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CEFIXIME AND OFLOXACIN IN THE ERA OF ANTIBIOTIC RESISTANCE REVIEW OF ITS USE IN UTI

Microbiology

KEYWORDS:

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Clinical context

Urinary tract infection (UTI) is a common bacterial infection that frequently contributes to morbidity in the hospitalized and out-patients.1 Worldwide, around 150 million people are estimated to suffer from asymptomatic and symptomatic UTIs each year. UTIs due to multidrug resistant (MDR) uropathogens have increased concern globally since the last 2 to 3 decades.[2] Microorganisms have developed resistance to the newer and more potent antimicrobial agents thereby limiting the therapeutic options.1 Escherichia coli has been reported to be a common uropathogen, accounting for 75 to 90% of the UTI isolates.[1,3] The resistant E. coli has shown to impair the antimicrobial therapy of the commonly-used antimicrobial agents. E. coli is also reported to be MDR due to presence of antibiotic resistant genes in its transferable R-plasmid. Therefore, the situation of prevailing MDR uropathogens is crucial for deciding the proper use of antimicrobial drugs in order to fight against MDR UTIs.[1]

Some authors recommend cefixime as a first line antibiotic in community-acquired URTI.[4] It is a potent broad-spectrum antibiotic with excellent efficacy in community acquired infections resistant to macrolides.[5] Ofloxacin has been recommended as the drug of choice for the empirical treatment of UTI.[3] It belongs to a new generation of fluorinated quinolones and is active against most gram-negative and many gram-positive bacteria.[6] Ofloxacin has shown to be effective against acute and chronic UTIs, is well tolerated and has a unique feature of being exempted from plasmid-borne bacterial resistance.[6]

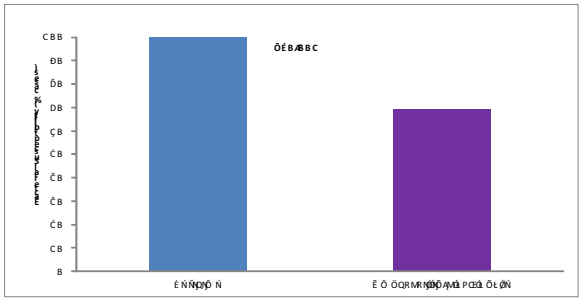
[7]**Efficacy and safety of cefixime in UTIs**

Cefixime was found to have greatest activity against E. coli, which was the most frequently isolated bacteria causing uncomplicated acute UTIs.8 In a study by Chaudhary et al, around 61 of the 65 patients (93.85%) with UTI recovered after cefixime therapy, administered twice a day for 7-10 days. Cefixime was well-tolerated with minor side-effects such as nausea, gastritis and drowsiness.[5] Another study has also demonstrated the efficacy of cefixime prophylaxis for UTIs associated with urinary tract anomalies.[9]

Cefixime vs amoxycillin + clavulanic acid

Francois et al evaluated the comparative efficacy and safety of cefixime with amoxycillin + clavulanic acid in urinary tract infections. Bacterial susceptibility was found to be greater with cefixime (100% of cases) than with amoxycillin-clavulanate (69%) ($p<0.0001$; Figure 1).[10]

Figure 1 Bacterial susceptibility to cefixime and amoxicillin-clavulanate



Cefixime is effective against resistant strains of uropathogens.

- A study was conducted to investigate the activity of cefixime against pathogens of UTIs resistant to ciprofloxacin or producing extended-spectrum -lactamases (ESBL). Cefixime was found to inhibit around 85.7% of non-ESBL-producing E. coli isolates, whereas ciprofloxacin inhibited 80.2% of these isolates. It inhibited around 80-90% of ciprofloxacin-resistant isolates and was active against less than 20% of ESBL-producing isolates.[11]

- In a study by Smith et al, >99% of E. coli isolates were susceptible to cefixime including those resistant to ampicillin.[12]

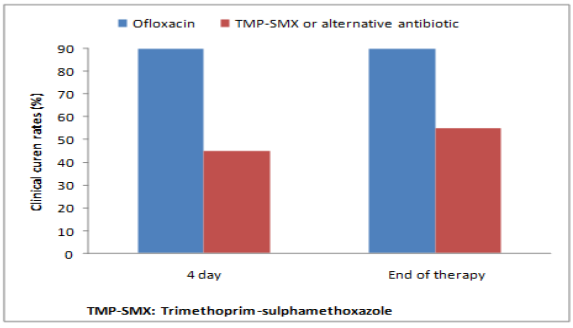
Efficacy of ofloxacin in UTIs

In a study conducted by Raz et al, ofloxacin was found to cure around 94% of women after 3 days of therapy. Around 86% of women were found to be free of symptoms and urinary cultures were found to be negative in around 80% of women after follow up at 28th day. Therefore, ofloxacin is effective in treating uncomplicated UTI in young women.[13]

Ofloxacin vs TMP-SMX and other antibiotics

Reida et al in a randomized study compared ofloxacin with trimethoprim-sulphamethoxazole (TMP-SMX) or an alternative antibiotic in patients with UTIs. The clinical cure rate (asymptomatic patient with sterile urine) at 4-day was found to be 90% with ofloxacin, which was significantly greater than 48% for the comparison group ($p=0.003$) and the rate at end of therapy (7-day) was 90% with ofloxacin, against 57% ($p=0.015$) as shown in Figure 2. Bladder cell biofilm eradication was significantly greater with ofloxacin therapy than the other antibiotic group on day 4 (62 vs 24%; $p=0.005$) and day 7 (67 vs 35%; $p=0.014$). Therefore, ofloxacin was better than TMP-SMX or alternative antibiotics in relieving infection and eradicating bladder cell biofilm of patients with UTI.[14]

Figure 2 The clinical cure rates in patients with urinary tract infections on ofloxacin and alternative antibotics[14]



Ofloxacin is effective against resistant strains of uropathogens

Cefixime and ofloxacin were found to be effective against E. coli strains resistant to ampicillin from positive urine cultures.15

Summary

Cefixime is recommended as a first-line antibiotic in community-acquired URTI by few authors. It has greatest activity against E. coli that frequently causes UTIs. Ofloxacin is active against most Gram-

negative and Gram-positive bacteria and is effective against acute and chronic UTIs. In the era of antibiotic resistance, studies have reported cefixime to be effective against bacteria resistant to other drugs. Ofloxacin was effective in the treatment of UTIs compared to TMP-SMX and against E. coli strains resistantto ampicillin. Therefore, cefixime and ofloxacin is considered as a rationale combination to treat UTIs.

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