



Effect of Antibiotic Prophylaxis on Infectious Complications in Patients with Asymptomatic Bacteriuria Undergoing Urologic Surgery

Efecto de la profilaxis antibiótica sobre las complicaciones infecciosas en pacientes con bacteriuria asintomática programados a cirugía urológica

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Abstract

Keywords

- ▶ asymptomatic bacteriuria
- ▶ urinary tract infection
- ▶ bacteremia
- ▶ sepsis
- ▶ surgical wound infection
- ▶ urologic surgical procedures
- ▶ urologic surgery

Objectives To identify the effect of duration of surgical antibiotic prophylaxis (SAP) and other variables on infectious postsurgical complications in patients with asymptomatic bacteriuria (ASB) undergoing urological surgery.

Methods We conducted an observational study of a cohort of patients with ASB scheduled for urologic surgery at three health service providers in Colombia. The study population comprised all patients with planned urologic surgery who had ASB prior to surgery from April 2018 to January 2019. The intervention evaluated was the duration of preoperative SAP, and the outcome variable was the development of any postoperative infectious complications for up to 30 days after the procedure.

Results The present study included 184 patients with ASB scheduled for urologic surgery.

The median duration of preoperative SAP ($p = 0.49$) or of 1 dose SAP (risk ratio [RR] = 1.24; 95% confidence interval [CI]: 0.45–3.39) were not statistically different in patients with postsurgical infectious complications. Infectious complications were more frequent among patients with benign prostatic hyperplasia (RR = 6.57; 95%CI:

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1.98–21.76) and hospitalization in the preceding 3 months (RR = 8.32; 95%CI: 2.69–25.71).

Conclusion One dose of antimicrobial therapy is sufficient to avoid infectious complications in patients with ASB. There were other factors associated with postsurgical infectious complications, such as benign prostatic hyperplasia and hospitalization in the preceding 3 months.

Resumen

Palabras clave

- ▶ bacteriuria asintomática
- ▶ infección del tracto urinario
- ▶ bacteriemia
- ▶ sepsis
- ▶ infección de la herida quirúrgica
- ▶ procedimientos quirúrgicos urológicos
- ▶ cirugía urológica

Objetivos Identificar el efecto de la duración de la profilaxis antibiótica quirúrgica (PAQ) y otras variables sobre las complicaciones infecciosas posquirúrgicas en pacientes con bacteriuria asintomática (BA) sometidos a cirugía urológica.

Métodos Se realizó un estudio observacional de una cohorte de pacientes con BA programados para cirugía urológica en tres instituciones de salud en Colombia. La población de estudio comprendió a todos los pacientes programados para cirugía urológica y con BA en el periodo de Abril del 2018 a Enero 2019. La intervención evaluada fue la duración de la PAQ preoperatoria, y la variable de resultado fue el desarrollo de cualquier complicación infecciosa posoperatoria hasta 30 días después del procedimiento.

Resultados El estudio incluyó a 184 pacientes con BA programados para cirugía urológica. La mediana de duración de la PAQ preoperatoria ($p = 0,49$) o 1 dosis de PAQ (razón de riesgo [RR]: 1,24; intervalo de confianza [IC] del 95%: 0,45 a 3,39) no fueron estadísticamente diferentes en pacientes con complicaciones infecciosas posquirúrgicas. Las complicaciones infecciosas fueron más frecuentes entre los pacientes con hiperplasia prostática benigna (RR: 6,57; IC del 95%: 1,98 a 21,76) y hospitalización en los 3 meses anteriores (RR: 8,32; IC del 95%: 2,69 a 25,71).

Conclusión Una dosis de terapia antimicrobiana es suficiente para evitar complicaciones infecciosas en pacientes con BA. Hubo otros factores asociados con complicaciones infecciosas posquirúrgicas, como hiperplasia prostática benigna y hospitalización en los tres meses anteriores.

