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Original article

Rational Use of Antibiotic Prophylaxis Prior to Rigid Cystoscopy: a Randomized Controlled Trial

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Abstract The objective of this study was to assess the need for using antibiotic in patients undergoing rigid cystoscopy. It was conducted as a randomized controlled trial by comparing the infection rate of patients receiving antibiotic prophylaxis with those who received a placebo 1 hour prior to rigid cystoscopy during July 2015 and March 2016. The samples were patients aged above 18 years who were indicated for cystoscopy and were randomly enrolled into 2 groups: (1) the experimental group (33 patients) who received ofloxacin 200 mg, and (2) the control group (33 patients) who received placebo. The urinary tract infection was determined by the occurrence of bacteriuria and febrile urinary tract infection (UTI). Independent samples t-tests and Fisher's exact tests were used, and the significant p-value was set at 0.05 level. It was found that there was no difference in demographic data between the two groups. In addition, there was no statistically significant difference on the occurrence of bacteriuria and febrile UTI between the two groups. None of the patients had adverse effects due to the method used in our study. Thus, it is highly likely that antibiotic prophylaxis has no role in reducing either infection or asymptomatic bacteriuria relating to the cystoscopy. Therefore, antibiotic prophylaxis is not recommended. The results of this study can be used as a guideline for clinicians to use antibiotics more effectively; which is in line with the global movement on the rational drug use. However, larger trials should be performed to verify the results.

***Keywords*: cystoscopy; antibiotics; prophylaxis; UTI; urinary tract infection; RCT; randomized controlled trial; rational drug use**

Introduction

Cystoscopy constitutes an essential procedure used for both surveillance and diagnostic purposes in patients with pathology or disease of lower urinary tract. Being meticulously performed by highly experienced urologists notwithstanding, the procedure inevitably entails some risk, e.g., urinary tract infection (UTI), pain, and bleeding[1, 2].

As mentioned above, UTI is a potential complication with rate of approximately 10%.[3] Consequently, the use of prophylactic antibiotics would be sensible to address this issue particularly in elderly, smokers, previous recurrent UTI and immunocompromised persons.[4-7] The routine use of such prophylaxis, however, is currently still controversial. The guidelines for the use of antibiotics for this purpose have suggested the practitioners to weigh risks of drug resistance against benefits of UTI prevention.[5,8-12]

Despite being the standard practice, a flexible cystoscopy is not prevalently performed in most hospitals in Thailand. As in our institution, only rigid cystoscopies were available during the period of this study. Each year, our hospital performs cystoscopy around 200 to 300 cases. The use of antibiotics prophylaxis varies in each case depending on each physician's opinions. Antibiotics prophylaxis is usually recommended for patients with certain conditions such as elderly, underlying diseases or obesity. Thereby, the aim of this study is to determine advantages of antibiotic prophylaxis in patients undergoing rigid cystoscopy.

Methods

The study was approved by the Ethical committee, EC 004/58, at our institution. There were 66 patients who were indicated for cystoscopy and enrolled for the study between July 2015 and March 2016. All patients were thoroughly explained, informed and committed to participating in the research. The patients who were excluded from this study included the age under 18 years, a history of UTI within a month, antibiotics taken 2 weeks before, an allergy to quinolones, and comorbidities, e.g., heart valve replacement, cardiac murmur, and placement of orthopedic or vascular prosthesis, in which prophylactic antibiotics were required.

The table of random numbers was used to allocate our samples into the experimental group and control group. Each group consists of 33 patients equally. The experimental group was given a 200 mg ofloxacin tablet an hour before the procedure while the control group received a placebo instead. The placebo was made from corn flour and shaped mimicking the given antibiotic. In addition, both physicians and patients were blinded to whether the patients were receiving a real tablet or placebo.

Complications were detected at the recovery room, and urine was sent for culture. Approximately 4 weeks after the procedure, all patients were reevaluated at the time of follow-up. They were evaluated for febrile UTI and bacteriuria. Our clues for the suspicion of febrile UTI included fever, dysuria, and any symptoms arisen after the procedure. If there were any clues, the midstream urine for urinalysis and culture would be required. In case the urinalysis revealing the number of white blood cells (WBCs) increases, the patient would be diagnosed with febrile UTI. The patients diagnosed with febrile UTI would be treated with a standard of care.

Statistical analyses

Demographic and clinical data, i.e., febrile UTI and bacteriuria, between groups were compared by independent samples t-tests and Fisher's exact tests. Significant difference was set at p-value<0.05. For all statistical analysis, SPSS software version 15.0 (SPSS Inc., Chicago, IL) was used. Data are expressed as mean±SD.

