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REVIEW ARTICLE

Asymptomatic bacteriuria, to treat or not to treat

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Abstract

Asymptomatic bacteriuria (ASB) is a common incidental finding in hospitals and health facilities during general examination of patients. Due to the new trend of giving antibiotic treatment without regulation in certain infections, it is important stablishing criteria to avoid over usage of antibiotics during the general or intrahospitalary examination of patients. This text summarizes the main characteristics of ASB, diagnostic criteria, definitions and assessment of treatment in defined populations.

Introduction

Asymptomatic bacteriuria (ASB) is the presence of one or more species of bacteria growing in an appropriately collected urine specimen (≥105 colony-forming units [CFU]/mL or ≥108 CFU/L) from a patient without symptoms of urinary tract infection (UTI) (1). ASB is common in healthy women and in adults and children with urologic abnormalities associated with impaired voiding (1). This pathology is nowadays relevant for physicians due to its recurrence in general population, specifically to stablish which population should receive treatment and which not. UTI are responsible for an estimated 7 million office visits, 1 million emergency rooms visit, and 100.000 hospitalizations each year (2). Healthcare providers, including general physicians, often prescribe unnecessary antibiotic treatment for asymptomatic bacteriuria, contributing to the

worldwide concern of antibiotic resistance. According to the Centers for Disease Control and Prevention (CDC), in their 2019 Antibiotic Resistance Report, each year antibiotic resistance bacteria and fungi cause at least an estimated 2,868,700 infections and 35,900 deaths only in the United States; thus the importance of avoiding the use of antibiotics in patients without a correct screening (3).

In order to accomplish a correct screening for ASB, it is important to establish the threshold of bacteriuria for distinguishing urethral contaminations from a voided clean catch specimen, and for isolation of bacteriuria in specimens collected through straight catheterization, which are less likely getting a urethral, vaginal (in women) or fecal contamination.

Definitions

Asymptomatic bacteriuria refers to patients who have no symptoms associated to UTI (e.g., common symptoms of cystitis: dysuria, frequency, urgency, suprapubic pain and pyelonephritis symptoms: fever, chills, flank pain, nausea and vomiting) (2,4). It is important to define the types of recollection of urine for ASB, since according to the method of recollection, depends the threshold for diagnosis.

In **voided clean-catch specimens**, the threshold is a quantitative count ≥105 CFU/mL. For women, it is necessary a second specimen, preferably in two weeks, to assess the growth of the same organism over the same quantitative threshold. For men, a single specimen over the threshold is sufficient for making diagnosis (5).

In **catheterized specimens**, the threshold for asymptomatic bacteriuria is a quantitative count ≥105 CFU/mL, and it is not necessary to repeat the sample for confirmation. Specimens collected through catheter, are less likely to have urethral contamination. Patients with long-term indwelling catheters often have low-level bacteriuria, often with multiple organisms, which reflects catheter contamination (5).

Methodology

The content of this review was made from electronic searches from the following sources:

- Cochrane's database.
- EBSCO database.
- Pubmed database.
- JAMA guidelines.
- UpToDate database.
- Searches of selected journals of Infectology, Surgery, and Obstetrics.

The keywords used for the search were: Asymptomatic bacteriuria, urinary tract infection; antibiotic, incidence, prevalence, renal transplant.

Used MeSH terms: Urinary Tract Infections, Urologic Diseases, Male Urogenital Diseases, Female Urogenital Diseases and Pregnancy Complications.

The search was made from October 2019 to July 2020, the total of articles included was 18, from 25 articles reviewed.

Epidemiology

ASB is common especially in elderly patients, patients in long-term facilities, and hospitalized patients. The prevalence increases with age, ranging from 0% in men aged 68 to 79 up to 5.4% in men aged 90 to 103. In women, this prevalence descends from 13.6% among women aged 68 to 79, to 2.4% among women aged 90 to 103 (6). In patients with kidney transplant, the prevalence is from 2 to 24% (6).