Introduction

Asymptomatic bacteriuria (ASB) is defined as isolation of bacteria in the urine of an individual without signs or symptoms of urinary tract infection.¹ Its incidence varies among different population groups, ranging from 7 to 27% in diabetic individuals to between 1.9 and 9.5% in pregnant women and between 1 and 5% in premenopausal women. Asymptomatic bacteriuria is also frequently found in persons with spinal cord injury (between 23% and 89%),² users with indwelling urethral catheters, and patients scheduled for urologic surgery.^{3,4}

According to the recommendation contained in the Guidelines on Urological Infections, ASB should not be treated, except in pregnant women, since it reduces the risk of pyelonephritis and premature births; and in patients prior to urological surgery with anticipated mucosal disruption, in view of the risk of presenting with infectious complications such as bacteremia, sepsis, or urinary tract infection.^{1,3,5–9} However, the duration of surgical antibiotic prophylaxis (SAP) has not been clearly established, due to the lack of studies that compare different antibiotic initiation times.¹⁰

Initially, in 2005, the Infectious Diseases Society of America (IDSA) guidelines recommended a short treatment, without specifying the number of days.¹ More recently, the 2017 urologic infection guidelines recommend that ASB should be treated prior to endourologic procedures that involve mucosal disruption, although, once again, without specifying the duration of antibiotic treatment.⁸ The IDSA 2019 ASB guidelines suggest a short course of 1 or 2 doses, as opposed to prolonged antibiotic treatment, based on 2 clinical trials that compared single- to multiple-dose long-term therapy.¹¹

The lack of studies targeted at evaluating the optimal duration of SAP in patients with ASB means that the duration of antibiotic treatment in urology has not become a standard scientific practice.¹² Furthermore, the studies that have been conducted have proposed initiating prophylaxis anywhere from 1 to 7 days prior to the procedure, without ascertaining differences in terms of the outcome for each initiation time,⁷ thereby potentially generating improper use of antibiotics.¹³

Bearing in mind that > 30% of the patients with planned urologic procedures have ASB,¹⁴ and that this condition poses a risk factor for postsurgical infectious complications,

it is essential to ascertain the effect of the duration of SAP prior to these procedures.

The aim of the present study was to analyze the effect of the duration of antibiotic prophylaxis and of other variables on postsurgical infectious complications in a cohort of patients with ASB undergoing urological procedures.

Methods

Study Type and Study Population

We conducted an observational study of a cohort of patients with ASB scheduled for urologic surgery at three median- to high-complexity hospitals, situated in two cities in Colombia. We included patients undergoing urological surgery from April 2018 to January 2019, and who had been screened to detect ASB prior to surgery. The intervention evaluated was the duration of preoperative SAP.

Asymptomatic bacteriuria was defined as a bacterial isolate in a voided urine sample having a count $> 10^5$ (CFU/ml), assessed as being from a person who does not exhibit signs or symptoms of urinary tract infection.¹⁵ The following urologic procedures were included: tumors of the bladder or the urethra, open prostatectomy, transurethral resection of the prostate, ureterolithotomy, nephrolithotomy, and ureterorenoscopy. Patients with immunosuppression secondary to glucocorticoid use, under radiotherapy or chemotherapy treatment, with urinary tract infections, as well as those < 18 years old, were excluded.

The antibiotic regimen was established from the date of detection of ASB until 30 days after surgery or the development of postsurgical infectious complication. Patients received antibiotic prophylaxis as follows: preoperatively, considering the isolated micro-organism and its susceptibility profile; and perioperatively between 30 and 60 minutes before the procedure, according to the institutional protocol. The duration of antibiotic treatment prior to surgery was empirically determined by the urologist or by an infectious disease physician. All patients underwent the following 2-stage follow-up: stage 1, by telephone at 15 days after the intervention; and stage 2, 30 days after surgery.

Dependent and Independent Variables

The outcome variable was the development of any postoperative infectious complications, whether in the form of surgical wound infection, urinary tract infection, bacteremia or sepsis, in line with the Centers for Disease Control and Prevention (CDC) criteria.^{15,16} Infectious complications were captured by the principal investigator during follow-up and/or at the postoperative monitoring appointment. All cases were confirmed by an infectious disease physician external to the study and blinded to the duration of the SAP.

