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Brief communication

Bacterial sensitivity to fosfomycin in pregnant women with urinary infection



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ABSTRACT

The aim this study was to determine the *in vitro* susceptibility to fosfomycin of bacteria isolated from urine samples of pregnant women with urinary tract infection. Samples of urine culture with bacterial growth of pregnant women were collected from clinical laboratories in Tubarão, state of Santa Catarina, Brazil, between September 2012 and May 2013. In the experimental stage, the colonies were tested for sensitivity to fosfomycin by using the Kirby–Bauer method. The following information relating to the samples was also collected: patients' age, colony count, type(s) of identified bacterial(s) and result of the antimicrobial sensitivity test. Student's t-test was used for mean comparison. A total of 134 samples were selected for the study. The age of the subjects ranged from 15 to 40 years (mean 26.7). Escherichia coli (Gram-negative) and Staphylococcus aureus (Gram-positive) were the most commonly identified species. In 89% of cases, the microorganisms were sensitive to fosfomycin. E. coli and S. aureus were the main species of bacteria responsible for urinary tract infections in women in the study area. The most prevalent microorganisms in pregnant women with urinary tract infection were susceptible to fosfomycin.

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Urinary tract infections (UTI) are common during pregnancy due to hormonal and anatomo-physiological changes that facilitate the growth and dissemination of bacteria in the maternal urinary tract.¹ It is estimated that 5–10% of women develop some kind of UTI during pregnancy.² Asymptomatic bacteriuria is the most common situation, followed by acute cystitis and pyelonephritis.³ These infections have potentially serious consequences for maternal and fetal health if they are not properly treated.¹

The choice of antimicrobial agents should preferably consider the urinalysis results, which allow for pathogen identification, in addition to antimicrobial susceptibility testing that indicates the susceptibility of microorganisms to specific groups of antimicrobials.⁴ However, the correct choice of an antimicrobial agent to treat UTI during pregnancy is complex because it requires full attention to maternal and fetal safety, in addition to ease of use, access, and cost of treatment.⁵

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Knowing the sensitivity of the etiological agents against antimicrobial drugs available, linked to relevant epidemiological data, helps to make appropriate therapeutic decisions based on updated scientific information for adequate treatment, which shortens the symptomatic period and prevents the possibility of recurrences and complications. However, in recent years, the problem of antimicrobial resistance has become very common, mainly because the antimicrobials once so successful, are no longer effective against several bacterial species responsible for infections in the urinary tract.^{3–6}

Although the introduction rate of new classes of antibiotics on the market is limited, some old drugs such as fosfomycin can still provide a temporary solution to the emerging problem of resistance, since they have proven to be effective against the prevailing pathogens.

The aim of this study was to demonstrate the *in vitro* antibacterial susceptibility to fosfomycin of bacteria taken from urine samples of pregnant women with UTI.

This study was approved by the Research Ethics Committee of the University of Southern Santa Catarina in November 29, 2012 (code number 12.289.4.01.III).

The study was conducted in two stages: first, an epidemiological cross-sectional study to collect data related to urine cultures of pregnant women performed in laboratories of the city of Tubarão, Santa Catarina, Brazil, between September 2012 and May 2013; in the second stage, in vitro antibacterial susceptibility to fosfomycin of isolated bacterial colonies from the urinary tract of pregnant women was evaluated.

Thus, the samples consisted of positive urine cultures obtained from the participating laboratories, as well as the following information contained in the reports or patients' records: colony count, identification of isolated species, antimicrobial susceptibility of the tested agents, and age of pregnant women.

The sample size was calculated according to the average annual number of live births in that city, which was 2470, and represented the estimated total number of annual pregnancies in the last decade (2001–2010), according to data from the Information System on Live Births.

The study sample was collected during nine months, and the final sample size of 186 pregnant women took into account the average annual number of pregnancies adjusted for the 9-month period (1853 pregnancies), and the percentage of UTI in pregnancy of 10%, as reported in the literature.² For a confidence level of 95%, a minimum of 126 urine samples would have to be obtained.

The inclusion criteria included positive urine culture of pregnant women living in the city of Tubarão, Santa Catarina, according to Kass' classification, regardless of symptoms. There was no access to clinical information regarding the patients' signs and symptoms. Samples characterized by dehydrated cultures were excluded from the study because of possible contamination by non-pathogenic environmental fungi or other contaminant external agents. Cultures in which the necessary information was unavailable or inaccessible for any reason were excluded as well.

Information about the age of participating pregnant women, date of urine culture, and date of birth were retrieved from records and reports of the participating laboratories.

The selected samples were tested for sensitivity to fosfomycin by the disk diffusion method known as the Kirby–Bauer method, as recommended by the Clinical and Laboratory Standards Institute, described in document M100-S23, as of January 2013, and based on studies of Minimum Inhibitory Concentration. The disc used was SENSIBIODISC CECON Fosfomicina® for antibiogram in standard concentration of 200 mcg of the drug, approved by the Brazilian Ministry of Health (Registration No. 10000600103) for testing Grampositive and Gram-negative bacteria isolated from human urinary tract.

All data obtained in both stages of the study were organized and stored in Excel spreadsheet (Microsoft Office 2010) and analyzed with the use of descriptive statistics, and presented in a narrative, tabular, or graphical form. Statistical analysis was performed using the Statistical Product for Service Solutions v.20.0. Student's t test was used for mean comparison. The confidence level was set at 95%.

A total of 139 samples were selected for the study, of which five (3.6%) were excluded; three because of contamination and two due to lack of laboratory antimicrobial susceptibility testing results.

The age of participants ranged from 15 to 40 years (mean 26.7; SD 6.2). The most commonly identified microorganism was Escherichia coli (66.2%), followed by Staphylococcus aureus (14.3%), Klebsiella pneumoniae (3.8%), Enterobacter (3.0%), and others (12.7%).

The antimicrobial agents tested for antimicrobial sensitivity included nalidixic acid, ampicillin, sulphazotrim, ciprofloxacin, norfloxacin, and nitrofurantoin (Table 1).

Eighty-nine percent of the microorganisms were sensitive to fosfomycin. Intermediate or resistant isolates included the strains of E. coli (5.9%; n = 8), S. aureus (2.2%; n = 3), Staphylococcus sp. (1.5%; n = 2), Enterococcus sp. (0.7%; n = 1), and Staphylococcus saprophyticus (0.7%, n = 1).

The mean age of pregnant women with UTI caused by microorganisms sensitive to fosfomycin was 26.6 years (SD 6.2), whereas the mean age of those with UTI caused by resistant microorganisms was 27.2 years (SD 6.3), [p=0.731].

Relative sensitivity of the two most commonly isolated bacteria in this study to the orally administered antimicrobials safe for use during pregnancy is shown in Table 2.

E. coli was the most commonly identified microorganism, which supports the findings of other studies that indicate the predominance of this species in community-acquired UTIs among pregnant and non-pregnant women of different age-groups. ^{2,4–7} E. coli, in addition to be part of the normal intestinal microbial flora, is able to invade and remain in the urinary tract due to structural factors that facilitate adherence, which justify its predominance when compared to other species of the same family (Enterobacteriaceae), also causing UTI. ⁸

Among the Gram-positive microorganisms, about 15% of the samples revealed the presence of *S. aureus* as the etiologic agent of UTIs. A study performed in a health center in Curitiba, Paraná that evaluated 120 urine samples of men and women with suspected UTI found a prevalence rate similar to that of this study, and *S. aureus* was isolated in 18.2% of cases. However, these findings differ from those of other studies in Portugal that found 0.9% of *S. aureus* in urine samples of

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