

Prospective evaluation of the efficacy of antibiotic prophylaxis before cystoscopy

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ABSTRACT

Background: The aim of this study was to prospectively compare single-dose intravenous antibiotic prophylaxis vs. no prophylaxis before minor cystoscopic procedures, including punch biopsy and transurethral resection (TUR) of small bladder tumors.

Materials and Methods: A total of 200 patients with a mean age of 47.3 years old (range: 19–84 years old) with initial negative urine cultures were recruited. All patients underwent a diagnostic cystoscopy. Patients were then randomized into 2 groups: One group that did not receive antibiotics (100 patients) and the other group that received antibiotic treatment (100 patients with a single intravenous dose of cefoperazone). All patients had urine analysis and urine cultures on the second day after the operation. Additionally, clinical parameters including fever and dysuria were recorded. In 15% of the patients, incidental additional interventions such as punch biopsy or TUR of a small bladder tumor that were similarly distributed in both groups were performed.

Results: In 1 patient from the antibiotic group and 2 patients from the no prophylaxis group, the urine cultures after cystoscopy were positive. No statistically significant difference was observed between these groups based on the microbiological and clinical parameters.

Conclusion: The current study provides evidence that no antibiotic prophylaxis is required before diagnostic cystoscopy in patients without bacteriuria. But, the absolute risk of infection was small, suggesting that a much larger study is required.

Key words: Antibiotic prophylaxis, cystoscopy, urinary tract infection

DOI: 10.4103/0970-1591.52914

INTRODUCTION

Periodic cystoscopic examinations remain the mainstay procedure in the management of superficial bladder tumors to monitor tumor recurrence and progression.^[1] Furthermore, cystoscopic investigations are included as the inevitable standard diagnostic tool in the evaluation of patients with microscopic or macroscopic hematuria.^[2] Consequently, cystoscopy is one of the most commonly performed urological investigations. However, no standard applications are strongly constructed in terms of applying routine antibiotic prophylaxis against urinary tract infection before cystoscopic examinations. The main drawback of providing strict clinical guidelines about antimicrobial prophylaxis in cystoscopic examinations is the lack of prospective, well-designed randomized trials with a sufficient number of patients.^[3] While earlier reports suggested routine antimicrobial prophylaxis before cystoscopies, recent studies have favored no prophylaxis

during these instrumentations.^[4] Karmouni, *et al.*,^[5] declared that a debate on the necessity of antimicrobial prophylaxis was present. They designed a prospective study including 126 patients to solve this complicated issue, revealing no benefit of prophylaxis in terms of decreasing urinary tract infections. In another clinical observation including over 2200 patients, the authors recommended the use of prophylactic antibiotics.^[6] Therefore, in the current clinical practice, some urologists may prefer to use an antimicrobial agent for prophylaxis before cystoscopic investigations. Moreover, unnecessary extensive utilization of prophylactic antimicrobial agents, in fact, may provide the emergence of resistant microorganisms.^[7] In conclusion, there is a need for further prospective studies to clarify this issue.

The aim of this randomized trial was to prospectively compare the efficacy of a single-dose intravenous antibiotic prophylaxis against no prophylaxis before cystoscopic examinations.

MATERIALS AND METHODS

A prospective randomized trial was designed to assess 200 consecutive patients who underwent diagnostic cystoscopy either for check-up of a superficial bladder tumor

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or for evaluation of hematuria. Patients with subsequent incidental interventions, including punch biopsy and transurethral resection (TUR) of a small bladder tumor were also recruited. The local ethical committee approved the trial. Patients who used antibiotics for any reason during the last month were excluded from the study. Moreover, patients requiring antibiotic prophylaxis for infective endocarditis or those with positive urine cultures were also not included. Patients were then prospectively randomized into 2 groups in terms of having antibiotic prophylaxis. Randomization was performed using tables of random numbers and using a block randomization. All patients were informed that they were participating in a randomized study. Then, patients read and signed an informed consent form. All potential side effects, particularly the occurrence of urinary tract infections and sepsis (the most severe adverse effects that would cause premature termination of the trial) were explained. While the first group received no antibiotic prophylaxis, the second group had a single dose of intravenous cefoperazone (1 g) as a third-generation cephalosporin with a certain efficacy against gram-negative uropathogens at the time of induction of anaesthesia. All patients had a clean midstream urinalysis and urine culture tests preoperatively. These tests were repeated on the second postoperative day. A growth of more than 10^5 microorganisms/ml was regarded as significant bacteriuria. Microscopic analysis of the urinary sediment was utilized to determine pyuria as over five leukocytes identified under high-power magnification. Additionally, clinical parameters including fever, dysuria, and frequency were evaluated for at least 1 month after the procedure. All patients had a follow-up visit at the first month.

