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MEZLOCILLIN THERAPY IN CHILDREN*

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Although there have been developments in the field of antibiotic therapy during the past few years, the treatment of infectious diseases caused by gram-negative bacteria and staphylococci still continues to be a serious problem due to resistance to antibiotics. The spectrum of carbenicillin includes both gram-negative microorganisms (Pseudomonas aeruginosa, Enterobacter cloacae and indole positive Proteus species) and bacteria sensitive to penicillin. Ticarcillin, in addition to the same properties, is two to four times more effective than carbenicillin when Pseudomonas species are concerned. Unfortunately, neither carbenicillin nor ticarcillin is sufficiently effective against Klebsiella and Serratia groups or E. coli with TEM-type beta-lactamases. Mòreover, carbenicillin and ticarcillin are liable to produce various side effects as fairly heavy doses are essential for them to be effective against pseudomonas[1,2]. Therefore, new antibiotics from the penicillin group, known as ureidopenicillins have been developed. Of these, mezlocillin and azlocillin have been used clinically[2,7].

Mezlocillin has an acyl-ureido side chain in its structure and is a semi-synthetic penicillin derivative which encompasses a wide and unique antibacterial spectrum. Until now, in vivo and in vitro studies have shown that mezlocillin is more effective than ampicillin, carbenicillin and cephalotin in the treatment of E. coli, indole positive Proteus species, Klebsiella, pseudomonas and anaerobic infections. It is also effective against all microorganisms sensitive to penicillin. Studies have shown that mezlocillin is more effective when used in combination with aminoglycosides[2-7].

There has been so much misuse of antibiotics in Turkey that frequently great difficulties are encountered when trying to combat effectively gram-negative bacteria

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and/or staphylococcal infections. It was against this background that the present study was undertaken and on the realization that there were no data available, in the medical literature in English, on the use of mezlocillin in the pediatric age group.

Material and Methods

Mezlocillin was used on 18 patients (14 boys and 4 girls). Their ages ranged from 44 days to 13 years with a mean of 5.5 years (Table I). Diagnoses of the patients are given in Table II. In no patient had there been any response to antibiotic treatment of various combinations during a mean period of fourteen days (Table III).

According to the severity of the infection, mezlocillin in amounts of 100-250 mg/kg/day, was given intravenously in three daily doses and was in some cases combined with aminoglycosides. After the symptoms and the clinical and laboratory findings of the infections were under control, mezlocillin was administered intramuscularly. Response to the therapy was determined by clinical and laboratory findings and the absence of bacterial growth in the cultures. Complete blood counts and urinalysis were carried out; SGOT, SGPT, BUN and creatinine levels were checked before and seven to ten days after treatment, in order to determine any side effects.

Results

The most important problem in our patients was high fever along with other persistent findings indicating infection related to their primary disease, which could not be overcome with various antibiotic combinations. Mezlocillin was effective in all of them. It corrected abnormal clinical findings and fever was brought under control (Table IV).

There was bacterial growth in the pus, blood, urine and cerebrospinal fluid cultures of 12 patients. Of these six were Staphylococcus aureus, four were Pseudomonas aeruginosa and two were Enterobacter aerogenes. Antibiograms were performed in nine and all of them were found to be sensitive to mezlocillin (Table V).

During the course of treatment, hemoglobin values, white blood cell counts, urinalysis, SGOT, SGPT, BUN and serum creatinine levels reflected only those changes brought about by the patients' primary diseases (Table I).

Discussion

The most important point which should be kept in mind in determining the effectiveness of mezlocillin is that all patients included in this study were severely infected and no clinical or laboratory response could be obtained through treatment with

