not to give antibiotic prophylaxis. The interest of this study is that is a clinical study without intervention, but with a well designed method in clinical habitual practice comparing two antibiotic prophylaxis with no prophylaxis. As different studies<sup>(1-3,8,9)</sup> have used quinolones and phosphomycin as prophylaxis in flexible cystoscopy, asserting its usefulness in the reduction of bacteriuria and infection, we established that the main objective of this study is to analyse the role of ciprofloxacin and phosphomycin versus not carrying out any prophylactic treatment in patients subjected to flexible cystoscopy, evaluating the presence of urinary tract infections, bacteriuria, as well as other variables that will be mentioned in the following section.

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**Table 1.** Characteristics of patients performed flexible urethrocytostcopy with antibiotic prophylaxis with ciprofloxacin 500 mg (group 1), phosphomycin 3 gr (group 2) and without (group 3).

	Group 1	Group 2	Group 3	p
Sex				
Men	73.3%	77.4%	80.6%	
Women	26.7%	22.6%	19.4%	
Smoking				0.03
Yes	35%	14.5%	19.4%	
No	30%	25.8%	25.8%	
Ex-smoking	35%	59.7%	54.8%	
Bladder instillations				0.16
Yes	35%	41.9%	25.8%	
No	65%	58.1%	74.2%	
Diabetes mellitus				0.99
Yes	28.3%	27.4%	27.4%	
No	71.7%	72.6%	72.6%	
Immunosuppression				0.21
Yes	10%	16.1%	6.5%	
No	90%	83.9%	93.5%	
LUTS*				0.31
Yes	38.3%	41.9%	51.6%	
No	61.7%	58.1%	48.4%	
Indication				0.59
Tumor Follow-up	63.3%	62.9%	51.6%	
Haematuria	16.7%	19.4%	16.1%	
Mictional symptoms	8.3%	6.5%	14.5%	
Others	11.7%	11.2%	17.8%	
Diagnosis				0.001
Normal	56.7%	58.1%	38.7%	
Bladder tumor	25%	35.5%	27.4%	
Urothelial edema	10%	1.6%	0%	
Strength bladder	6.7%	0%	6.5%	
Others	1.6%	4.8%	27.4%	

\*LUTS: Lower urinary tract symptoms

## MATERIALS AND METHODS

The prospective non-randomised study included 184 patient candidates for flexible cystoscopy. These were performed by 3 different urologists according to their usual individual clinical practice, with one of them using 500 mg ciprofloxacin as antibiotic prophylaxis, another with 3 g of phosphomycin as prophylaxis, and another without using any prophylaxis. All patients had a urine culture performed to check for the absence of urinary infection before inclusion in the study. The patients were divided into 3 groups:

- Group 1: 60 patients, who took 500 mg ciprofloxacin 1 hour before being subjected to flexible cystoscopy.
- Group 2: 62 patients, who took 3 g phosphomycin 1 hour before being subjected to flexible cystoscopy.
- Group 3: 62 patients, with no prophylaxis before being subjected to flexible cystoscopy.
- Inclusion criteria: Males and females aged over 18 years in whom a flexible cystoscopy according to routine clinical practice was indicated (presence of hematuria, voiding symptoms, bladder tumour revision).
- Exclusion criteria: Patients with a bladder catheter or

**Table 2:** Results of urinary culture after flexible cystoscopy. No statistically differences were observed between groups ( $p = 0.31$ ).

	Group 1	Group 2	Group 3
Urinary culture positive	15%	22.6%	12.9%
Urinary culture negative	85%	77.4%	87.1%

suprapubic drainage line, patients who had a urinary infection in the previous month, patients with a ureteral catheter or nephrostomy line, and patients with urethral stenosis.

· Primary variables analyzed: Urinary infection symptoms during the 7 days after the cystoscopy, attending an emergency department or Primary Care clinic due to infection symptoms, bacteriuria (by urine culture at 7 days), and the type of microorganism present in cases of infection.

· Secondary variables: Age, gender, concomitant diseases, presence of prior lower urinary tract symptoms, reason for cystoscopy, result of the cystoscopy, and bladder instillations.

· Statistical analysis: The proportions and means of the variables recorded in the study was analyzed first, followed by a statistical analysis of the results, by applying an ANOVA test for the analysis of the qualitative-quantitative variables, and the chi-squared test for the analysis of the qualitative variables. The normality of the variables was checked using the Kolmogorov-Smirnov test, and the analysis of variance with the Levene test. A multivariate analysis was performed using binary logistic regression.  $P \leq .05$  was considered significant. The analysis was performed using the program SPSS 17.0 for Windows.

· Calculation of sample size: At least 180 patients needed to be included in the study, considering a beta error of 80% and alpha error of 5%, in order to obtain a statistically significant difference between the groups, and taking into account an estimated percentage loss of 5% and a precision of 3%. The patients were included in each following routine clinical practice of each urologist that perform cystoscopy.

· Ethics: All patients were informed about the study and gave their informed consent to participate in it. The Ethics Committee of our Health Area approved the conducting of the study. In this study urologists for 3 different Hospitals have participated. Each urologist has assessed and checked the patients in our health area for urinary tract infection after flexible cystoscopy. If urinary tract infection was present after the procedure a correct antibiotic treatment and follow up has been practiced.