Rigid cystoscopic investigations were performed in the urology operation room. A 24 Fr rigid endoscope under irrigation with sterile 0.9% NaCl solution was used in all the cases. Activated glutaraldehyde solution 2% was applied for 30 minutes to sterilize the endoscopic instruments. The external genitalia were prepared with chlorhexidene solution. Lidocaine gel 2% was introduced into the urethra for topical anaesthesia. While in the majority of female patients no subsequent anaesthesia was used, male patients received either general anaesthesia with a laryngeal mask or spinal anaesthesia. All operations were performed as out-patient procedures. However, hospitalization for 1 or 2 days was preferred in 17 patients who required a subsequent punch biopsy or TUR.

Statistical analyses were carried out using the Statistical Package for the Social Sciences-SPSS Inc, Chicago, IL, USA for Windows, Version 6.00 software. The level of statistical significance used was 0.05. A Student's *t*-test and Fisher's exact tests were used for statistical analysis.

RESULTS

The demographic characteristics of the patients are summarized in Table 1. No statistical difference was

Table 1: Patient characteristics

	Group I (prophylaxis)	Group II (no prophylaxis)
Number of patients	100	100
Patient age (mean \pm SD)	58.9 \pm 5.2	56.3 \pm 5.4
Female (n)	38	41
Diagnostic cystoscopy (n)	28	25
Check-up cystoscopy (n)	72	75
Punch biopsy (n)	7	9
Transurethral resection for tumor (n)	8	6

detected regarding age and gender between the groups. The indications for cystoscopy are also presented in Table 1. These two groups were similar with regard to the distribution of cystoscopy indications.

In the beginning, a total of 22 patients with positive urine cultures before cystoscopy were not included in the study. Urine cultures revealed the growth of *Escherichia coli* in a majority (19/22) of these cases. In all these patients, urinalysis also revealed pyuria. Interestingly, pyuria was seen in an additional 28 patients without any bacterial growth on the urine cultures. It should be emphasised that those with pyuria only were not excluded. The main interesting issue regarding pyuria without positive cultures was that the majority of these patients (25/28) had received six courses of intravesical Bacillus Calmette-Guérin (BCG) treatment for the management of a superficial bladder tumor during the previous 3-month period. In all patients, including the ones who were excluded from the study, only one case had positive urine culture without pyuria in an ordinary urinalysis.

The study groups were comparable regarding urine cultures and clinical parameters. The post-operative urine cultures were positive in 1 patient from the antibiotic group and 2 patients from the no prophylaxis group. Isolated microorganisms were *E. coli* in 2 patients and *Klebsiella pneumoniae* in the remaining patient. No difference was observed between the groups ($P = 1.000$). Two of these patients with positive cultures had complaints of dysuria and frequency while the third patient was asymptomatic. Additionally, 2 patients, one from each group, had dysuria without associated positive culture results. No fever or any other severe symptom was detected in any patient. In conclusion, no difference was observed between these groups based on the microbiological and clinical parameters.

A total of 16 patients underwent a punch biopsy mainly for hyperemic locations in order to exclude carcinoma *in situ* during the cystoscopy. At least one bladder tumor was detected by cystoscopy in the other 14 patients. Consequently, complete TURs of these tumors were performed. Simultaneously, 12 patients (5 patients from the first group and 7 patients from the second group) who

underwent TUR had urinary catheters for 1 day. Although the numbers of patients having these supplementary procedures are quite few, no symptoms developed in all these patients, with invasive interventions from both groups. Also, urine cultures were negative for all these patients.

DISCUSSION

Cystoscopic examinations are extensively performed for the diagnosis and management of benign or malignant urological diseases. These invasive investigations, however, may be associated with marked morbidity. Furthermore, the urinary tract is the most common site of nosocomial infections, of which instrumentation and catheterization are the major predisposing aspects.^[8] Moreover, urological invasive procedures may account for, at least as a predisposing factor, up to 10% of the nosocomial infections.^[9] The risk of severe infections and sepsis, although minimal, is present.^[4] On the other hand, unnecessary consumption of prophylactic antibiotics may result in the emergence of resistant microbial strains.^[7] In general practice, antibiotic prophylaxis is commonly overprescribed.^[10]