In healthy young premenopausal nonpregnant women, the prevalence of ASB is 1% to 5% (7). The Clinical Practice Guideline from the Infectious Diseases Society of America (IDSA) reported similar prevalence (table 1). In healthy pregnant women, the prevalence is 1.9% 2- 9.5% (8).

Regarding the most common pathogens in ASB according to a specific population are *Escherichia coli*, *Klebsiella pneumonia*, *Proteus mirabillis* and *Enterococcus faecalis* in community-dwelling older women; among institutionalized patients and patients with long-term indwelling urinary catheters, the most common pathogens are *Pseudomonas aeruginosa*, *Morganella morganii*, and *Providencia stuartii* (7).

Pathophysiology

There are diverse factors that affect the course of the pathology, such as pathogens, hosts or both. The microbiology of ASB is similar to most of UTI. Regarding the pathogen factors, specifically in *E. coli*, several studies stablish that certain strains are more capable of causing symptomatic disease than others. These studies explain the virulence via fimbrial adhesins of *E. coli*. There is a hypothesis that suggests that certain strains of *E. coli* that cause ASB and its colonization are "uroprotective" against infection with more invasive uropathogens (9).

Other important factors are the host responses in ASB. For example, an article published in Lund University of Sweden reports an interesting model previously proved in mice, where reduced levels of neutrophils Toll-Like Receptor 4 may lead to asymptomatic bacterial carriage (10).

Population	Prevalence (%)
Children	
Boys	<1
Girls	1-2
Healthy women	
Premenopausal	1.0-5.0
Pregnant	1.9-9.5
Postmenopausal (age 50-70 yrs)	2.8-8.6
Persons with diabetes	
Women	10.8-16
Men	0.7-11
Elderly persons in the community (age >70 yrs)	
Women	10.8-16
Men	3.6-19
Elderly persons in a long-term care facility	
Women	25-50
Men	15-50
Persons with spinal cord injury	
Intermittent catheter use	23-69
Sphincterotomy/condom catheter	57
Persons with kidney transplant	
First month post-transplant	23-24
1 mo to 1 yr post-transplant	10-17
>1 yr post-transplant	2-9
Persons with indwelling catheter use	
Short-term	3-5/day catheter
Long-term	100

Table 1. Prevalence of ASB according to specific population. Own elaboration from (2,7,13) data.
ASB: asymptomatic bacteriuria

Diagnosis

- Lack of signs and symptoms of urinary tract infection.
- Diagnosis based on urine specimen collected in manner that minimizes contamination.
- For asymptomatic women, 2 consecutive voided urine specimens with isolation of same bacterial strain in quantitative counts ≥ 100,000 CFU/mL.
- For asymptomatic men, single voided urine specimen with one bacterial species isolated in quantitative count ≥ 100,000 CFU/mL.
- For women or men with indwelling catheter, single catheterized urine specimen with one bacterial species isolated in quantitative count ≥ 100,000 CFU/mL (5,8,11).

Management

There is no evidence for routine screening or treating ASB in general, non-pregnant population. Several trials have failed to find a clear benefit of treating this pathology. In order to assess the effectiveness and safety of antibiotics treatment for asymptomatic bacteriuria in adults, a systematic review from the Cochrane Renal Group was made. The analysis was made in Israel, it included nine studies (1,614 participants), comparing antibiotics to placebo or no treatment for asymptomatic bacteriuria, excluding pregnant women, catheterized participants, patients with urinary stents, nephrostomy tubes, kidney or other transplant recipients, spinal cord injury and hospitalized patients (1). According to the consulted bibliography, it is not suggested the screening and treatment of ASB. There exist certain exceptions in which screening and treatment is highly recommended; including pregnant women, patients undergoing urologic intervention, and recent renal transplant recipients (1).

No differences were observed between antibiotic therapy versus no treatment of ASB for the development of symptomatic UTI, complications or death. Antibiotics were superior to no treatment for the bacteriological cure but with significantly more adverse events. There was no clinical benefit from treating asymptomatic bacteriuria (11).