The main independent variable was the duration of preoperative SAP. Other independent variables were gender, age, arterial hypertension, diabetes mellitus, urological cancers, nephrolithiasis, and benign prostatic hyperplasia (HPB). Additionally, data were also gathered on the site where SAP was received and its duration in the postoperative period (POP), prior manipulation of the urinary tract (surgery or endoscopic

procedure) in the preceding 3 months,^{8,14} antibiotic use in the preceding 3 months, type of urologic intervention, micro-organism isolated, multiresistant micro-organism,¹⁷ as well as hospitalization in the preceding 3 months.

All isolates were identified by different clinical laboratories using the standard method. The susceptibility profile was defined by reference to the Clinical & Laboratory Standards Institute (CLSI) cutoff values.

Statistical Analysis

The independent variables were compared considering the development of postsurgical infectious complications. To establish significant differences with the categorical variables, the chi-squared test was used; numerical variables were compared using the Mann-Whitney U-test statistic; and the risk ratios (RRs) with their 95% confidence intervals (CIs) were calculated for the independent variables. A log-binomial regression model was fitted for explanatory purposes, in which we included the confounding variables; the interactions; and those identified by other studies as having a degree of clinical importance, which proved to be statistically significant. All data analyses were performed using the RStudio 3.5 software package (R Foundation, Vienna, Austria).¹⁸

Ethical Considerations

The present study was submitted to and approved by the Universidad CES University research ethics committee (Record no. 123, Study 631), and by the ethics committees of the respective participating institutions. The main investigator entered into a confidentiality agreement with the institutions. All patients signed an informed consent form to participate in the study.

Results

A total of 184 patients with ASB underwent urological surgeries. Most patients were males ($n = 114$; 61.96%) with BPH ($n = 76$; 41.30%). Arterial hypertension was the most frequent comorbidity ($n = 57$; 30.98%). The median age was 63 years old (range: 18 to 88 years old). The two main micro-organisms identified were *Klebsiella pneumoniae* ($n = 36$; 19.56%) and *Escherichia coli* ($n = 70$; 38.04%). Micro-organisms resistant to ≥ 3 groups of antibiotics were identified in 41.85% ($n = 77$) of the patients.

In this cohort, the density of incidence of postsurgical infectious complications was 4.27 per thousand patients/day, and the proportion of the incidence was 11.96%. Half of the patients received > 5 days of antibiotics as prophylaxis in the preoperative period, with 29 days as the maximum. The most used antibiotics in preoperative SAP were fluoroquinolones ($n = 58$; 31.18%) and aminoglycosides ($n = 28$; 15.05%); 15.22% ($n = 28$) of the patients received 1-dose antimicrobial therapy before the procedure. Surgical antibiotic prophylaxis was extended across the POP in 73.66% of the patients ($n = 137$) for a median of 7 days postoperatively (► **Table 1**).

The duration of SAP was found to have no effect on postsurgical infectious complications. The median duration

Table 1 Effect of antibiotic prophylaxis on postsurgical infectious complications in patients with asymptomatic bacteriuria ($n = 184$)

DATA	INFECTION ($n = 22$)	<i>p</i> -value	Crude RR (95%CI)
SAP ADMINISTRATION SETTING			
Ambulatory care	6 (6.59)	0.04	0.38 (0.16–0.93)
Hospital care	16 (17.20)	Ref.	Ref.
DURATION OF PREOPERATIVE SAP			
One dose	4 (14.29)	0.75	1.24 (0.45–3.39)
> One dose	18 (11.54)	Ref.	Ref.
TYPE OF PREOPERATIVE SAP			
Fluoroquinolones	5		
Aminoglycosides	4		
Two antibiotics	3		
Narrow-spectrum cephalosporins	2		
Nitrofurantoin	0		
Carbapenems	3		
Extended-spectrum cephalosporins	2		
Penicillins + beta-lactamase inhibitors	2		
Penicillins	1		
Antipseudomonal penicillins	0		
Phosphonic acids	0		
Folate antagonists	0		
Monobactams	0		
Polymyxins	0		
SAP IN THE POP			
No	5 (10.64)	Ref.	Ref.
Yes	17 (12.41)	0.95	1.17 (0.45–2.99)