The results of studies on the antimicrobial prophylaxis in endoscopic procedures are confusing. The current trial presented no statistical difference of antibiotic usage before minor cystoscopies against urinary tract infection. Rane, *et al.*,^[11] proposed that a single dose of gentamicin reduced the infection rate from 21 to 5% in 162 patients with flexible cystoscopies. Similarly, Lugagne, *et al.*,^[12] observed that there was an unexpectedly high rate of infection after the cystoscopic examinations without prophylactic antibiotics even in the presence of sterile urine. A large randomized trial including over 2200 patients suggested the use of prophylactic antibiotics that reduced symptomatic bacteriuria from 10.2 to 2.5% in the prophylaxis group.^[6] On the other hand, recent trials were particularly against the use of prophylactic antibiotics. Wilson, *et al.*,^[13] rarely observed infection (0.85%) when no prophylactic antibiotics were used after cystoscopic examinations. They also indicated that further studies are needed to solve the problem of the necessity of prophylactic antibiotics. In 138 patients who underwent a diagnostic cystoscopy in an outpatient setting with previously sterile urine, the safety of cystoscopy without routine administration of post-operative antibiotics was established.^[14] Similarly, Tsugawa, *et al.*,^[15] reported that prophylactic administration of antibiotics was not required for a urethroscopy or urethrocytography in their randomized trial of 78 patients with sterile urine. In a double-masked, randomized trial to compare the efficacy of prophylaxis with placebo for preventing urinary tract infections during combined urodynamics and cystourethroscopy, no benefit of antibiotic prophylaxis was seen.^[16]

One of the main concerns during the simple endoscopic investigations is the possible detection of an abnormality

in the bladder requiring subsequent invasive procedures. In the current study, either punch biopsy or TUR was required in 30 patients (15%). According to the results of this study, these procedures were also not associated with an increased risk of urinary tract infection in patients with previously sterile urine. Interestingly, in the literature, a very limited number of trials addressing the use of prophylaxis before TUR of bladder tumors were present. Delavierre, *et al.*,^[17] reported no benefit of prophylactic antibiotics before transurethral bladder tumor resections in their prospective randomized trial of 61 patients. Consequently, further prospective trials with a sufficient number of patients are needed to definitively illuminate the issue regarding antibiotic prophylaxis before TUR of bladder tumors.

According to our results, pyuria detected by urinalysis predicted bacterial growth on urine cultures in the majority of the cases, except for patients who received recent BCG instillations that may cause an inflammatory response. Therefore, urinalysis may be used as a screening tool to confirm the absence of bacteriuria in order to safely avoid the use of antibiotic prophylaxis through a cost-effective approach.

In the current study, the most predominant pathogen isolated from the midstream urine specimens obtained from the patients before and after the cystoscopy was *E. coli*. This finding was similar to previous observations.^[4,11]

The major limitation of this study is the fact that the absolute risk of bacteriuria is very low after cystoscopic instrumentations. Therefore, a much larger study or a meta-analysis is required. Furthermore, the issue of the need for antibiotic prophylaxis before cystoscopies is still unclear. A recent prospective placebo-controlled trial indicates the use of antibiotics in flexible cystoscopies.^[18] Bacteriuria may be associated with remarkable clinical consequences for a particular patient. On the other hand, unjustified usage of prophylactic antibiotics is first associated with the development of antimicrobial resistance, which in turn may lead to fatal consequences for an individual patient. Secondly, one should also consider the potential side effects of these drugs. Moreover, cystoscopic investigations are one of the commonly performed urological procedures, particularly in monitoring superficial bladder tumors. The cost of the unjustified use of prophylactic antibiotics during cystoscopies would create a significant burden in the health system. The available data suggest that the cost effectiveness of the use of antibiotic prophylaxis depends on the underlying rate of urinary tract infection. In the present study, it was very low making antibiotic use not worthwhile despite twice as many infections in the no antibiotic group, whereas in some other studies it was higher, resulting in significant benefit. Conclusively, any data that provide recent information from different countries on the necessity of prophylactic antibiotics should be regarded as important in order to construct clinical guidelines or a meta-analysis.

CONCLUSION

This prospective randomized trial suggests that the prophylactic use of antibiotics before cystoscopy is unnecessary in patients without bacteriuria, which is in line with the European Association of Urology guidelines.^[19] However, we should state that the current study shows no evidence of a statistical benefit of antibiotics before cystoscopic investigations but that either a larger study or a meta-analysis would be definitive. Moreover, this trial provides an insight for subsequent trials to investigate the position of antibiotic prophylaxis before TUR of bladder tumors.

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How to cite this article: Cam K, Kayikci A, Erol A. Prospective evaluation of the efficacy of antibiotic prophylaxis before cystoscopy. *Indian J Urol* 2009;25:203-6.

Source of Support: Nil, **Conflict of Interest:** None declared.

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