## RESULTS

The mean age of the patients in Group 1 was 65.3 (12.5) years, 66.7 (10.8) years in Group 2, and 66.9 (10.8) years in Group 3, which was not statistically significant ( $P = .7$ ). **Table 1** summarizes the variables recorded: gender, smoking, bladder instillations, as well as the presence of diabetes mellitus, immunosuppression and lower urinary tract symptoms, the reason for cystos-

copy, and its results. The analysis of the urine culture performed 7 days after cystoscopy showed the presence of bacteriuria in 15% of the patients in Group 1, compared to 22.6% in the patients of Group 2, and 12.9% of Group 3 patients, with no statistically significant differences ( $P = .31$ ). The microorganisms isolated in 13% of the previously indicated Group 1 patients were: *E. coli* ( $n = 3$ ), *K. pneumoniae* ( $n = 1$ ), *E. faecalis* ( $n = 1$ ), *S. epidermidis* ( $n = 1$ ), and *P. mirabilis* ( $n = 3$ ); while in 22.6% of Group 2 they were: *E. coli* ( $n = 2$ ), *K. pneumoniae* ( $n = 6$ ), *E. faecalis* ( $n = 3$ ) and others ( $n = 2$ ), and in 12.9% of Group 3 they were: *E. coli* ( $n = 2$ ), *E. faecalis* ( $n = 1$ ), *P. mirabilis* ( $n = 1$ ) and others ( $n = 4$ ). Only 1 patient in Group 2 went to the emergency department due to symptoms of a urinary infection arising from the flexible cystoscopy, and only 1 patient from Group 1 went to primary care due to urinary infection symptoms. A multivariate analysis was performed to determine the relationship between different factors and the appearance of bacteriuria, which included age ( $P = .8$ ), smoking ( $P = .4$ ), presence of diabetes ( $P = .2$ ), immunosuppression ( $P = .6$ ), and lower urinary tract symptoms ( $P = .7$ ), observing a lack of relationship between these and the appearance of bacteria in the urine.

## DISCUSSION

The use of antibiotic prophylaxis in flexible cystoscopy is controversial. Despite the European Urology Association clinical guidelines<sup>(10)</sup> recommending its use only in high risk patients, in usual clinical practice it depends to a great extent on the preferences of the urologist. Manson, in a study with 138 patients, stated that the routine use of an antibiotic did not prevent the appearance of bacteriuria and thus, was not indicated<sup>(11)</sup>. Rané et al.<sup>(12)</sup>, on the other hand showed that the use of gentamicin in a single dose decreased the rate of urinary infection after flexible cystoscopy, and administering it as a prophylactic would be indicated. Karmouni et al.<sup>(13)</sup>, after conducting a study with 126 patients, stated that the use of antibiotic prophylaxis did not decrease the incidence of urinary tract infection and therefore, it would not be necessary to use it. On the other hand, Trinchieri et al. stated that the use of levofloxacin reduced the incidence of urinary infection after endoscopic procedures in the urinary tract<sup>(9)</sup>. However, Wilson et al.<sup>(14)</sup> did not observe a benefit in the administration of norfloxacin in patients subjected to flexible cystoscopy in terms of urinary infection incidence. On the contrary to this last study, Johnson et al.<sup>(8)</sup> did observe a benefit of another quinolone, ciprofloxacin, in the prevention and reduction of bacteriuria after flexible cystoscopy. However, in our study, after analyzing the different variables and comorbidities, we observe that the use of prophylaxis with ciprofloxacin did not reduce the presence of bacteriuria or the urinary infection symptoms, suggesting, according to our results, that its use is not recommended. For their part, Cam et al.<sup>(15)</sup> and Jiménez et al.<sup>(16)</sup>, did not observe any benefit of antibiotic prophylaxis with phosphomycin in a population with no risk factors and appropriately selected; although they stated that further studies are necessary to establish the real risk in these types of patients. In a study by García-Perdomo et al.<sup>(17)</sup>, using 500 mg levofloxacin compared to placebo, no statistically significant decrease in bacteriuria or urinary infection was observed between both groups. Therefore, they did not recommend the use of this an-

tibiotic as prophylaxis, unlike other studies<sup>(8,9)</sup> that did recommend the use of quinolones as prophylactics. We are in accordance with the study by Garcia-Perdomo, in that the use of quinolones as a prophylactic does not reduce the presence of bacteriuria. The recent studies by Herr<sup>(18,19)</sup>, with a very large cohort of patients, showed that antibiotic therapy before cystoscopy does not appear to be necessary in patients who do not have signs or symptoms of a urinary tract infection, although these results cannot be extrapolated to another health area, and the responsibility for whether to use it or not falls uniquely on the urologist. As can be observed in the data presented here, and in the literature, as well as that indicated by Mossanen et al.<sup>(20)</sup>, there is a wide variability in antibiotic prophylaxis in urological procedures. Therefore, it is important to perform further studies in order to achieve a better understanding of the reasons for this variability in prophylaxis, with the aim of decreasing complications and improving the outcomes of the procedures routinely performed by urologists.

## CONCLUSIONS

As a conclusion, despite the limitations of our study, due to the number of patients and not being a clinical trial, it is clear on looking at the results, that we do not believe that the use of ciprofloxacin or phosphomycin is routinely indicated as antibiotic prophylaxis in the performing of flexible cystoscopy regardless of other concomitant factors.

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