Determination of Antimicrobial Activity of Cefaclor on Common Respiratory Tract Pathogens in Pakistan

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Abstract

Objective: To determine the antimicrobial activity of Cefaclor against common respiratory tract pathogens isolated from patients in Pakistan.
Setting: Department of Microbiology, Liaquat National Postgraduate Medical Centre, Karachi.
Method: A laboratory analysis was done on 466 isolates of respiratory tract pathogens collected from 13 laboratories from all over Pakistan. Antibiotic sensitivity test was done by Kirby Bauer disc diffusion method and MIC of Cefaclor was determined by 'E' test.
Result: Of the 163 Streptococcus pneumoniae, 87 Moraxella catarrhalis and 216 Haemophilus influenzae > 95% isolates were susceptible to Cefaclor. The MIC 90 of all these pathogens were <2 ug.
Conclusion: Resistance of respiratory tract pathogens to the 2nd generation Cephalosponn, Cefaclor is very low. MIC 90 of Cefaclor against all three common respiratory tract pathogens is < 2 ug , which indicates that Cefaclor would be effective in more than 90% of cases infected with these bacteria (JPMA 52:7,2002).

Introduction

Respiratory tract infection is one of the most common diseases prevalent in the community with high mortality rates specially in developing countries1. Knowledge of the susceptibility pattern of bacteria most often involved in such infections is very important because in majority of cases sputum culture and susceptibility testing is not requested and empirical treatment is given. The susceptibility pattern of common bacterial isolates serves as a guideline for the choice of appropriate antibiotics.
The three frequently encountered respiratory pathogens include Streptococcus pneumoniae, H aemophilus influenzae and Moraxella catarrhalis2. The sensitivities of these isolates have recently been changing and relative resistance has been on the rise hence surveillance of resistance in local population has become very important.
Cefaclor, an oral semi-synthetic 2nd generation cephalosporin is effective against various respiratory pathogens. Efficacy and safety of Cefaclor in respiratory infection amongst
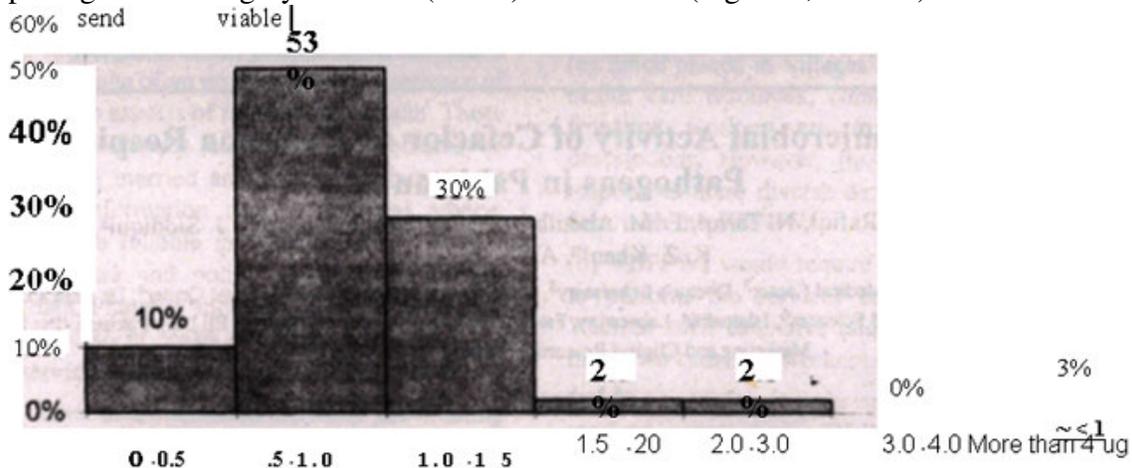
Pakistani children has been documented. In this study Cefaclor was found to be a safe and efficacious drug in the treatment of bacterial respiratory tract infections among Pakistani children3. The present communication is based on the determination of the MIC of Cefaclor against H. influenzae, S. pneumoniae and M catarrhalis isolated from clinical samples collected from all over Pakistan, to know the MIC of Cefaclor for the common respiratory pathogens and establish its suitability for treating respiratory infections in Pakistan.

Material and Methods

A total of 13 Laboratories from all over Pakistan participated in the study. These laboratories were asked to isolates of S. pneumoniae, H. influenzae and M catarrhalis from patients presenting at out-patient clinics during 1999 - 2000. The isolates were received in the central lab and were confirmed using standard ASM technique4. 'E' test (AB Biodisk, Solna, Sweden) strips of Cefaclor were used according to the manufacturer's instructions to determine the MIC of common respiratory tract pathogens. The sensitivity of the organisms were categorized into susceptible, intermediate and resistant based on the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS)5. MIC of Cefaclor _1 ug/mi was taken as sensitive, 2 ug/mi as intermediate and _4 ug/mI as resistant. Disc sensitivity test was carried out by Kirby-Bauer disc diffusion method6. The following organisms were included as control strains: S. pneumoniae ATCC 49619, H. influenzae ATCC 49247, M catarrhalis ATCC 12429.

Results

A total of 466 viable isolates were received; among these 216 were H.influenzae, 163 were S. pneumoniae and 87 were M cat arrhal is.The isolates were mainly from sputum and remaining were from CSF and blood. Disc sensitivity method showed that all three pathogens were highly sensitive (>95%) to Cefaclor. (Figure 1, Table 1).

