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A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF PROPHYLACTIC ANTIBIOTICS IN PREVENTING FEMALE URINARY TRACT INFECTION AFTER URODYNAMIC STUDY

Hypothesis / aims of study

To study the effectiveness of prophylactic antibiotics in reducing female urinary tract infection (UTI) after urodynamic study (UDS). The hypothesis is that prophylactic antibiotic can reduce the prevalence of post-UDS UTI.

Study design, materials and methods

All women who had been referred to the authors' Urodynamic Clinic were invited to participate. Clinical research ethics approval was obtained from the authors' institution. A "screen-and-treat" protocol was adopted for detection of pre-existing asymptomatic UTI [1]. Specifically, an Midstream urine (MSU) culture for bacteria was collected at the time of first consultation, which was four weeks before the UDS. Women with UTI were recalled for a course (seven days) of antibiotics according to sensitivity, and the UDS were postponed, until the repeated MSU result became normal. On the day of UDS, urine was also checked for leukocytes and nitrite by Multistix® (Bayer Diagnostics Manufacturing Ltd., South Wales, UK) reagent strip. UDS was cancelled in women with either significant leucocytes (one '+' or above) or nitrite (one '+' or above) in their urine. An MSU culture was repeated and another UDS appointment was arranged if the culture had become negative. This has been the standard practice at the authors' unit to screen for any pre-existing asymptomatic UTI before UDS. Immediately before the UDS, those who gave informed consent were randomised into Group A (Prophylactic Augmentin) or Group B (Placebo). Group A would receive single oral dose of Augmentin (amoxycillin 250mg + clavulanic acid 125mg, GlaxoSmithKline, Middlesex, UK). Group B would receive single oral dose of placebo. The allocation and dispense of the study drug was by sequentially numbered opaque sealed envelopes prepared by a research nurse, and the procedure was concealed from the investigators who performed the UDS. Each envelope contained one tablet of Augmentin 375mg or placebo, which was identical in shape, size, and colour. Subjects were instructed to take the tablet 30 minutes before the UDS. We chose Augmentin as our study drug as it had been shown to be an effective beta-lactamase-stable oral antibiotic in the treatment of UTI (uncomplicated and complicated, recurrent, and nosocomial) and bacteriuria [2]. The single-dose regimen was more economical, easier to administer, and carried a lower risk of inducing bacterial resistance than multiple-dose regimen [3]. All subjects had standardised UDS, which comprised uroflowmetry, filling and voiding cystometry, with a Dantec Menuet (Dantec Medical A/S, Skovlunde, Denmark) multichannel urodynamic machine. Each UDS was performed with strict aseptic technique. The urodynamic procedures and diagnoses were in accord with the standards prescribed by International Continence Society. MSU was collected for bacteriology two days after the UDS.

The primary outcome measure is the prevalence of significant bacteriuria after UDS. Significant bacteriuria is defined as ≥10E5 colony forming unit per ml (cfu/ml) in a clean catch MSU specimen. Other relevant data like the subjects' demographic, urodynamic, and related medical information were also collected.

130 consecutive female subjects (65 in each group) attending the Urodynamic Clinic for urinary incontinence were recruited. The prevalence of post-UDS UTI in our unit had been shown to be around 8%, and the sample size calculation is based on the reduction of UTI from 8% to 0%, with Type I error of 0.05 and power of 80%.

Results

The median age between Groups A and B are different, with Group A subjects being slightly younger but not reaching statistical significance (52 years [IQR 45, 61] vs. 55 years [IQR 48, 70]; p=0.05, Mann-Whitney U test). Otherwise the two groups were not different in terms of parity, BMI, UDS diagnoses, and prior continence procedures (p>0.05). Before the UDS one (1.5%) Group A subject had a significant MSU culture of $\geq 10^5$ cfu/ml; and no (0%) Group B subject had significant MSU culture. After the UDS one (1.5%) Group A subject had a significant MSU culture of $\geq 10^5$ cfu/ml; and eight (12.3%) Group B subjects had significant MSU culture. The difference between the post-UDS prevalence was statistically significant (p=0.02, Chi squared test). Of the eight MSU specimen with significant culture, one (12.5%) had a pure culture of *Klebsiella* species; four (50%) had *Escherichia coli*, and three (37.5%) had *Enterococcus* species.

Interpretation of results

UDS are associated with significant bacteriuria due to catheterisations. The prevalence of post-UDS bacteriuria as shown in this study is 12.3%. Enterobacteriaceae, in which *Escherichia coli* constitutes approximately half the uropathogens before and after UDS, remain the commonest bacteria isolated. All the bacteria isolated are commonly associated with uncomplicated UTI, i.e., occur mainly in otherwise healthy females with structurally normal urinary tracts and intact voiding mechanisms. However, even in patients with uncomplicated UTI, there may be considerable morbidity from recurrent symptomatic infections, and there is a small but well-documented risk of developing acute pyelonephritis, bacteraemia, and renal damage. We have shown that one single oral dose of Augmentin 375mg 30 minutes before UDS effectively reduced the post-UDS bacteriuria prevalence from 12.3% to 1.5%.

Concluding message

UDS could lead to female UTI despite a stringent screen-and-treat protocol. Single oral dose of Augmentin 375mg offers effective prophylaxis against post-UDS bacteriuria.

References
1. Am J Obstet Gynecol 2004;190:1234-40.
2. J Urol 1998;191-4.
3. BJU Int 1999;83:392-395.

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