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COMPARATIVE IN VITRO ACTIVITY OF CEFACLOR AND LORACARBEF AGAINST ESCHERICHIA COLI AND KLEBSIELLA STRAINS

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SUMMARY

In vitro activities of loracarbef and cefaclor were compared against 154 *Escherichia coli* and 46 *Klebsiella* clinical isolates. The susceptibilities to loracarbef and cefaclor were determined by Kirby Bauer disk diffusion method and microdilution tests. The susceptibilities of *E.coli* strains to loracarbef and cefaclor were found as 70% and 71%, respectively, by microdilution test and as 89% and 76% by disk diffusion tests. The susceptibilities of *Klebsiella* strains to loracarbef and cefaclor were found as 81% and 79%, respectively, by disk diffusion test, and as 64% for both antibiotics by microdilution tests.

ÖZET

Escherichia coli ve Klebsiella suşlarına sefaklor ve lorakarbefin in-vitro aktivitelerinin karşılaştırılması.

Lorakarbef ve sefaklorun 154 *E.coli* ve 46 *Klebsiella* suşuna in-vitro aktiviteleri karşılaştırılmıştır. Lorakarbef ve sefaklor duyarlılıkları Kirby Bauer disk difüzyon yöntemi ve mikrodilüsyon yöntemi kullanılarak belirlenmiştir. *E.coli* suşlarının lorakarbef ve sefaklor duyarlılıkları mikrodilüsyon yönteminde sırasıyla % 70 ve % 71, disk difüzyon yönteminde % 89 ve % 76 olarak, *Klebsiella* suşlarının lorakarbef ve sefaklor duyarlılıkları disk difüzyon yönteminde sırasıyla % 81 and % 79, mikrodilüsyon yönteminde her iki antibiyotik için de % 64 bulunmuştur.

INTRODUCTION

Loracarbef is an orally administered member of a new syntetic class of β-lactam antibiotics, the carbacephems, which is characterized by enhanced chemical stability. It is active against common pathogens associated with skin infections, otitis media, sinusitis, bronchopulmoner infections and urinary tract infections (12). In general, the oral cephalosporins have similar antibacterial characteristics but express some differences in their pharmacological properties (4). Loracarbef is similar to cefaclor in structure, solubility and microbiological activity, but it is significantly more stable in solution than cefaclor or any other therapeutically useful cephalosporins (9).

In this study, we have compared the in-vitro activities of loracarbef and cefaclor against 154 *E.coli* and 46 *Klebsiella* clinical isolates.

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MATERIALS AND METHODS

Bacterial isolates. All strains were isolated from clinical specimens. The strains were preserved in Mueller-Hinton Agar (MHA) (Difco), were covered with glycerol and were kept frozen at -30°C. Then these isolates were subcultured on MHA and the bacterial suspensions were prepared equivalent to the 0.5 McFarland standard.

Antibiotic susceptibility tests. Loracarbef and cefaclor were kindly provided by Lilly Research Laboratories. The susceptibility of cefaclor and loracarbef has been determined by Kirby Bauer disk diffusion method and microbroth dilution tests according to NCCLS M100-S8 guidelines (7). Zone diameters of ≤ 14 mm indicated resistance and ≥ 18 mm indicated susceptibility in disk diffusion test. For these strains ≤ 8 μg/ml minimal inhibitory concentration (MIC) values were evaluated as susceptible and ≥ 32 μg/ml as resistant in microdilution test.

RESULTS

In microbroth dilution tests for loracarbef and cefaclor the susceptibilities of *E.coli* strains were found to be 70% and 71%, respectively. The MIC_{50} of both loracarbef and cefaclor was 4 μg/ml and the MIC_{90} was 32 μg/ml for both antibiotics. The susceptibilities of *E.coli* strains by disk diffusion tests for loracarbef and cefaclor were 89% and 76%, respectively.

Loracarbef susceptibility of *Klebsiella* strains was found to be 64% by microdilution tests and 81% by disk diffusion tests. Cefaclor susceptibility of *Klebsiella* strains was found to be 64% by microdilution and 79% by disk diffusion. The MIC_{50} values of both loracarbef and cefaclor were 8 μg/ml and MIC_{90} were 32 μg/ml for *Klebsiella* strains.

DISCUSSION

Cefaclor has been noted to be more active in vitro against a variety of Gram positive and Gram negative organisms including staphylococci, streptococci, *Haemophilus influenzae, Escherichia coli, Klebsiella pneumoniae* and *Proteus mirabilis* than such cephalosporins like cephalexine and cephradine (2,8). Loracarbef has been shown to exhibity equivalent or greater in vitro potency than those antibiotics against a range of bacterial species (4).

Loracarbef, a carbacephem which has structural similarities to cefaclor, is a novel β-lactam antibiotic. The dihydrothiazine ring of the cephalosporin molecule contains a sulphur atom and substituting this with a carbon atom gives the corresponding carbacephem analogue (6).

Recently introduced parenteral cephalosporins have proved valuable in the management of life threatening infections but oral agents are often more convenient for the treatment of less severe conditions, and their clinical applications have been diverse. Cefaclor has offered advantage due to its greater potency against a range of pathogens despite a significant degree of instability in serum and buffer (2). Loracarbef is more active than cefaclor with its greater chemical stability and comparable resistance to hydrolysis by bacterial β-lactamases (4,5).

Studies by Cao et al (3) showed that MIC_{90} of loracarbef and cefaclor for *E.coli* was 16 mg/l. For *K.pneumoniae* MIC_{90} of loracarbef was 8 mg/l, and MIC_{90} of cefaclor was 32 mg/l. MIC_{90} of both loracarbef and cefaclor for *K.oxytoca* was 128 mg/l. On the other hand Shelton and Nelson (11) reported that MIC_{90} of loracarbef for *E.coli* was 2 μg/ml and

MIC_{90} of cefaclor was > 8 μg/ml. Preston and Turik (10) demonstrated that 85% of *E.coli* were susceptible to cefaclor at the NCCLS interpretive breakpoints. Another study from our country demonstrated that the susceptibility of loracarbef was 82% for *E.coli* and 37% for *Klebsiella* (1).

In our study, according to the results we obtained from *E.coli* strains, the MIC_{50} of loracarbef and cefaclor was 4 μg/ml and MIC_{90} was 32 μg/ml in both antibiotics. When we compared the results of disk diffusion susceptibility tests for loracarbef with that of cefaclor, loracarbef seems to be more effective in *E.coli* strains, but the results of microbroth dilution tests for the two anibiotics were similar. The results of susceptibility test of loracarbef and cefaclor for *Klebsiella* strains are as follows; MIC_{50} of both loracarbef and cefaclor was 8 μg/ml and MIC_{90} of both loracarbef and cefaclor was 32 μg/ml.

The widespread antibiotic use is often cited as a factor in the emergence of bacterial resistance to antibiotics and the results obtained from our study supports this fact. The higher results concerning the MIC_{50} and MIC_{90} values of both antibiotics may be related to the antibiotic misuse in our country. According to these data in order to prevent the development of resistance, the widespread antibiotic use should be restricted.

KAYNAKLAR

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