Results

Our demographic data revealed no significant difference between the two groups in terms of gender (p=0.500), age (p=0.270), body mass index (BMI) (p=0.431), and indications for cystoscopy (p=0.126). The data regarding the risk factors for febrile UTI encompassing age above 60 years (p=0.401) and presence of benign prostate hyperplasia (BPH) (p=0.158), smoking (p=0.390), diabetes mellitus (p=0.269), or urinary catheterization (p=0.500), also had shown no difference (Table 1).

Of the 66 samples, there were 2 positive urine cultures at the time before cystoscopy, one in the experimental group and another one in the control. After undergoing the procedure, there were 8 positive cultures, 3 (9.09%) and 5 (15.15%), in the experimental group and control group, respectively (Table 2). However, the difference was not statistically significant. All cultures demonstrated only Escherich-

Table 1 Demographic data in the experimental and the control groups

	Ofloxacin (n=33)	Placebo (n=33)	p-value (χ^2)
General			
Gender (male:female)	18:15	19:14	0.500
Age (±SD years)	62.52 (±16.20)	63.36 (±14.42)	0.270*
BMI (±SD kg/m2)	24.09 (±4.70)	23.23 (±4.20)	0.431*
High-risk groups			
Age above 60 years	19	21	0.401
Smoking	8	10	0.390
Diabetes mellitus	8	5	0.269
Benign prostatic hyperplasia	11	16	0.158
Indwelling catheterization	4	5	0.500
Indications for cystoscopy			0.354
Evaluation of voiding symptoms	16	22	
Evaluation of hematuria	9	2	
Evaluation of bladder lesion	3	1	
Evaluation of recurrent UTI	1	4	
Evaluation of urethral obstruction	2	2	
Evaluation of metastasis	2	2	

*All variables are expressed as χ^2 (Fisher's exact test) except age and BMI expressed as independent samples t-tests

Table 2 Comparison of bacteriuria and febrile UTI in the experimental and control groups

	Ofloxacin (n=33)	Placebo (n=33)	p-value (χ^2)
Asymptomatic bacteriuria prior to cystoscopy	1	1	0.754
Asymptomatic bacteriuria following cystoscopy	3	5	0.354
Febrile UTI	Nil	Nil	

ia coli as a culprit organism. There was no febrile UTI and also no life-threatening complications found in the both groups.

Discussion

The study aimed to compare procedure-related complications after undergoing cystoscopy between those who received antibiotic prophylaxis and those who did not. According to the literature, the rate of urinary tract infection can reach up to 10% after the procedure,[3] some practices of prophylactic antibiotics for patients undergoing cystoscopy are recommended to reduce infective complications.[4,5] Such antibiotics as oral ciprofloxacin or trimethoprim-sulfamethoxazole as well as intravenous gentamicin have been proposed for that purpose and found that the rate of bacterial infection or bacteriuria can be lowered compared to the control group.[8,13] A systematic review also demonstrated that transurethral urological surgery has more benefits compared with transabdominal urological surgery. Considering 42 studies with a total of 7,496 patients, the antibiotic prophylaxis seems to have a positive role in preventing urinary tract infections resulting from the transurethral urological surgery in patients with preoperative sterile urine.[14-16]

In spite of the benefits of antibiotic prophylaxis, all outcomes in the literature are not homogeneous. Some revealed no role of antibiotics in reducing the rate of urinary tract infection after being given flexible cystoscopy.[12,17-22] Others, with a study of urodynamic evaluation, found that prophylactic antibiotics still had some roles in patients with certain conditions.[1,6,19,22,23] In addition, in 2 randomized controlled trials and a meta-analysis shown the same results which claim that there is no statistically significant difference between antibiotic and placebo group, and there was no recommendation to the use of antibiotic prophylaxis in order to prevent UTI in patients undergo cystoscopy.[9,24,25] In a study of patients with bladder tumor, antibiotics also had no prophylactic role in reducing infections resulting from outpatient flexible cystoscopy.[19]

Antibiotic prophylaxis can be both considered beneficial and non-beneficial with regard to the aforementioned procedure, hence no consensus in standard guidelines for prevention of infection in patients undergoing cystoscopy. As mentioned above, the use of such prophylaxis is still debatable. Benefits of antibiotics are not only questionable, but routine use of them also entails increasing the risk of drug resistance[12]. The authors are concerned about this issue and therefore conduct this study to determine whether antibiotic prophylaxis is still necessary for prevention of urinary tract infection in the patients who undergo for cystoscopy. Unfortunately, flexible

cystoscopies could not be performed in a widespread manner in our country. As in our institution, the only available procedures are rigid cystoscopies at that time. As a consequence, the outcomes of this study would address only the question in the given condition. However, it would be possible to imply the results from the study to the practice of flexible cystoscopy since, in a randomized comparison, the effectiveness of each procedure reportedly was the same. The only difference is that the pain experienced during rigid cystoscopy is higher compared with that experienced during flexible cystoscopy.[26]

As previously mentioned, there were only 8 positive cultures, 3 and 5, in the experimental group and control group, respectively. This difference was not statistically significant. There was no febrile UTI in the both groups. Consequently, antibiotic prophylaxis appears not to be necessary prior to the rigid cystoscopy. Since there was no incidence of urinary infection in our study, larger group of patients should be assessed in the next study.

