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EVALUATION OF CEFTAZIDIME ANTIMICROBIAL ACTIVITY IN INFECTIONS CAUSED BY BURNS

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ABSTRACT

In vitro evaluation of ceftazidime antimicrobial activity in infections caused by burn and its comparison to the other antibiotics is presented.

In vitro tests for susceptibility to ceftazidime and other antibiotics were carried out on 744 bacterial strains collected from burn infections. The results have shown that generally ceftazidime was more active against *Pseudomonas aeruginosa* and other gram-negative bacilli like *Klebsiella pneumoniae*, *Escherichia coli*, and Proteus than amikacin, gentamicin, tobramycin, carbenicillin, kanamycin, and streptomycin in terms of potency and activity. In addition, and according to our *in vitro* studies we suggest that ceftazidime could be considered a valuable alternative to other antibiotics in the treatment of burn infections caused by *P. aeruginosa* and other gram-negative bacilli.

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INTRODUCTION

The appearance and existance of resistant bacterial strains in infections caused by burns has produced many difficulties. However, by observing the bacterial resistance in many of the antibiotics, we studied *in vitro* activity of ceftazidime, a new drug from the third generation of cephalosporins, and compared it to the other antibiotics.

Ceftazidime possesses a broad spectrum of antibacterial activity against both gram-positive and gram-negative beta-lactamase producers.[10,14,19]

Ceftazidime has high resistance to betalactamase, but there are reports about its sensitivity against *Pseudomonas aeruginosa*.[4,7,13,16] In this study 744 serotyes of different microorganisms such as *P. aeruginosa*, *S. aureus*, *K. pneumoniae*, *P. mirabilis*, *E. coli*, etc. were evaluated for antibiotic susceptibility by the disk susceptibility test, minimum inhibitory concentration antibiotic susceptibility test (MIC), and the result of sensitivity and resistance to the antibiotics have been considered.

MATERIAL AND METHOD

Specimens were sent to the microbiology dept. from the burn section at Ghaem Hospital for isolation, identification and bacterial susceptibility test. 744 microorganisms isolated were *P. aeruginosa*, *S. aureus*, *K. pneumoniae*, *P. mirabilis*, *E. coli*, and 48 serotypes from other bacteria.

Cultures

(A) Mueller-Hinton media for antibiotic susceptibility by agar-gel diffusion.

(B) Trypticase soy broth for antibiotic susceptibility by MIC method.

Antibiotics

In this study we used 30 mg ceftazidime disks for antibiotic susceptibility by gel diffusion and ceftazidime powder for MIC method.

Method

(1) Antibiotic susceptibility test by gel diffusion

Table I. Assay protocol for tube dilution method

no	liquid medium	antibacterial solution	liquid medium with bacteria	concentration of antibiotic (mg/ml)
1	—	4 ml	2 ml	64
2	2 ml	2 ml (from tube no. 1	2 ml	32
3	2 ml	2 ml (from tube no 2)	2 ml	16
4	2 ml	2 ml (from tube no. 3)	2 ml	8
5	2 ml	2 ml (from tube no. 4)	2 ml	4
6	2 ml	2 ml (from tube no. 5)	2 ml	2
7	2 ml	2 ml (from tube no. 6)	2 ml	1
8	2 ml	2 ml (from tube no. 7)	2 ml	0.5
9	2 ml	2 ml (from tube no. 8)	2 ml	0.25
10	2 ml	——	2 ml	positive control
11	4 ml	——	—	negative control

(Kerby-Bauer method)

(2) Tube dilution method: in tube dilution method we used 11 sterile tubes. 2 cc of culture medium (liquid form) were added into tubes 2 to 10. 4 cc of antibiotic solution (128 mg/ml) was added to tube 11. Serial dilution was made by addition of 2 cc from tube 1 to tube 2, transfer of 2 cc from tube 2 to tube 3, discarding the last 2 cc from tube 9, and addition of 2 cc culture medium which had bacteria ($10\text{-}10^7$/ml) to tubes number 1 to 10.

All tubes were incubated for 16-20 hrs at 35-37°C.