Older patients also had reported no benefits in treatment or screening. Even though rates of incidence in the elderly, asymptomatic bacteriuria is not associated with an increased risk of adverse outcomes, also, antimicrobial treatment has no benefit in those patients (5).

A review of ASB in patients with diabetes mellitus concluded that although ASB is relatively common in diabetic women, the lack of evidence in treatment and different scenarios such as renal function and chronic urinary disease makes more difficult the physician's decision to treat patients with diabetes (12). Other studies concluded that the incidence of ASB increases in this population, but there is no significant benefit in treatment of ASB (5).

There are few exceptions in the screening and treatment of ASB, such as pregnancy, patients undergoing urologic intervention and renal transplant recipients. In these groups (table 2) ASB has been associated with adverse outcomes (5,6). Assessing the correct screening and treatment for ASB can also be useful for improving patient

Population	Screen	Treat	Notes
Healthy patients	×	×	
Pregnant women	✓	✓	Consult national guidelines
Postmenopausal women	×	×	
Women with recurrent uncomplicated UTI	×	×	The treatment of ASB may be potentially harmful
Diabetes	×	×	
Elderly institutionalized patients	×	×	
Patients with renal transplants	×	×	
Prior to surgery	✓	✓	Only in case of urological procedure entering urinary tract and breaching the mucosa
Patients with indwelling catheters	×	×	

Table 2. Exceptions in screening and treatment of ASB. Extracted and adapted from Tommasso *et al.* (6)

outcomes and experience while reducing intrahospitalary costs, such as described in the guideline of JAMA (13).

In pregnant women, an optimal duration of treatment is not stablished; generally, a 4-7 day course or 2-7 day course is sufficient. No single antibiotic has been shown to be superior to another. Options of treatment include penicillin, cephalosporins, fosfomycin, nitrofurantoin (avoided at end of pregnancy and in patients with glucose-6-phosphate dehydrogenase deficiency), trimethoprim (avoided in first trimester of pregnancy) and sulphonamides (avoided in third trimester). Cotrimoxazole and ciprofloxacin (both Pregnancy Class C) are generally avoided in the 1st trimester and in late 3rd trimester when alternatives exist due to potential for adverse events. Giving the correct treatment during pregnancy is important for reducing the incidence of maternal pyelonephritis, preterm birth, and infant low birth weight, although overall quality of evidence low (8).

In patients undergoing a genitourinary surgery, is recommended antimicrobial prophylaxis (14). This include ciprofloxacin (500 mg orally or 400 mg intravenous) or trimethoprim-sulfamethoxazole (one 160/800 mg tablet orally).

In patients undergoing joint arthroplasty, it is not recommended performing urinalysis or culture in patients without urinary symptoms; if a patient is found to have prior to the surgery ASB, it is not recommended the use of antibiotics (15).

Patients undergoing surgery for kidney transplantation are treated for ASB within three months of transplant in order to prevent symptomatic UTI, which has been associated with an increased risk of acute allograft rejection (16). The most common regimens are ciprofloxacin (250 mg orally twice daily) and amoxicillin (500 mg orally three times daily) in patients with normal renal function; and nitrofurantoin (100 mg orally twice daily) when there is impaired renal function (17).

Patients with spinal cord injury often have atypical manifestations of UTI, thus there is no role for screening or treating ASB. Although these patients have a high prevalence of ASB, due to the increased risk of drug-resistant uropathogens it is necessary to avoid antibiotic therapy (18).

Conclusion

Nowadays, the evidence and access to laboratory tests give young physicians another view for treating or referring patients from office visits. The clinical importance of this topic is huge for two simple reasons: first, the optimal and quick identification of ASB in general population and susceptible population, and second, avoiding antimicrobial resistance worldwide due to the incorrect use of them. The importance of avoiding the use of antibiotics when there is not a correct screening ensures the goal of preventing antibiotic resistance. Antibiotics prescription is not a kitchen's recipe, it has to be adapted to the patient. Identifying ASB and the population at risk give physicians a valuable tool for general practice.

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