

## COMPARISON OF THE EFFECTIVENESS OF MEZLOCILLIN AND AMPICILLIN/PENICILLIN THERAPIES IN CHILDHOOD LOWER RESPIRATORY TRACT INFECTIONS\*

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### SUMMARY

Mezlocillin is a semisynthetic penicillin with a broad antibacterial spectrum of activity. The efficiency of mezlocillin therapy has been investigated by various studies in respiratory tract infections. Ampicillin and tobramycin or penicillin and chloramphenicol combinations are being used for the treatment of lower respiratory tract infections in our pediatrics clinic. This study has been performed in order to test the effectiveness of mezlocillin in comparison with ampicillin and penicillin in children with bronchopneumonia. Seventy-three patients who were hospitalized in the Ankara State Hospital have been enrolled in the study. Thirty of the patients received mezlocillin (200 mg/kg/day-intravenous), 22 received ampicillin and tobramycin, and 21 received penicillin and chloramphenicol combinations. For each group, the patients have been chosen randomly. Clinical trial cure rates were 80 % for mezlocillin, 82 % for ampicillin and tobramycin combination, and 86 % for penicillin and chloramphenicol combination. There were no significant differences in relation to clinical cure rate, the hospitalization period and to the side-effects. Our preliminary data suggest that mezlocillin, ampicillin and tobramycin, or penicillin and chloramphenicol therapies have similar efficacy in the treatment of lower respiratory tract infections.

### ÖZET

*Alt solunum yolu infeksiyonlarının tedavisinde mezlosilinin etkinliğinin ampisilin ve penisilin ile karşılaştırılması.*

Mezlosilin geniş antibakteriyel spektruma sahip semisentetik bir penisilindir. Çeşitli çalışmalarda solunum sistemi infeksiyonlarında mezlosilinin etkinliği araştırılmıştır. Kliniğimizde alt solunum yolu infeksiyonlarının tedavisinde genellikle ampisilin ve tobramisine veya penisilin ve kloramfenikol kombinasyonları uygulanmaktadır. Bu çalışma çocukluk yaş grubunda, alt solunum yolu infeksiyonlarının tedavisinde başarı ile kullanılabilceği yolunda çalışmalar bulunan mezlosilinin etkinliğini ampisilin ve penisilin tedavileri ile karşılaştırmak amacıyla yapılmıştır. S.B. Ankara Hastanesi Çocuk kliniğinde bronkopnömoni tanısı ile tedaviye alınan 73 hasta çalışmaya alınmıştır. Çalışmaya alınan 30 hastaya mezlosilin, 22 hastaya ampisilin ve tobramisine, 21 hastaya ise penisilin ve kloramfenikol tedavileri uygulanmıştır. Klinik başarı oranı mezlosilin için % 80, ampisilin ve tobramisine için % 82, penisilin ve kloramfenikol için ise % 86 bulunmuştur. Gruplar arasında istatistiksel açıdan anlamlı bir fark saptanmamıştır. Çalışmamızda infeksiyonun şiddetindeki ağırlığın tüm tedavi gruplarında klinik başarıda düşüşe neden olduğu görülmüştür ( $p=0.00006$ ). Bu çalışmanın

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sonuçları ile çocukluk yaş grubu alt solunum yolu infeksiyonlarının tedavisinde mezlosilin, ampisilin ve tobramisin veya penisilin ve kloramfenikol tedavilerinin benzer şekilde etkin oldukları sonucuna varılmıştır.

## INTRODUCTION

The initial introduction of aqueous penicillin-G for treatment of streptococcal and staphylococcal infections was an important pharmacological landmark. The emergence of penicillinase-producing *Staphylococcus aureus* prompted the development of the penicillinase-resistant penicillins. The search for a penicillin with additional antimicrobial activity against the *Enterobacteriaceae* and *Pseudomonas aeruginosa* led to the development of the carboxypenicillins (carbenicillin, ticarcillin, and temocillin) and the ureidopenicillins (mezlocillin, azlocillin, piperacillin and apalcillin) (3, 10, 12, 13). The acylureido penicillin mezlocillin is active against Gram positive, Gram negative, and anaerobic bacteria. It easily penetrates the outer membrane of Gram negative bacteria. Its antibacterial spectrum consists of *Staphylococcus aureus*, *Streptococcus faecalis*, *Klebsiella*, *Haemophilus influenzae*, *Escherichia coli*, *Enterobacter spp.*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, and anaerobic microorganisms (6, 12). The efficiency of mezlocillin therapy has been investigated by various studies in respiratory and urinary tract infections, as well as septicemia, meningitis and various infections of the neutropenic patients (1, 2, 4, 5, 11).

Ampicillin and tobramycin or penicillin and chloramphenicol combinations are being used for the treatment of lower respiratory tract infections in our pediatric clinic. This study has been performed in order to test the effectiveness of mezlocillin in comparison with ampicillin and penicillin in children with bronchopneumonia.

## METHODS

Seventy-three patients (36 females, 37 males; ages ranging between 2-72 months) who were hospitalized in the Ankara State Hospital with the diagnosis of bronchopneumonia have been enrolled in the study. The diagnosis was established with clinical, laboratory and radiographic findings (7). Fever, cough, dyspnea, nausea and vomiting and feeding difficulty was investigated, white blood-cell count and radiographs were carried out before treatment. Signs of heart failure including tachycardia, tachypnea, increased work of breathing, pallor, hepatomegaly and also side effects were observed daily. Patients having heart failure signs were digitalised. The cases were divided into three groups according to the severity of the disease as mild, moderate or severe.

