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The Connection Between Endourological Procedures and Occurrence of Urinary Infections

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ABSTRACT

Introduction: Endoscopic surgery and endourological procedures imply the use of special instruments that are introduced into the urinary system through the urethra and percutaneous techniques that allow ante grade access to the urinary tract. The risk of urinary tract infection after endourological procedures and the use of antibiotic prophylaxis for these procedures is a question about which there is no unique opinion. **Goal:** The objective of this study was to determine the connection between endourological procedures and occurrence of urinary infections and to analyze the risk factors of urinary infection for patients who were hospitalized at the Urology Clinic of the Clinical Center University of Sarajevo (CCUS). **Material and methods:** The research was conducted as a prospective study on a sample of 208 patients of both genders, who were hospitalized at the Urology Clinic of the CCUS and to whom one of endourological procedures was indicated either for diagnostic or therapeutic purposes. All patients were clinically examined prior to endoscopic procedures and after the treatment attention was focused on the symptoms of urinary tract infections. **Results:** Analysis of the presence of postoperative bacteriuria shows that it has been more common in men or in 48 cases (28.1%) compared to women with 8 cases (21.6%) ($p > 0.05$). Preoperative catheterization was statistically significantly more present in patients who have had a postoperative bacteriuria (16 or 28.6%) compared to those without bacteriuria (8 or 5.3%) ($p < 0.05$). Analysis of the average duration of postoperative catheterization shows that patients with postoperative bacteriuria had longer duration of postoperative catheterization of 1.97 ± 0.14 days (range 1-20 days) compared to those without postoperative bacteriuria with 1.4 ± 0.4 days (range 0-5 days) and with a statistically significant difference ($p < 0.05$). Antibiotic prophylaxis in relation to the occurrence of postoperative bacteriuria did not show a statistically significant difference ($p > 0.05$). Analysis of the correlation coefficient indicates that a statistically significant effect on the occurrence of postoperative bacteriuria have preoperative bacteriuria, duration of postoperative catheterization and duration of hospital stay, as well as the total duration of hospitalization before and after endourological treatment ($p < 0.05$). **Conclusion:** It is important to emphasize that the endourological procedures are safe procedures in terms of urinary tract infections. This study should lay pathway to establishment of guidelines for the application of antibiotic prophylaxis in endourological procedures. This would standardize the perioperative use of antibiotics, taking into account the local prevalence of pathogens and antibiotic resistance, but keeping the individual approach to each patient, considering all risk factors for the development of urinary infection after endourological procedures..

Key words: urinary infection, endourology, risk factors.

1. INTRODUCTION

Endoscopic surgery and endourological procedures imply the use of special instruments that are introduced into the urinary system through the urethra and percutaneous techniques that allow ante grade access to the urinary tract (1, 2). The risk of urinary tract infection after endourological procedures and the use of antibiotic prophylaxis for these procedures is a question about which there is no unique opinion (3-6). Practice has proved that every urological procedure with use of instruments is associated with an increased risk of urinary tract infections

and bacteremia.

Classification of transurethral surgery according to Cruise and Ford into clean, clean-contaminated and contaminated is more complex, compared to open urological surgical procedures (7-10). Traditionally endourological procedures are classified as clean-contaminated, because the genitourinary tract is colonized with micro flora, even in case of sterile urine presence (1).

The importance of risk factors for urinary tract infections as a result of endourological procedures is not yet known. There are no international standards for the assessment of risk factors

for the development of urinary infections after endourological procedures. EAU/ESIU announced a new categorization of risk factors for urinary infections, called ORENUC system (1). According to the present system of risk factors for urinary infection classification ORENUC the risk factors are divided into six groups (1).

Today the general risk factors for urinary tract infections are known, such as patients of older age, immune deficiency, malnutrition, obesity, diabetes mellitus, smoking, hypoalbuminemia. In order to assess the general risk factors related to the patient the ASA score is used, which is primarily focused on the assessment of anesthetic risk, but also indicates the general health of the patient. The higher the ASA score the greater is the risk of infectious complications. As specific risk factors for the development of urinary tract infection are considered preoperative bacteriuria, urethral catheter, stones in the urinary tract and a history of previous urogenital infections (15).