Cefaclor in

Sensitivity pattern	H. influenzae No.	%	S. pneumoniae No.	%	M. catarrhalis No.	%
Resistant	6	3	4	3	1	1
Intermediate	4	2	2	1	1	1
Sensitive	206	95	157	96	85	98
Total	216	100	163	100	87	100

Table I. Sensitivity profile of three common respiratory tract pathogens against Cefaclor (disc diffusion method). Figure 1. MIC for H. influenzae with Cefaclor.

The results matched the MIC determined by E-test.

94% of H. influenzae and S. pneumoniae had MIC of 2ug/ml while 98% M catarrhalis had MIC of 2ug/ml (Table 2, Figures 1,2,3). The MIC 90 of all three pathogens to Cefaclor were <2ug. (Table 3).

Table 3. MIC 50 and 90 of Cefaclor to common respiratory tract pathogens.

Orgnaism	Total	MIC 50	MIC 90
S. Pneumoniae	163	0.5	1.0
H. influenzae	216	1.0	1.5
M. catarrhalis	•87	1.5	2.0
Total	446	1.0	2.0

Discussion

Constant surveillance studies are essential for containment of antimicrobial resistance profiles. Such programmes help generate information on resistance at local, national and international levels to guide the prescribing physicians. Local information should be used in clinical management and to update treatment guidelines, educate prescribers and to guide infection control policies. In developing countries reliable laboratory data of resistance profile is inadequate and MIC are not usually carried out particularly for H influenzae and S. pneumoniae for which MIC are needed to determine the actual degree of resistance. The results of this in vitro study confirm and extend the scope of the previous surveillance programmes undertaken globally and in Pakistan. Accordingly we have shown more than 94% H. influenzae, S. pneumoniae and 98% Mcatarrhalis sensitive to Cefaclor.

In a previous study performed in Pakistan among children with acute respiratory tract infection showed 100% sensitivity to CefaFlor as ompared@to 31% Desistant to Cotrimoxazole and 39% resistance to Chloramphenicol[7]. Similarly in 1993 the global surveillance study of Cefaclor showed > 90% susceptibility of common respiratory bacterial pathogens to this antibiotic[8]. The efficacy and safety of Cefaclor in respiratory infection among Pakistani children has also been determined [3] showing 93% in vitro sensitivity and 97% in vivo response to the use of Cefaclor for respiratory tract infections[3]. Over 138 in vitro studies have been performed and evaluated across USA since 1989. Ninety seven percent of all H influenzae (Beta-lactamase positive and negative) strains tested (over 14000 isolates) were susceptible to Cefaclor. Only 3% of all

isolates tested were intermediate or resistant to Cefaclor9. In anOther study, the susceptibility of 1688 isolates of H. influenzae were evaluated out of which 97% were susceptible to Cefaclor 10.

In a study done in United States, in vitro activity of 26 antimicrobials against the isolates of H. influenzae, M catarrhalis and S. pneumoniae isolates was evaluated. Cefaclor was found active against the penicillin-susceptible S. pneumoniae isolates. The MIC5O and MIC9O were 0.5 and lug/ml respectively. Cefaclor was not active against penicillin-resistant S. pneumoniae11. A local surveillance study shows that in Pakistan still we do not have high-level penicillin-resistant S. pneumoniae12.

M catarrhalis, previously considered a harmless upper-respiratory tract pathogen in humans, is now recognized as the etiological agent of significant number of diseases. These include a variety of infections, like conjunctivitis, otitis media, sinusitis, endocarditis, meningitis, septicemia and pneumoniae, particularly in patients with underlying compromised pulmonary function13,14. In the 1970's Beta-lactamase producing strains of M catarrhalis were beginning to be identified15. Now more than 90% of all M. catarrhalis isolates produce B-lactamase and are resistant to ampicillint6. However, most isolates still remain susceptible to second generation cephalosporins such as Cefaclor, to macrolides and to miscellaneous antibiotics such as chloramphenicol, tetracycline and trimethoprim/sulfamethaxazole17.

Numerous studies have confirmed the in vitro activity of Cefaclor against M catarrhalis. In one of a large multi-centre multinational collaborative studies, entitled Alexander Project, involving 15 centers throughout the world evaluated the susceptibility of 6,385 community-acquired lower respiratory tract pathogens to 15 antimicrobial agents. Out of 818 isolates of M catarrhalis 82% were 13-lactamase producers and more than 90% isolates were susceptible to Cefaclor18.

One important point to mention is the variation in sensitivity reporting of Cefaclor or any other antibiotic, which are subject to chemical instability. A chemically unstable antibiotic can result in significant variation in test results. The inoculum size, composition and quality of test media, pH of the solvents and diluents, delays in procedure and duration and temperature of incubation may also contribute to variability of susceptibility tests with any antibiotics including Cefaclor19. In addition variation between laboratories and individuals in reading zone sizes can also influence the reported susceptibilities. The MIC 90 of all common respiratory pathogens in this study is <2ug which indicates that even in empiric therapy cefaclor would be effective in more than 90% of cases. The present study adds valuable information on the activity of Cefaclor (MICs not tested before) against respiratory tract pathogens isolated in Pakistan. The results of this study clearly indicate that Cefaclor is still very effective against common respiratory tract pathogens. Such data will help the clinicians to select the most appropriate antibiotic against these pathogens and will contribute in lowering the resistance rate to different antibiotics as misuse of antibiotics usually give rise to resistant pathogens.

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