In conclusion, it appears that antibiotic prophylaxis has no role in reducing either infection or asymptomatic bacteriuria related to the rigid cystoscopy. In other words, the results support rational drug use. However, a larger trial should be conducted to assure the aforementioned results.

Conflicts of interest

We have no conflict of interest to declare.

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บทคัดย่อ: ความสมเหตุสมผลในการให้ยาปฏิชีวนะเพื่อป้องกันการติดเชื้อในทางเดินปัสสาวะสำหรับผู้ป่วยเข้ารับการส่องตรวจท่อปัสสาวะด้วยกล้องชนิดแข็ง: การศึกษา แบบสุ่ม ในกลุ่มอาสาสมัครควบคุม

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** หน่วยศัลยกรรมทางเดินปัสสาวะ สาขาวิชาศัลยกรรม ศูนย์การแพทย์ปัญญานันทภิกขุชลประทาน มหาวิทยาลัยศรีนครินทรวิโรฒ; ** สาขาวิชาศัลยกรรม ศูนย์การแพทย์ปัญญานันทภิกขุชลประทาน มหาวิทยาลัยศรีนครินทรวิโรฒ*

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การศึกษานี้เปรียบเทียบผลการติดเชื้อในทางเดินปัสสาวะในผู้ป่วยที่เข้ารับการส่องตรวจท่อ-ปัสสาวะด้วยกล้องส่องชนิดแข็งระหว่างกลุ่มที่ได้รับยาปฏิชีวนะและกลุ่มที่ได้ยาหลอกเพื่อเป็นแนวทางในการใช้ยาอย่างสมเหตุสมผล ผู้ศึกษาได้คัดเลือกอาสาสมัครอายุ 18 ปีขึ้นไปที่เข้ารับการส่องตรวจท่อปัสสาวะด้วยกล้องส่องชนิดแข็งซึ่งไม่มีภาวะติดเชื้อ ในทางเดินปัสสาวะ นำมาก่อนในช่วงระหว่างปีพ.ศ. 2558 - พ.ศ. 2559 จำนวนทั้งสิ้น 66 ราย โดยสุ่มเลือกโดยใช้ตารางสุ่ม เพื่อแยกอาสาสมัคร เป็นสองกลุ่ม ได้แก่ กลุ่มที่ได้ยาปฏิชีวนะ Ofloxacin 200 mg. และกลุ่มที่ได้ยาหลอกก่อนทำการ ส่องตรวจประเมินผลการติดเชื้อในทางเดินปัสสาวะโดยการเพาะเชื้อแบคทีเรียในปัสสาวะและอาการไข้ที่เกิดจากการติดเชื้อ ในทางเดินปัสสาวะ การคำนวณทางสถิติใช้ independent samples t-test และ Fisher's exact test โดยให้ค่าความเชื่อมั่น $p<0.05$ ในการยืนยันความแตกต่างอย่างมีนัยสำคัญ ผลการศึกษาพบว่ากลุ่มอาสาสมัครทั้งสองกลุ่ม ที่ได้จากการสุ่ม ไม่มีความแตกต่างด้าน demographic data เมื่อวิเคราะห์ผลการติดเชื้อในทางเดินปัสสาวะ ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ ทั้งนี้ไม่พบภาวะไม่พึงประสงค์ในอาสาสมัครที่เข้าร่วมการวิจัยนี้ ในการวิจัยนี้ให้ผลที่สะท้อนว่าการให้ยาปฏิชีวนะแก่ผู้ป่วย ที่เข้ารับการส่องตรวจท่อปัสสาวะด้วยกล้องส่องชนิดแข็งไม่มีความจำเป็น สนับสนุนการใช้ยาอย่างสมเหตุผลที่ไม่ต้องให้ยาปฏิชีวนะก่อนเข้ารับการตรวจ ทั้งนี้อาจจำเป็นต้องทำการวิจัยในกลุ่มตัวอย่างที่เพิ่มขึ้นเพื่อให้มั่นใจในผลที่ได้ต่อไป

คำสำคัญ: **การติดเชื้อทางเดินปัสสาวะ; การส่องกล้องตรวจท่อปัสสาวะ; ยาปฏิชีวนะ; ป้องกัน; การศึกษาเปรียบเทียบ; การใช้ยาอย่างสมเหตุผล**