Abbreviations: CI, confidence interval; POP: Postoperative period; RR, risk ratio; SAP: surgical antimicrobial prophylaxis.

of preoperative SAP ($p = 0.49$) and 1-dose SAP (RR = 1.24; 95%CI: 0.45–3.39) were not statistically different in patients with postsurgical infectious complications. Similarly, SAP in the POP did not display significant differences in terms of infected patients (RR = 1.17; 95%CI: 0.45–2.99) (►Table 1). Administration of preoperative SAP on an ambulatory basis was greater among patients who did not develop infectious complications (RR = 0.38; 95%CI: 0.16–0.93) (►Table 1).

Postsurgical infectious complications were greater among patients with diabetes (RR = 2.50; 95%CI: 1.09–5.76), BPH (RR = 3.05; 95%CI: 1.30–7.11), hospitalization in the preceding 3 months (RR = 4.94; 95%CI: 1.91–12.81), indwelling urinary catheters (RR = 2.30; 95%CI: 1.06–4.97), as well as endourological intervention in the preceding 3 months (RR = 2.23; 95%CI: 1.03–4.84). Asymptomatic bacteriuria with multidrug-resistant bacteria was present in 41.40% of the patients, and its incidence was higher in infected patients (50.0 versus 40.74%); however, without statistical significance (RR = 1.39; 95%CI 0.64–3.04) (►Table 2).

The factors found by the multivariate analysis to be associated with postsurgical infectious complications were

BPH (RR = 6.57; 95%CI: 1.98–21.76) and hospitalization in the preceding 3 months (RR = 8.32; 95%CI: 2.69–25.71). Surgical antibiotic prophylaxis-related variables were not included in the model due to lack of statistical significance (►Table 3).

Discussion

This is the first prospective study in Latin America to assess the effect of duration of SAP on postsurgical infectious complications in patients with ASB scheduled for urologic surgery. The results indicate that one dose of antimicrobial therapy preoperatively is sufficient to prevent postsurgical infectious complications in patients with ASB. We found other factors associated with postsurgical infectious complications, such as benign prostatic hyperplasia and hospitalization in the preceding 3 months. Also, the administration of preoperative SAP on an ambulatory basis was greater among patients who did not develop infectious complications.

The IDSA guideline for the management of ASB (2019)¹¹ recommends that, in patients with planned urologic

Table 2 Factors associated with postsurgical infectious complications in patients with asymptomatic bacteriuria ($n = 184$)