The most important risk factors for postoperative bacteriuria are preoperative bacteriuria, duration of postoperative catheterization, and length of hospital stay, as well as overall also preoperative and postoperative. It is of great importance in everyday urological practice to identify and control risk factors for the development of urinary infection after endourological procedures, with the main objective to minimize occurrence of infectious complications.

2. GOAL

The objective of this study was to determine the connection between endourological procedures and occurrence of urinary infections and to analyze the risk factors of urinary infection for patients who were hospitalized at the Urology Clinic of the Clinical Center University of Sarajevo (CCUS).

3. MATERIAL AND METHODS

The research was conducted as a prospective study on a sample of 208 patients of both genders, who were hospitalized at the Urology Clinic of the CCUS and to whom one of endourological procedures was indicated either for diagnostic or therapeutic purposes. We analyzed data from patient histories, laboratory tests taken at admission and after endourological procedures, and also the operational programs for endoscopic procedures. All patients were clinically examined prior to endoscopic procedures and after the treatment attention was focused on the symptoms of urinary tract infections. Upon hospitalization at the Urology Clinic, from all patients were taken midstream, first morning urine for bacteriological examination, for three consecutive days and then again urine was taken 48 hours after the endoscopic procedure (also for three consecutive days).

All data are presented in charts by absolute number of cases, relative number of cases, mean with standard deviation, standard error of mean and range of values. To test the difference we used chi-square test with Yates correction for small samples, Fisher exact test and one-way analysis of variance (ANOVA), and in order to test the influence of various parameters on the occurrence of bacteriuria Spearman test of nonlinear, rank correlation. Results of statistical tests with $p < 0.05$ or at the confidence level of 95% were considered statistically significant. Data analysis was performed using the statistical package IBM SPSS Statistics v21.0, MedCalc v12.7 and Microsoft Excel 2010.

Figure 1. Postoperative bacteriuria according to gender

Figure 2. The relationship of age and postoperative bacteriuria

Figure 3. Relationship of catheterization and postoperative bacteriuria

4. RESULTS

Research results are presented on figures 1-8.

Analysis of the presence of postoperative bacteriuria shows that it has been more common in men or in 48 cases (28.1%) compared to women with 8 cases (21.6%). Statistical analysis indicates that there is no significant difference in the presence of postoperative bacteriuria in relation to gender ($p > 0.05$).

There was no statistically significant difference in the prevalence of postoperative bacteriuria by age groups ($p > 0.05$). Preoperative catheterization was statistically significantly more present in patients who have had a postoperative bacteriuria (16 or 28.6%) compared to those without bacteriuria (8 or 5.3%) ($p < 0.05$). Postoperative catheter was placed in almost all cases—196 patients or 94.2%, or it was not placed only in individual cases after cystoscopy and urethral stent installation.

The duration of postoperative catheterization, with the exclusion of nine patients who were discharged with a catheter, was 3.9 ± 2.1 days, with the longest postoperative catheterization of 20 days. Analysis of the average duration of postoperative catheterization (with the exclusion of nine patients who were discharged with a catheter), shows that patients with postoperative

Figure 4. Relationship between duration of postoperative catheterization and postoperative bacteriuria

Figure 5. Duration of preoperative hospitalization and postoperative bacteriuria

Figure 6. Duration of postoperative hospitalization and postoperative bacteriuria

bacteriuria had longer duration of postoperative catheterization of 1.97 ± 0.14 days (range 1-20 days) compared to those without postoperative bacteriuria with 1.4 ± 0.4 days (range 0-5 days) and with a statistically significant difference ($p < 0.05$).

We did not record a statistically significant difference in the prevalence of postoperative bacteriuria according to the type of surgery ($p > 0.05$). Also a statistically significant difference in the presence of postoperative bacteriuria by the presence of comorbid diseases was not recorded ($p > 0.05$). Antibiotic prophylaxis in relation to the occurrence of postoperative bacteriuria did not show a statistically significant difference ($p > 0.05$). Analysis of the average values indicate that there is a statistically significant difference according to the presence of postoperative bacteriuria in relation to the hospitalization duration, as preoperative and postoperative, as well as total duration of hospitalization ($p < 0.05$). Analysis of the correlation coefficient indicates that a statistically significant effect on the occurrence of postoperative bacteriuria have preoperative bacteriuria, duration of postoperative catheterization and duration of hospital stay, as well as the total duration of hospitalization before and after endourological treatment ($p < 0.05$).