TABLE I

Clinical and Laboratory Findings of the Patients on whom Meziocillin was Used

Case no.	Age (years), sex	Diagnosis*	Antibiotics used previously** (duration in days)	Culture	Sensitivity to meziocillin	Meziocillin dose (g/day)	Laboratory findings*** SGOT (U)	SGPT (U)	BUN (mg/dl)	Creatinine (mg/dl)
1	3 M	TOF	pen, genta (12)	S. aureus (pus)	?	3 × 0.75	–	–	13/13	0.5/0.5
2	9/12 F	TA	pen, genta, carb (22)	Ps. aeruginosa (pus)	+	3 × 1	–/30	–/45	–/12	–/0.5
3	2 M	purulent meningitis	pen, chlora, amp (19)	– (CSF)	–		–/20	–/19	10/10	0.5/0.5
4	13 M	osteomyelitis	met, genta, ceph (20)	S. aureus (pus)	+	3 × 3	11/22	11/22	12/14	0.3/0.6
5	4 M	TOF	pen, genta (20)	– (pus)	–	3 × 1.5	–	–	–	–
6	1 M	urinary infection (nephrotic syndrome)	pen, genta, carb, netil (15)	Ps. aeruginosa (urine)	+	3 × 1	94/67	140/30	–	–
7	13 M	urinary infection (rupture of bladder)	ceph, genta (11)	Ps. aeruginosa (urine)	+	3 × 2	–	–	–	–
8	7 M	urinary infection	pen, genta (16)	Ps. aeruginosa (urine)	+	3 × 2	–	–	45/20	1.2/1.2
9	6 F	multiple abscesses, ALL	met, genta (10)	S. aureus (pus)	?	3 × 1.5	7/22	8/19	–/10	–/0.3
10	2/12 M	gastroenteritis, septicemia	pen, genta (5)	(died on the third day of treatment)	?	3 × 0.2	–	–	–	–
11	6 M	brain abscess	pen, chlora, ceph, tetra, sm, met, genta (16)	– (pus)	–	3 × 1	–/22	–/19	–/11	–
12	5/12 M	pyoderma gangrenosum	pen, genta, ceph (7)	– (pus)	–	3 × 0.3	–	–	–	–
13	8 M	empyema	pen, genta, met (16)	S. aureus (pus)	?	3 × 2	10/10	12/12	10/10	0.8/0.3
14	10 M	osteomyelitis, septic arthritis	pen, genta, met, ceph (12)	S. aureus (pus)	?	3 × 2	–	–	–	–
15	13 F	purulent meningitis	pen, genta (10)	– (CSF)	–	3 × 3	–/22	–/11	10/17	0.8/0.8
16	11 F	abscess, ALL	met, trimetho (14)	S. aureus (pus)	?	3 × 3	–	–	16/10	–
17	44/365 M	septicemia	pen, genta (8)	Enterobacter aerogenes (blood)	+	3 × 0.3	–	–	–/10	–/0.5
18	18/12 M	purulent meningitis	pen, chlora, genta, ceph (26)	Enterobacter aerogenes (CSF)	+	3 × 0.5	15/22	10/19	10/11	0.5/0.5

* TOF: tetralogy of Fallot, TA: tricuspid stress, ALL: acute lymphoblastic leukemia.

** pen: penicillin, genta: gentamicin, met: methicillin, chlora: chloramphenicol, carb: carbenicillin, ceph: cephalotin, netil: netilmicin, tetra: tetracycline, sm: streptomycin, trimetho: trimethoprim and sulfamethoxazole, amp: ampicillin

*** before/after the treatment

TABLE II

Clinical Diagnoses of the Cases

Diagnosis	Number of cases
Cyanotic congenital heart disease (postoperative)	3
Purulent meningitis	3
Brain abscess	1
Osteomyelitis, septic arthritis	2
Empyema	1
Urinary tract infection	3
Pyoderma, abscess	3
Septicemia	2
TOTAL	**18**

TABLE III

Duration of Antibiotic Therapy Before Mezlocilin Therapy

Duration (days)	Number of cases
5-10	5
11-15	5
16-20	6
21-25	1
26-30	1
TOTAL	**18**

various antibiotic combinations. Almost all of them were complicated cases and the involved areas were relatively difficult for antibiotic penetration such as an abscess pouch, joint cavities, bone tissue, brain and meninges. Infections of the urinary system caused by Pseudomonas, Enterobacter and Staphylococcus species were resistant to almost all antibiotics produced in Turkey. When all these facts are considered, the destruction of these resistant pathogens would seem to present many dif-

ficulties. However, mezlocillin corrected the clinical and laboratory findings related to the various infectious diseases.

TABLE IV

Persistent Clinical Findings Before Mezlocillin Therapy and Response to Mezlocillin

Clinical findings	Number of cases	Time needed for response (days)
Fever	15	7 (approx.)
Diarrhea	1	9
Cough, respiratory distress	1	9
Neck rigidity	1	3
Abscess	1	10
Vomiting	1	9

TABLE V

Results of the Cultures Taken from the Patients

Culture	Number of patients studied	Number of cultures that revealed growth	Microorganism	Sensitivity to mezlocillin
Pus	10	6	S. aureus	3/6
		1	Ps. aeruginosa	1/1
Blood	1	1	Enterobacter aerogenes	1/1
Urine	3	3	Ps. aeruginosa	3/3
CSF	3	1	Enterobacter aerogenes	1/1
TOTAL	**17**	**12**		**9/12**

Although the side chains in the alpha position are different[3], many properties of mezlocillin resemble those of carbenicillin; for instance many pharmacokinetic effects such as pK values, protein-binding properties, and solubility in lipids, are similar to those of carbenicillin. The most important advantage of mezlocillin over

carbenicillin is that it is more effective with a lower dose and has a wider antibacterial spectrum[2-7]. Since mezlocillin is effective in lower doses, side effects such as coagulation disorders and electrolyte imbalance are very rare[1-7].

We do not know whether the microorganisms that grew in the cultures of our patients had penicillinase activity (beta-lactamase) or not[8]. In earlier studies[2,4], mezlocillin had been reported to be ineffective against microorganisms with penicillinase activity, but antibiograms in our patients' cultures showed them to be sensitive to mezlocillin.

Therefore, it is concluded that mezlocillin can safely be used alone or in conjunction with an aminoglycoside such as gentamicin or netilmicin in children, especially in the case of staphylococcal, pseudomonas and enterobacterial infections.

Summary

This is, as far as we know, the first detailed study in the English medical literature concerning the pediatric use of mezlocillin. In the study mezlocillin was used in 18 patients between the ages of 44 days and 13 years with severe and complicated infections who had previously not responded to various antibiotic combinations. Mezlocillin therapy was effective in all of them, and there were no serious side effects.

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