The results were evaluated microscopically for turbidity and cylinder motion. The tube without turbidity and least concentration would be the MIC for ceftazidime.

Positive control tube must be turbid (tube no. 10), and tube no. 11 (negative control) must be without turbidity.

RESULTS

Study on 744 isolated microorganisms from burn infections showed 222 *P. aeruginosa* and 213 *S. aureus*. Other microorganisms isolated included *K. pneumoniae*, *P. mirabilis* and *E. coli*, with frequency of 174, 51, and 36, respectively. 48 other microorganisms were also isolated.

Table II shows the results of identification of 744 strains of microorganisms isolated from burn infections in Ghaem hospital of Mashhad University from July 1987 to June 1989. Pseudomonas was the genus most frequently isolated and most common species was *Pseudomonas aeruginosa* and other microorganisms isolated from burn infections were *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *E. coli* and 48 serotypes of other microorganisms.

Table II. Identification of 744 strains of microorganisms isolated form burn infections

Microorganism	No. of strains	Percentage
Pseudomonas aeruginosa	222	29.8%
Staphylococcus aureus	213	28.6%
Klebsiella pneumoniae	174	23.4%
Proteus mirabilis	51	6.8%
E. coli	36	4.8%
other microorganisms	48	6.8%

Table III. Activity of ceftazidime compared with other antibiotics against 222 strains of *P. aeruginosa*

Antibiotic	No. of strains	Percentage S	Percentage R
ceftazidime	222	100	0
amikacin	222	76	24
tobramycin	222	23	67
gentamicin	222	18	82
carbenicilin	222	15	85
trimethoprim	222	9.5	90.5
sulfamethoxazole	222		

Table IV. Activity of ceftazidime compared with other antibiotics against 213 strains of *Staphylococcus aureus*

Antibiotic	No. of strains	Percentage S	Percentage R
ceftazidime	213	34	66
chloramphenicol	213	61	36
lincomycin	213	48	52
gentamicin	213	46	54
cephalothin	213	34	66
cloxacillin	213	31	69
trimethoprim	213	30	70
sulfamethoxazole	213		

DISCUSSION

Amikacin, tobramycin and gentamicin have been known as effective antibiotics against *P. aeruginosa* with a sensitivity of 95 to 100%, 51% and 48%

In our study it was 100% for ceftazidime, 76% for amikacin, 23% for tobramycin, 18% for gentamicin and 15% for carbenicillin (Table III).

Ohkoshi and co-workers proved that the anti-pseudomonas activity of ceftazidime is 16 to 32 times more than the anti-pseudomonas activity of cefotaxime and moxalactam, and 4-5 times more than ceftriaxone. The antibacterial activity of ceftazidime is more than carbenicillin, azlocillin and piperacillin. On the other hand, ceftazidime shows anti-pseudomonas activity to those which are resistant to penicillin and

Table V. Activity of ceftazidime compared with other antibiotics against 174 strains of *Klebsiella pneumoniae*

Antibiotic	No. of strains	Percentage S	Percentage R
ceftazidime	174	96	4
amikacin	174	74	26
trimethoprim sulfamethoxazole	174	43	57
cephalothin	174	33	67
gentamicin	174	19	81
tobramycin	174	15	85
kanamycin	174	12	88

Table VI. Activity of ceftazidime compared with other antibiotics against 51 strains of *Proteus mirabilis*

Antibiotic	No. of strains	Percentage S	Percentage R
ceftazidime	51	100	0
gentamicin	51	58	42
amikacin	51	29	71
tobramycin	51	23	77
trimethoprim sulfamethoxazole	51	20	80
cephalothin	51	12	88

Table VII. Activity of ceftazidime compared with other antibiotics against 36 strains of *E. coli*

Antibiotic	No. of strains	Percentage S	Percentage R
ceftazidime	36	100	0
amikacin	36	100	0
kanamycin	36	67	33
gentamicin	36	50	50
tobramycin	36	50	50
cephalothin	36	42	58

aminoglycosides. In the study of 202 serotypes of *P. aeruginosa*,ceftazidimewith concentration was effective in 100 percent of cases, and gentamicin was only effective for 70% of the cases.[10,15,17]

