Meningococcal disease, prognostic factors and cefotaxime therapy

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Twenty-four children diagnosed as having meningococcal disease have been investigated with respect to prognostic factors, and were prospectively randomized to receive cefotaxime (150 mg/kgjday in two divided doses) or penicillin G in standart doses. All strains were susceptible to cefotaxime and penicillin G. Hypotension (55%) was the most important prognostic factor. Clinical cure rates for cefotaxime (91%) and penicillin G therapy (70%) groups were insignificantly different. No adverse drug reactions or severe side effects were noted in either group. The therapy regimes were similar for rates of complications. Overall mortality rate was 20.8% (9% for cefotaxime group and 30% for penicillin G group). Although the study group are small we may suggest that cefotaxime is found to be as safe and effective as penicillin G for the treatment of meningococcal disease in children, and offers the advantage of twice daily administration. [Turk J Med Res 1994; 12(6): 257-260]

Key Words: Meningococcal disease, Cefotaxime

Despite effective therapeutic approach, the prognosis of fulminant meningococcal disease is very poor. Epidemiological studies Indicate a mortality rate of between 5 and 20% (1-6). The success of treatment depends on the rapid clinical evaluation and correct estimation of the prognosis and appropriate antimicrobial therapy. Many scoring systems for meningococcal disease were proposed by various authors (6-9). Penicillin is currently recommended as the drug of choice for meningococcal infection (10-13). Alternatively, cephalosporins are effective for therapy of meningococcal disease (14-17).

The aim of this study was to evaluate the prognostic factors on admission and the clinical efficacy of cefotaxime, a third generation cephalosporin in meningococcal disease in children.

PATIENTS AND METHODS

Twenty-four patients diagnosed as having meningococcal infection (13 cases had meningitis with or without meningococcemia, and 11 had meningococcemia without meningitis). The diagnosis was based on the clinical findings, positive blood or cerebrospinal fluid (CSF) cultures and on the presence of meningococci In smears from CSF and petechiae.

The clinical assessment was made within the first hour of admission. Prognosis was based on the practical and reliable scoring system of Tüysüz et al (6). The parameters in their scoring system are three easily diagnosed clinical signs -hypotension, diffuse petechiae, sensorial changes- and two easily performed laboratory investigations-peripheral white blood cell (WBC) and CSF analysis. Blood pressure was measured every 30 minutes until the patient was stabilized. Hypotension was defined as systolic blood pressure below the 5th percentile with respect to sex and age, disturbed consciousness as sensorial variability between somnolence and coma, and diffuse petechiae as uncountable; and confluent petechiae and meningitis as the presence of clinical signs and more than 100/mm3 leucocytes in CSF or the presence of fewer leucocytes with positive CSF culture and smear. The serogroups of *Neisseria meningitidis* could not be demonstrated for technical reasons. Routine tests (complete blood count, urinalysis, serum electrolytes, CSF sugar and protein) were obtained on admission in all patients.

The patients were randomly assigned to recieve cefotaxime or penicillin G for antimicrobial therapy. All

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strains were susceptible to cefotaxime and penicillin G. 11 children were treated intravenously with cefotaxime, 150 mg/kg/day in two divided doses for 5 days. Penicillin G, 500 000 units/kg/day in 6 divided doses was administred for 7 days in the 13 children. The patients were evaluated for clinical status by the same physician every 6 hours. Lumbar puncture was performed every other day until the CSF inflammation profile had returned to near normal values (i.e. protein <40 mg/dl, WBC count, <20 cells/mm^3, glucose >65 mg/dl).

Analysis of data for significance for the age and therapy groups were used for Student's t and Fisher's exact tests.

RESULTS

The ages of 24 patients ranged from 2 months to 12 years. 8 patients were female and 16 were male. Mortality was seen in 5 of 24 children (20.8%). Table 1 gives the relationship between age and mortality rate. Mortality rate for children aged 3-12 years is insignificantly higher than that of those aged 0-2 years (p>0.05). The prognostic value of the factors which were analysed is also given in Table 1. Hypotension was the most important parameter affecting the outcome (p<0.01).

Some characteristics of the two therapy groups are shown in Table 2. The clinical features and recovery time of each group are similar (p>0.05). CSF cultures became sterile and the inflammation profile had returned to normal in all patients with meningitis on the third day of therapy. This was the time when the repeat CSF culture and examination were performed.

One of 11 cases (9%) in the cefotaxime group and 4 of 13 cases (30%) in the penicillin G group died within 12 hours of admission to the hospital. These 5 patients were older than 2 years of age. Case fatality rates were insignificantly different for the two treatment groups (p>0.05). No adverse drug reactions were observed in any of the 24 patients. Two patients receiving cefotaxime had mild diarrhea. Detectable complications occurred in 3 of the 19 survivors. In the cefotaxime group, one patient developed necrotic skin lesions alone. In the penicillin G group two patients developed necrotic skin lesions and one arthritis.