5. DISCUSSION

Sometimes difficult to distinguish bacteriuria caused after urological instrumentation from urine contamination with periurethral flora (1). Most common cause of UTIs is *E. coli*, with a greater incidence of infection also occurring other bacteria such

Figure 7. Relation of the total hospitalization and postoperative bacteriuria

Figure 8. Analysis of the correlation coefficient by individual risk factors for occurrence of postoperative bacteriuria.

as *Proteus spp.*, *Klebsella spp.*, *Enterobacter spp.*, *Pseudomonas spp.*, *Acinetobacter spp.* *Staphylococcus saprophyticus* is associated with uncomplicated urinary tract infections in young women. Aim of the Global Prevalence Study - GPIU study is to examine the urinary infections and infections of the operative field in urological patients, the prevalence of hospital infections, pathogens, bacterial resistance and antibiotic use in the prophylaxis and treatment at urological departments around the world. According to the GPIU study results, *E. coli* is responsible for 31% of urinary tract infections, followed by *Pseudomonas spp.* (13%), *Klebsiella spp.* (10%), *Proteus spp.* (6%) and *Enterobacter spp.* (6%). Gram-positive uropathogen *Enterococcus spp.* is isolated in 10% of patients (1).

According to GPIU study resistance of *E. coli*, *Klebsiella spp.* and *Proteus spp.* is less than 45% to the commonly used antibiotics. According to the study, *Enterococcus spp.* and *Pseudomonas spp.* have resistance over 70% to majority of antibiotics.

Today there are many different opinions about the importance of antibiotic prophylaxis for certain endourological procedures. Use of antibiotic prophylaxis in high-risk patients is accepted and even recommended practice, but use in low-risk patients remains a controversial issue, especially about the type and duration of antimicrobial treatment.

Most authors agree that in low-risk endourological procedures, in the absence of risk factors and if the preoperative urine sample is sterile, antibiotic prophylaxis may be unnecessary. In the preoperative preparation of patients, any infections, especially urinary tract infections must be verified and treated. If an infection is present and intervention cannot be delayed, antibiotic therapy should be given on an empirical basis before surgery and then continued after surgery, while it is desirable to be done according to the antibiotic resistance chart when it is available. Preoperative urinary infections, especially recurrent, are recognized as a high risk for postoperative infection

and must be treated before the surgery. The importance of preoperative bacteriuria is not yet sufficiently established, but it is proven that patients with preoperative bacteriuria have higher incidence of gastroenteritis and sepsis.

One result of our study is that preoperative bacteriuria which is found in 26.4% patients had a statistically significant effect on the occurrence of postoperative bacteriuria. The end point of perioperative prophylaxis in urology is debatable. It is generally believed that the main objective is the prevention of symptomatic or febrile genito-urinary infections, such as acute pyelonephritis, prostatitis, epididymitis, sepsis and serious wound infections. The question is whether this should be extended to asymptomatic bacteriuria or less severe wound infections, which can be easily treated on out-patient basis. Asymptomatic bacteriuria after TURP or other endourological procedures may disappear spontaneously, usually without clinical significance.

Antibiotic prophylaxis and antibiotic therapy are two different concepts that are used but in everyday practice very often identified as the same. Antibiotic prophylaxis aims to prevent hospital infection that occurs due to diagnostic and therapeutic procedures. Antibiotic prophylaxis is only one of several measures to prevent infection and can never compensate for poor hygiene and poor surgical technique. Published literature suggests that antibiotic prophylaxis is unnecessary after the completion of endoscopic procedures. Therapeutic doses of antibiotics are given in cases where infection, bacteriuria at the time of endoscopic procedures, vitalized tissue or stones are present. In some cases, such as the treatment of patients with infected catheters or stones, concomitant infection cannot be eradicated prior to the procedure. In these cases, the goal of preoperative antibiotic therapy is to suppress the bacteria, prior to the surgery. Further continuation of the administration of antibiotics is more therapeutic than prophylactic and may include period longer than 24 hours after the surgery, depending on the patient's risk factors and the importance of morbidity related to infection. For TUR of the prostate, there are studies that have shown that administration of antibiotics for less than 72 hours has an advantage over the single dose of prophylactic antibiotics. Practice at the Urology Clinic CCUS is administration of prophylactic dose of antibiotics for period longer than 24 hours, usually during whole hospitalization (1). It is recommended to use different drugs for the prophylaxis and treatment of urinary tract infections after endourological procedures, provided to leave "strong" antibiotics for treatment. The ideal antibiotic should cover the broad spectrum of microorganisms, which has limited resistance, causes few side effects, outperforming virulence, it is easy to apply and is based on the local prevalence of microorganisms. In cases where the prevalence of resistant strains is large, empirical therapy should start with broad-spectrum antibiotics, and if possible, therapy should be according to the findings of susceptibility testing of the agent as soon as possible to change to the narrow spectrum antibiotic. Rational prophylaxis should be based on a combination of antibiotics. One agent most probably will not provide the broadness of protection that is adequate for prophylaxis. The ideal situation would be if each health institution adopts its own recommendations for the selection of prophylactic antimicrobial drug. The ultimate goal being pursued is that in the near future antimicrobial prophylaxis and empirical antibiotic treatment is determined individually for each patient based on risk factors,