Arnonff et al, Bayer et al, and Chattopadhyay et al reported some cases of *P. aeruginosa* which are resistant to ceftazidime, but in our study all serotypes were sensitive to ceftazidime.[1,2,6]

According to a study by Tehran Medical School, gentamicin, cephalothin, trimethoprim- sulfamethoxazole and lincomycin were the most active antibiotics against strains of *S. aureus* with activity of 98%, 97% 94%, and 88%, respectively.[22] A study conducted by Imam Reza Hospital shows that all strains are sensitive to amikacin and have activity of 66.4% to gentamicin.[21]

Our study shows increased resistance of the staphylococcus serotypes. Chloramphenicol, lincomycin, gentamicin, cephalothin, and cloxacillin had activity of 61%, 48%, 46%, 34%, and 31% against serotypes of *S. aureus,* respectively. In this study ceftazidime showed

Table VIII. Antibacterial activity of ceftazidime against different microorganisms isolated from burn infections by MIC method

Microorganism	Results of Ghaem Microbiology Dept		Results of Glaxo Microbiology Dept	
	Mic 90 mcg/ml	Mic 50 mcg/ml	Mic 90 mcg/ml	Mic 50 mcg/ml
P. aeruginosa	8	3	4	1
S. aureus	32	16	8	8
K. pneumoniae	8	2	1	0.5
E. coli	4	0.5	0.25	0.13
P. mirabilis	2	1	0.06	0.06

only 34% activity against serotypes of *S. aureus* isolated from burn infections (Table IV).

In general, ceftazidime has a high stability against staphylococcus penicillinase. Researchers of Glaxo Lab. showed that 90.1% of the Staphylococcus infections have been treated by ceftazidime.

On the other hand only 81% of staphylococcus infections could be treated by other antibiotics.[10] Glaxo Microbiology Lab showed that amikacin, tobramycin and gentamicin have sensitivity for 90-100% of *Klebsiella pneumoniae* serotypes.[9] Our study shows the activity of amikacin, trimethoprim-sulfamethoxazole, cephalothin, gentamicin and tobramycin against serotypes of *K. pneumoniae* in 74, 43, 33, 19, and 15% of cases, respectively. In this study ceftazidime was effective in 96% of cases (Table V).

Glaxo Microbiology Lab showed sensitivity of amikacin, tobramycin and gentamicin to proteus in 96 to 100% of the cases.[22] The study performed by Imam Reza Hospital of Mashhad shows activity of amikacin in 95.6% and gentamicin in 56.6% of the cases.[21] In our study, gentamicin, amikacin, and tobramycin had activity against Proteus in 58, 29, and 23% of cases respectively. The most effective antibiotic was ceftazidime which had activity in 100% of the cases (Table VI).

Glaxo Lab proved sensitivity to amikacin, gentamicin, and tobramycin in 96 to 100% of *E. coli* serotypes. The study of Imam Reza Hospital showed activity of amikacin in 90%, gentamicin in 58%, and kanamycin in 33.8% of cases.[21] Our study shows the sensitivity of ceftazidime and amikacin in 100% of cases. Kanamycin, gentamicin and tobramycin were effective in 67, 50, and 50%, respectively. Reports by Watanabe showed sensitivity of 98% on gram-negative organisms which correlated with the study on organisms such as *P. aeruginosa, Klebsiella, E. coli* and Proteus.[20] Chattopadhyay indicated the same results as ours about activity of ceftazidime on *P. aeruginosa*.[6]

Resistance of microorganisms against ceftazidime depends on the production of enzyme by the organism. Hiraboka et al found two kinds of cephalosporinases in *E. coli* and *P. vulgaris*.[11]

Epidemiological studies indicate that the important microorganisms causing infection in burn patients are *P. aeruginosa*, Enterobacter, and *S. aureus*. Our results indicate that ceftazidime has good activity against gram-negative microorganisms in comparison to other antibiotics such as gentamicin, amikacin, tobramycin, carbenicillin, etc. From our study and studies undertaken by others we can conclude that ceftazidime is the best choice for treatment of burn infections.

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