

Problem of antibiotic resistance in patients with acute bacterial cystitis and treatment options

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Acute bacterial cystitis (ABC) is one of the most common community-acquired (CA) infections. We curiously read the systematic analysis article “Management of community-acquired acute bacterial cystitis in Turkey” by Coşkun et al. about determining the adequate antibiotherapy for ABC in our country (1).

That study objectively revealed the potential antibiotherapy resistance generally assigned by clinicians based on long-term personal experience and dissolved the suspicions. Accordingly, trimethoprim-sulfamethoxazole (SXT), amoxicillin-clavulanate (AMC), and 1st and 2nd generations of cephalosporins that are used empirically in Turkey are not reliable because serious resistance has been detected for antibiotics used in the traditional treatment of CA-ABC. For example, more than 20% resistance is suggested for SXT, amoxicillin-clavulanate, cefazolin, and cefuroxime. With this study, fosfomycin and nitrofurantoin were shown to have an excellent effect on *E. coli*, the most common agent for CA-ABCs. This systematic analysis showed resistance rates of more than 20% for quinolones like ciprofloxacin that are widely used in Turkey for adult ABC. On the other hand, aminoglycosides, 3rd and 4th generation cephalosporins, and piperacillin-tazobactam were found to be more reliable. However, none of these antibiotics can be comfortably used for outpatients. For that reason, fosfomycin and nitrofurantoin are the antibiotics that should be essentially used in place of the aforementioned ones. Antibiotic resistance generally is not an important issue for patients with first-attack CA-ABC. In these cases, despite the resistance to amoxicillin, ampicillin, or SXT, sensitivity to 3rd generation cephalosporins or quinolones is expected. However, quinolone resistance is often found in patients with recurrent ABC attacks. In such cases, bad sanitation or an underlying cause like ureterovesical reflux, urinary spasm, or nephrolithiasis may be present. In relatively elderly patients, obesity and diabetes mellitus are significant predisposing factors. In ABC cases with an underlying risk or patient cooperation problems, initiation of oral antibiotics like nitrofurantoin or fosfomycin empirically (until the urine culture results are obtained) may be reasonable.

Azap et al. reported extended-spectrum β -lactamase (ESBL) positivity of 6.3% (17 of 269) in noncomplicated CA-urinary tract infections (CA-UTI) cases and of 17.4% (34 of 195) in complicated CA-UTI cases in their 2010 study of 510 CA-UTI cases. In the same study, SXT, ciprofloxacin, and gentamicin resistance was found to be low in the ESBL-negative group at 4.6%, but this rate was 8 times higher in the ESBL-positive group (39.2%, $P < 0.001$) (2). However, this finding should not mean the initiation of carbapenem therapy in cases of CA-UTI caused by ESBL-positive members of Enterobacteriaceae. Noncarbapenem antibiotics (AMC, piperacillin-tazobactam, 3rd and 4th

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generation cephalosporins, etc.) may be used in these cases. With its 2009 regulation, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) focused on the definition “ESBL (+) Enterobacteriaceae” for the species isolated from UTIs, redefined the sensitivity zone radius and MIC values for 3rd and 4th generation cephalosporins (cefotaxime, ceftriaxone, ceftazidime, and cefepime), and suggested the use of noncarbapenem antibiotics in case of sensitivity (3).

Pullukcu et al. administered oral fosfomycin (3 g each 48 h, repeated for 3 doses) for 52 ESBL producers in cases with no systemic signs or symptoms (mean patient age: 55 ± 18.3 years), and 94% of patients responded well clinically. Microbiological response was obtained in 78% of the cases. Upon the 1-month follow-up, none of the patients showed a relapse. Meanwhile, 70% of the study group had risk factors including indwelling catheter, hemiparesis or quadriparesis, malignancy in urinary tract, other malignancies, diabetes mellitus, renal transplantation, nephrolithiasis, and recent urological intervention (4). Similar findings were also reported by some other researchers (5,6).

This approach forms an important treatment alternative for many centers with outpatients. It is a fact that fosfomycin is preferred more often for such cases today in Turkey. In cases of urinary tract infections by ESBL-positive Enterobacteriaceae, fosfomycin will thus be encountered as a carbapenem-sparing agent. Our personal observation depicts the positivity of this approach in obviating the unnecessary hospitalization of ABC patients and carbapenem dependence. As the development of new antibiotics declines, effective use of ‘old’ antibiotics and dynamic following of changes in antibiotic resistance have gained more importance. Prevention against ABC and the use of products from medicinal plants like cranberry will also ease the management of CA-ABC. In their study of 153 female patients, Avorn et al. reported that daily consumption of 300 mL of cranberry juice decreased bacteriuria and pyuria frequency by 42% (7). It was suggested to prevent the adherence of *E. coli* fimbrial subunits to the uroepithelium by competitive inhibition or blocking of fimbrial subunit functions (8).

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