DATA	INFECTION ($n = 22$)	<i>p</i> -value	Crude RR (95%CI)
Gender			
Female	5 (7.14)	0.11	0.48 (0.18–1.24)
Male	17 (14.91)	Ref.	Ref.
AGE (Years Old)			
> 63 years	12 (14.10)	0.40	1.40 (0.64–3.07)
≤ 63 years	10 (10.10)	Ref.	Ref.
HTA			
Yes	8 (13.60)	0.64	1.21 (0.54–2.73)
No	14 (11.20)	Ref.	Ref.
DM			
Yes	6 (25.00)	0.03	2.50 (1.09–5.76)
No	16 (10.00)	Ref.	Ref.
UROLOGIC CANCER			
Yes	1 (7.69)	0.62	0.63 (0.09–4.29)
No	21 (12.28)	Ref.	Ref.
NEPHROLITHIASIS			
Yes	8 (13.60)	0.64	1.21 (0.54–2.73)
No	14 (11.20)	Ref.	Ref.
BPH			
Yes	15 (19.74)	< 0.01	3.05 (1.30–7.11)
No	7 (6.48)	Ref.	Ref.
PRIOR ENDOUROLOGICAL INTERVENTION*			
Yes	10 (20.0)	0.05	2.23 (1.03–4.84)
No	12 (8.95)	Ref.	Ref.
PRIOR SURGERY*			
Yes	5 (14.71)	0.58	1.30 (0.51–3.27)
No	17 (11.33)	Ref.	Ref.
INDWELLING URINARY CATHETER			
Yes	10 (20.41)	0.03	2.30 (1.06–4.97)
No	12 (8.89)	Ref.	Ref.
URETERAL STENT			
Yes	1 (4.76)	0.28	0.37 (0.05–2.61)
No	21 (12.88)	Ref.	Ref.
PREVIOUS HOSPITALIZATION*			
Yes	17 (22.67)	< 0.01	4.94 (1.91–12.81)
No	5 (4.59)	Ref.	Ref.
ANTIBIOTIC USE*	16 (15.69)	0.08	2.14 (0.88–5.23)
Yes			
No	6 (7.32)	Ref.	Ref.
REASON FOR UROLOGIC INTERVENTION			
Tumor	1 (14.28)	Ref.	Ref.
Urologic cancer	1 (5.88)	0.51	0.41 (0.03–5.70)
Hydronephrosis	2 (8.33)	0.55	0.58 (0.06–5.52)
Benign Prostatic Hyperplasia	13 (18.57)	1.0	1.30 (0.20–8.52)

(Continued)

Table 2 (Continued)

DATA	INFECTION (n = 22)	p-value	Crude RR (95%CI)
Urinary incontinence	0	NA	NA
Lithiasis	5 (10.0)	0.56	0.70 (0.09–5.15)
NNIS SURGICAL RISK			
1	17 (11.80)	Ref.	Ref.
2	4 (10.26)	1.0	0.87 (0.31–2.42)
3	1 (100)	0.12	NA
MULTIDRUG-RESISTANT BACTERIA			
No	11 (14.30)	0.41	1.39 (0.64–3.04)
Yes	11 (10.3)	Ref.	Ref.

Abbreviations: AHT: arterial hypertension; CI: Confidence interval; DM: diabetes Mellitus; BPH: benign prostatic hyperplasia; NNIS: national nosocomial infections surveillance; RR: risk ratio.

* In the last 3 months.

Table 3 Regression analysis of factors associated with postsurgical infectious complications in patients with asymptomatic bacteriuria (n = 184)

ASSOCIATED FACTORS	Crude RR (95%CI)	Adjusted RR (95%CI) ¹
AGE (years old)		
>63	1.40 (0.64–3.07)	0.30 (0.09–0.97)
≤ 63	Ref.	Ref.
DIABETES MELLITUS		
Yes	2.50 (1.09–5.76)	2.27 (0.90–5.69)
No	Ref.	Ref.
BPH		
Yes	3.05 (1.30–7.11)	6.57 (1.98–21.76)
No	Ref.	Ref.
PRIOR HOSPITALIZATION		
Yes	4.94 (1.91–12.81)	8.32 (2.69–25.71)
No	Ref.	Ref.

Abbreviations: CI, confidence interval; BPH: benign prostatic hyperplasia; RR, risk ratio.

1. Age-adjusted RR, diabetes mellitus, benign prostatic hyperplasia, and hospitalization in the previous 3 months.

procedures, SAP should be administered as a short (one or two doses) rather than as a prolonged course. This recommendation is based on the findings of two clinical trials that compared the incidence of infectious complications in two groups, one that received a single dose, and another that was prescribed a longer regimen.¹⁹