Table **1.** Age and prognostic factors related to mortality of the 24 patients with meningococcal disease

		Died		
	No	No	%	p
Age				>0.05
0-12	7	0	0	
3-12	17	5	29	
Factors				
Hypotension				<0.01
M	9	5	55	
H	15	0	0	
Disturbed counsciousness				>0.05
(t)	8	4	50	
B	16	1	6	
WBC<10 000/mm^3				>0.05
M	8	4	50	
(-)	16	1	6	
Abscence of meningitis				>0.05
(+)	11	4	36	
H	13	1	7	
Diffuse petechiae<12h duration prior to admission				>0.05
(*)	12	4	33	
H	12	1	8	

Table2. Clinical features of 24 children with meningococcal disease

	Groups	
	Cefotaxime	Penicillin
No. of patients	11	13
Female/male	1/10	6/7
Age range	2 months-12 years	5 months-10 years
No. of patients with		
Meningitis	7	6
Meningococcemia without meningitis	4	7
Medium high prognostic score	3	**5**
Clinical recovery time*		
Fever <37°C (hours)	48	48
Arterial blood pressure>70 mmHg (hours)	17	20
Normal CSF (days)	3	3
Severe adverse effects	0	**0**
Survival	10(91%)	9 (70%)
Deaths*	1 (9%)	4 (30%)

•There is no significant difference (p>0.05).

DISCUSSION

Some epidemiological studies have suggested that mortality is high in young children (6,18,19), but many others have failed to demonstrate a correlation between mortality and age (1,7,8,20). In this study, the mortality rate of the children aged 3-12 years was insignificantly higher than that of the younger group. However, most of them died within one hour of admission to the hospital, and had endotoxic shock.

The mortality rate of hypotensive children was 55%, which was found to be a parameter strongly affecting the prognosis. This rate ranged between 30% and 50% according to various studies (1,6-8,21). The prognostic factors affecting mortality most were disturbed counsciousness (50%) and the peripheral WBC count decrease (50%). It has been demonstrated that the children with the disturbed counsciousness had

high mortality rate (6,9,20-22), but in three studies, impaired sensorium was not regarded as a prognostic factor (7,8,23). Many studies show that mortality rate increases in children with WBC counts lower than 10000/mm^3 (5,7-9,22,23). In the current study the mortality rate was 36% and 33% in patients without meningitis and with diffuse petechiae up to 12h prior to hospital admission, respectively. It has been suggested that the absence of meningitis during the clinical course is regarded as a poor prognostic factor (5,7,8,21,22,24). In several studies, correlation was found between diffuse petechiae and mortality (5,7,8). These factors are three easily performed laboratory investigations, and their determinations is practical and unexpensive.

We found no statistically significant differences in clinical and laboratory findings between the two therapy groups. Mortality rate of the patients receiving cefotaxime was insignificantly lower ($p>0.05$). Additionally, the children administered cefotaxime could be mobilized more easily after 2 or 3 days of intravenous therapy because at that time the drug was administered intramuscularly. This could not be possible with penicillin therapy because it was given intravenously six times daily.

The lack of adverse reactions with cefotaxime reflects its relatively wide therapeutic index (17). Our data indicate that cefotaxime was insignificantly more effective than penicillin G therapy in the clinical cure and offers the advantage of twice daily administration. Although the study groups are small, we may conclude that cefotaxime is an effective and safe alternative to penicillin G in meningococcal disease of pediatric patients.

MenIngokokal hastalık, prognostik faktörler ve sefotaksim tedavisi

Meningokokal hastalık tanısı alan 24 çocuk prognostik faktörler ve ileriye dönük olarak rastgele yöntemle sefotaksim (150 mg/kg/gün, iki eşit dozda) ve standart dozda penisilin G tedavisi yönünden incelendi. Üretilen meningokoklar sefotaksim ve penisilin G'ye duyarlı idi. Hipotansiyon (%55) en önemli prognostik faktördü. Sefotaksim için %91 ve penisilin G için %70 olarak bulunan klinik kür oranı anlamlı olarak farklı değildi. Hiçbir hastada ilaç reaksiyonu ve ciddi yan etki görülmedi. Her iki grupta komplikasyon oranı benzer idi. Mortalite oranı %20.8 (sefotaksim grubunda %9, penisilin G grubunda %30) idi. Çalışma grubu küçük olmasına karşın sefotaksimin çocukların meningokokal hastalığının tedavisinde penisilin G kadar etkili ve güvenilir olduğu, ve günde iki kez uygulanma avantajı sağladığı söylenebilir.

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