categories of contamination surgical procedures and antibiotic sensitivity in a given region. The risk of urinary tract infections after endourological procedure depends on the type of procedure performed, wherein the TUR of the prostate is associated with the highest risk of urinary tract infections. In this study, we did not find significant difference in the occurrence of postoperative bacteriuria between individual endourological procedures. Cystoscopy is the most commonly endourological procedure performed which belongs to clean procedures. According to studies cystoscopy is relatively safe procedure. The incidence of symptomatic urinary tract infection after cystoscopy with preoperatively sterile urine sample is 5% and the incidence of asymptomatic bacteriuria is between 10% and 35%.

In this study, the percentage of bacteriuria after cystoscopy is 1.8%. Since cystoscopy is the most common endourological outpatient procedure, it is very important that it belongs to safe procedures with very few complications. A study done by Rané and associates has compared the administration of one dose of parenteral gentamicin before cystoscopy with a flexible cystoscope, with placebo in 162 patients. The result was a reduction of the positive findings in urine from 21% to 5%. Compared with transurethral resection of the prostate, there is less data on infectious complications after transurethral resection of the bladder tumors. According to the literature, urinary infection after TURBT occurs in 2-39% of patients. Frequently endourological operations in hospitalized patients at the Urology Clinic are transurethral resection of bladder tumors. In this study in 25.3% of 83 patients who underwent TURBT was verified postoperative bacteriuria. After TURBT, most performed surgical procedure is TUR of the prostate. In a systematic review, Bootsma and colleagues concluded that "except for TURP and biopsy of the prostate, lacking a well performed studies that examined the need for antibiotic prophylaxis for endourological procedures". In patients who were scheduled for TURP and who do not have a urethral catheter, preoperative bacteriuria is found in more than 10%. Bacteriuria at the time TURP is performed increases the risk of febrile infection by 5-10%. In a meta-analysis of 32 studies, Berry and Barrett found the percentage of postoperative bacteriuria in 26% of 4260 patients and septicemia in 4.4%. According to other studies in 6-70% of patients bacteriuria occurs postoperatively. Febrile or symptomatic infection in 5-10% of cases and in sepsis 0-4%, with a mortality rate of 13%, which increases to 20% in men over 64 years of age.

Clinical trials have demonstrated that prophylaxis is effective in men who are subject to prostate TUR, but studies that have evaluated other procedures are limited. It is assumed that the risk of sepsis is similar like in any similar followed by mucosal bleeding and that antimicrobial therapy will produce similar benefits for all of these procedures. Studies have shown that a single dose or short administration of antibiotics (<72 h) reduces urinary tract infection in 66% and 71%. In this study of 48 patients who underwent TUR of the prostate, in 35.4% was verified postoperative bacteriuria. Our results show that preoperative catheterization was statistically significantly more present in patients who had postoperative bacteriuria (16 or 29.1%) compared to those without (8 or 5.2%). Analysis of the average duration of postoperative catheterization (with the exclusion of nine cases that were dismissed with still placed catheter), shows that patients with postoperative bacteriuria had placed catheter for 1.97 ± 0.14 days (range 1-20 days) compared to those without postoperative bacteriuria with