In a clinical trial, Sayin Kutlu et al.¹⁹ compared 59 patients with ASB who were scheduled for urologic surgery. They

were divided into 2 groups: the 1st group received a single dose of antibiotics 30 to 60 minutes prior to surgery; the 2nd group comprised patients who received antibiotic treatment until the urine culture tested negative (8 ± 3 days). In this study, no patient developed postsurgical infectious complications, yet the group of patients that received a prolonged antibiotic regimen registered a longer hospital stay ($p < 0.01$) and higher antibiotic treatment costs ($p < 0.01$). Our study compared all patients with ASB, taking into account different SAP duration modalities, showing that, as yet, there is no standard practice in place. Surgical antibiotic prophylaxis duration was also found to have no effect on the prevention of postsurgical infectious complications, results similar to those reported by Sayin Kutlu et al.¹⁹

Another prospective study evaluated 60 patients with ASB and spinal cord injury scheduled for urologic endoscopic procedures.²⁰ These patients were also divided into 2 groups: the first group of 35 patients received a single dose of antibiotic 30 minutes before the procedure; the second group of 25 patients received a regimen of 3 to 5 days. In this cohort, one patient in each group developed some postsurgical infectious complication, but the costs of antibiotic treatment and preoperative anxiety were lower in the group that received a single dose.¹⁹ Diagnostic cystoscopy accounted for most procedures included, 98.3% of the patients were male, and the study objective was not to compare infectious complications, but rather to compare the quality of life of the patients. In contrast, our study used a larger patient sample, included several urologic procedures, and focused especially on comparing postsurgical infectious complications.

We found that there are other factors that increase the risk of postsurgical infectious complications, such as comorbidities and having undergone hospitalization in the 3 months immediately preceding the procedure. These factors have already been described by previous studies.^{4,14} In a cohort of 2,201 patients scheduled for urologic procedures, Cai et al. found that patient comorbidities increased the risk of infectious complications.¹⁴ Similarly, our study also showed that BPH was more frequent in patients who developed postsurgical infectious complication.

The fact that a patient has been hospitalized is a factor that is associated with healthcare-related infections, due to exposure to invasive devices, contact with healthcare personnel, and use of antibiotics.^{21,22} In our study, postsurgical infectious complications were greater among patients who underwent hospitalization in the 3 months immediately preceding the urologic procedure.

Providing evidence to show that the duration of SAP has no influence on the risk of infectious complications has a direct impact on health care costs and prudent antibiotic use.²³ Among the strengths of the present study is the fact that it is the first prospective multicenter study to compare different SAP initiation times. Furthermore, since the participants were selected consecutively, the study can be considered as being free of selection bias. The evaluation of the outcome was subjected to a second evaluation by an infectious disease physician external to the study, who was biased toward the duration of SAP. Lastly, both pre- and postoperative antibiotic use were considered.

The present study has some limitations. Isolates were identified using the standard method, albeit at different clinical laboratories, in view of the fact that patient care depends on each institution. The small sample size did not allow for analysis by subgroup with a breakdown by urologic procedure or type of infectious complication. Even so, this ranks as the prospective study with the largest-sized sample to be conducted in Latin America on patients with ASB prior to urologic procedures. Taking into account the fact that urologists participated in the study, they might have prescribed antibiotics appropriately or prescribed wider-spectrum antibiotics, thus constituting a possible selection bias.

Based on these results, it is important to raise three aspects that will have to be studied in greater depth: one, the necessity and cost-effectiveness of screening and treating ASB prior to urologic procedures, bearing in mind the consequences in terms of urinary disbiosis and bacterial resistance; two, the need to consider whether the SAP received by patients in the perioperative period is sufficient to control the risk, as has been highlighted by some researchers^{14,24}; lastly, performing a study to evaluate the association between postsurgical infectious complications with benign prostatic hyperplasia and hospitalization in the preceding 3 months.

Conclusions

Duration of SAP has no effect on infectious complications. There are other variables that are associated with development of postsurgical infectious complications in patients with ASB scheduled for urologic surgery, such as BPH and hospitalization in the 3 months immediately preceding surgery. Lastly, the patients who did not develop infectious complications had the administration of preoperative SAP on an ambulatory basis.

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Conflict of Interests

The authors have no conflict of interests to declare.

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