Thirty patients received mezlocillin (200 mg/kg/day-intravenous); 22 received ampicillin (150 mg/kg/day-intravenous) and tobramycin (5 mg/kg/day-intravenous); 21 received penicillin-G (200,000 U/kg/day-intravenous) and chloramphenicol (60 mg/kg/day-intravenous). For each group, the patients have been randomly chosen. The administration route of antibiotics was switched to intramuscular injection, if the signs and symptoms of infection subsided within five days. Failure of the treatment was supposed when no response was obtained within 72 hours.

The statistical analysis included X-square test (for the comparison of group proportions) and one-way analysis of variance or Kruskal-Wallis analysis of variance (for the comparison of group means). The level of significance was assigned to  $p=0.05$ . The results were expressed as mean  $\pm$ SD.

## RESULTS

All three antibiotic groups were comparable according to sex and age.

The distribution of the patients according to the severity of bronchopneumonia was similar in all groups (Table 1).

Table 1. Distribution of the patients according to the severity of the disease.

Antibiotic administered	Mild		Moderate		Severe	
	n	%	n	%	n	%
Mezlocillin	9	30	9	30	12	40
Penicillin-G +chloramphenicol	4	19	11	52	6	29
Ampicillin +tobramycin	5	23	7	32	10	45

p=0.50

Mean white blood-cell counts was 11,760+4,800/mm<sup>3</sup> for mezlocillin group; 11,450+6,020/mm<sup>3</sup> for penicillin and chloromphenicol group; and 11,030+3,780/mm<sup>3</sup> for ampicillin and tobramycin group. No significant difference was found between the three groups.

Clinical trial cure rates were 80 % for mezlocillin, 86 % for penicillin and chloramphenicol, and 82 % for ampicillin and tobramycin combination. There was no significant difference in relation to clinical cure rates (Table 2).

Table 2. Comparison of clinical effectiveness.

Antibiotic administered	Treatment rate		Failure of treatment		Exitus	
	n	%	n	%	n	%
Mezlocillin	24	80	5	17	1	3
Penicillin-G +chloramphenicol	18	86	2	19	1	5
Ampicillin +tobramycin	18	82	2	9	2	9

p=0.80

The patients were divided into three age groups (0-2 months, 2.1-24 months and older than 24 months) in order to investigate the effect of the age on the treatment rate. No difference was found between the age groups (Table 3).

Table 3. Treatment rates for the age groups.

Age group (Month)	Treatment rate		Failure of treatment	
	n	%	n	%
0-2	9	69	4	31
2.1-24	42	82	9	18
>24	9	100	0	0

p=0.18

The clinical cure rate of all patients was investigated with regard to the severity of bronchopneumonia. The efficacy of treatment, decreased in severe cases ( $p=0.00006$ ) (Table 4); but the clinical effects in each antibiotic group could not be compared with regard to the severity of the disease, because the cases in each group were not enough for statistical analysis when they were classified according to the severity of the disease (Table 5).

Table 4. Clinical cure rate of all patients according to the severity of the disease.

Severity of disease	Treatment rate		Failure of treatment	
	n	%	n	%
Mild	18	100	0	0
Moderate	26	96	1	4
Severe	16	57	12	43

$p=0.00006$

Table 5. The effect of the severity of the disease on the response to the therapy.

Antibiotic administered	Severity of disease	Clinical effectivity	Failure of treatment
Mezlocillin n=30	Mild	9	0
	Moderate	8	1
	Severe	7	5
Penicillin +chloramphenicol n=21	Mild	4	0
	Moderate	11	0
	Severe	3	3
Ampicillin +tobramycin n=22	Mild	5	0
	Moderate	7	0
	Severe	6	4

Hospitalization period was  $8.2 \pm 2.7$  days for mezlocillin,  $6.3 \pm 3.3$  days for penicillin and chloramphenicol, and  $7.6 \pm 3.0$  days for ampicillin and tobramycin. There was no significant difference between the three groups.

Skin rash occurred in two patients on ampicillin and tobramycin therapy, but no other side-effect was observed during the therapy. There was no significant difference between the three drugs in relation to side-effects.

## DISCUSSION

Pneumonia in children requires immediate antibiotic treatment, and the identification of the causative microorganism is very difficult. The most common event that disturbs the defense mechanisms of the lung is a viral infection, preceding the development of bacterial pneumonia. *S.pneumoniae* is the most common bacterial pathogen in all age groups; *S.aureus* is the causative organism mostly in children under six months of age; *H.influenzae* is a frequent cause of infection under two years of age; and Group A streptococci is more common in 3-5 years of age (7, 9). Laboratory examinations such as white blood cell and neutrophil count, erythrocyte sedimentation rate and radiographic findings are generally suitable for differentiating bacterial and viral infections retrospectively (7, 11).

Mezlocillin is an expanded spectrum semi-synthetic penicillin for parenteral administration and it is effective when administered in lower doses than other penicillins; therefore electrolyte imbalances and coagulation disorders are rare in patients treated with mezlocillin (8). Mezlocillin has been tested in various studies for treating respiratory tract infections and authors concluded that it is a safe, effective and well tolerated antibiotic (2, 10, 11). Our results show that clinical cure rates were 80 % for mezlocillin, 86 % for penicillin and chloramphenicol combination and 82 % for ampicillin and tobramycin combination (Table 2). There was no significant difference in relation to clinical cure rates. No side-effect was observed in patients treated with mezlocillin in our study; this finding is also consistent with other studies (2, 10, 11).

In our study, the efficacy of treatment decreased in severely affected patients ( $p=0.00006$ ) (Table 4); but the clinical effectivity in each antibiotic group could not be compared, because the cases in each therapy group were not enough for statistical analysis when they were classified according to the severity of the disease (Table 5).

In conclusion, we commend that mezlocillin is also a safe and effective drug for the treatment of bronchopneumonia in children.

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