1.4±0.4 days (range 0-5 days) and with a statistically significant difference. In the literature, there is data that preoperative catheter significantly increase the incidence of bacteriuria before and after TURP or from 53% to 100% (5-10). Nosocomial bacteriuria develops in 25% of patients with catheter placed for more than 7 days with daily risk of 5%. Each additional day of catheterization is associated with a further risk increase by 3-10% for developing bacteriuria. Bacteriuria which occurs after catheterization that was short lasting, usually asymptomatic and is caused by a single microorganism. Extra luminal path for spread of bacteria, with the placed catheter involves the direct inoculation of the bacteria during the insertion of the catheter, and the other way is by migration within mucosal coating that is on the outside of the catheter. These bacteria are endogenous, originating from the gastrointestinal tract. Microorganisms can also enter through intraluminal space, when is enabled entry of the microorganisms through the lumen of the catheter due to the lack of a closed drainage system or contamination of urinary bags. These microorganisms originate from the outer environment, for example, hands of health care professionals, which is very important for the prevention of urinary tract infections associated with urethral catheter.

In this study, the highest level of resistance expressed by *E. coli* is on Trimethoprim/sulfamethoxazole (55%) and ampicillin (53%) followed by ciprofloxacin 17%, amoxicilline/clavulanic acid 16.6%, h 16.6% of gentamicin and cephalosin in 13.3%.

ESBL strains during this study were isolated in total of 7.5% cases preoperatively and in 5.5% of cases postoperatively. It was a case ESBL *E. coli* and *Enterobacter aerogenes*. According to the recommendations for perioperative antimicrobial prophylaxis during endourological procedures (recommendations for perioperative antibacterial prophylaxis in urology, Guidelines European Association of Urology, 2012 edition), trimethoprim-sulfamethoxazole is one of the recommended antibiotics for prophylaxis in endourological procedures. However, today it is known that there are differences in European countries in the bacterial spectrum and bacteria resistance, so antibiotic resistance is higher in Mediterranean countries compared to Northern Europe (1). The results of this study pertaining to antibiotic resistance indicate that *E. coli* exhibits the highest degree of resistance to trimethoprim/sulfamethoxazole in 55%. From this stems the fact that beside it is necessary to set up a proper indication for the application of antibiotics and to know the pharmacological properties of a prescribed antibiotics, it is necessary to know the regional profile and microbial pathogen resistance, all in order to make rational approach to the therapy.

6. CONCLUSIONS

A significant number of hospitalized urological patients undergoing one of endourological procedures for diagnostic or therapeutic purposes have preoperative bacteriuria or 26.4% (55 patients) of the total number of patients. Bacteriuria after endourological intervention was found in 26.9% (56 patients) of the total number of patients. In 5.8% (12 patients) in the postoperative period was verified symptomatic urinary infection.

Of the 153 patients who had preoperative sterile urine, 10.6% (22 patients) developed present postoperative bacteriuria. The most common preoperative microorganisms isolated from urine were: *Escherichia coli* (30.9%), *Enterococcus faecalis* (20%), *Proteus mirabilis* (9.1%), *Staphylococcus epidermidis* (7.3%), *Pseudomonas aeruginosa* (5.4%), *Streptococcus agalactiae* (5.4%) and

Enterobacter cloacae (5.4%). On the appearance of preoperative bacteriuria has influence preoperative presence of a catheter and duration of hospitalization prior to surgery. Statistically significant effect on the occurrence of postoperative bacteriuria have preoperative bacteriuria, duration of postoperative catheterization, and duration of hospital stay, as well as overall also preoperative and postoperative. In our study a statistically significant difference was not found in the prevalence of postoperative bacteriuria in relation to different age groups, gender, various comorbidity and in relation to different surgical procedures. At the Urology Clinic CCUS most commonly prescribed antibiotics for prophylaxis and treatment of infections after surgery are parenteral cephalosporines of third generation—Ceftriaxone and fluoroquinolone-ciprofloxacin. There is a known resistance of enterococci to cephalosporines, and in our study, during postoperative period commonly isolated bacteria were enterococci.

Statistical analysis of patients sample indicates that there is no significant difference in the presence of postoperative compared to preoperative bacteriuria. It is important to emphasize that the endourological procedures are safe procedures in terms of urinary tract infections. This study should lay pathway to establishment of guidelines for the application of antibiotic prophylaxis in endourological procedures. This would standardize the perioperative use of antibiotics, taking into account the local prevalence of pathogens and antibiotic resistance, but keeping the individual approach to each patient, considering all risk factors for the development of urinary infection after endourological procedures.

CONFLICT OF INTEREST: NONE DECLARED

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