

THE USE OF CEFOTAXIME IN SERIOUS AND PROBLEM SURGICAL INFECTIONS

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SUMMARY

Cefotaxime [HR 756], a third generation cephalosporin with pronounced antibacterial activity against the Enterobacteriaceae, was assessed in serious and problem antibiotic resistant infection. Good clinical success was achieved without observed untoward effects. The study suggests that due to its properties, cefotaxime could be used as a first-line antibiotic provided that the clinical situation warrants the use of a cephalosporin or aminoglycoside.

Key words - cefotaxime [HR 756], serious surgical infection, antibiotic resistant infection.

INTRODUCTION

INFECTION in surgical cases poses difficulties in management especially when the organism is a problem one or in instance where serious infection requires immediate antimicrobial intervention before bacteriological confirmation is available. In such situations, one is forced to use antibiotics with a broad spectrum and dependable efficacy even against the more difficult Enterobacteriaceae.

Cefotaxime (HR756, Hoechst) was chosen for this study as a representative of the third-generation cephalosporins. Cefotaxime is characterised by its beta-lactamase stability against the clinically important organisms (O'Callaghan, 1979),

its exceptionally high antibacterial activity against Enterobacteriaceae that betters that of the currently available cephalosporins (Hamilton-Miller *et al*, 1978; Chabbert and Lutz, 1978; Sosna *et al*, 1978), and even the aminoglycosides (O'Callaghan, 1979), and possible clinically useful activity against *Pseudomonas* (Stratford, 1978). Furthermore the relative renal non-toxicity of cefotaxime (Ninane, 1979; Clumeck 1979) is an important consideration in serious surgical infection as it does allow for greater leeway in the use of larger doses of the antibiotic if considered necessary.

MATERIAL AND METHODS

Adult patients of either sex were admitted to the study if they either had surgical infection of the severity that warranted immediate potent antibiotic treatment (7 patients). or whose infections had failed to respond to treatment with other antibiotic regimes (4 patients). Routine bacteriological and laboratory studies were done but treatment was commenced with cefotaxime and did not await the outcome of these studies. The study was an open one.

Treatment was initiated with cefotaxime 2Gm intravenously as a stat dose followed by 1 or 2Gm 6-8hrly depending on the clinical assessment of the severity of the infection.

Parameters monitored included temperature, pulse blood pressure and symptomatology of each case as well as the various laboratory investigations. Efficacy of the treatment was assessed globally and also any untoward effects of the drug were carefully looked into.

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RESULTS

Patients and Response

The patient characteristics and the infection for which they were treated with cefotaxime is given in Table I. The duration of infection before admission to hospital ranged from 3-25 days; the majority however being less than 5 days. Of the 11 cases treated, one with two episodes of

infection, the response was clinically graded as excellent in 3 instances and good in 7. Figure 1 gives an example of a typical response. There was one case which did not respond even to relatively large doses of 6-9Gm of cefotaxime a day. This case was later found to be suffering from a hepatoma and in retrospect was not considered to be appropriate for assessment of the antibiotic. Thus an overall success rate of 91.8% of patients could be said to have achieved in the study.

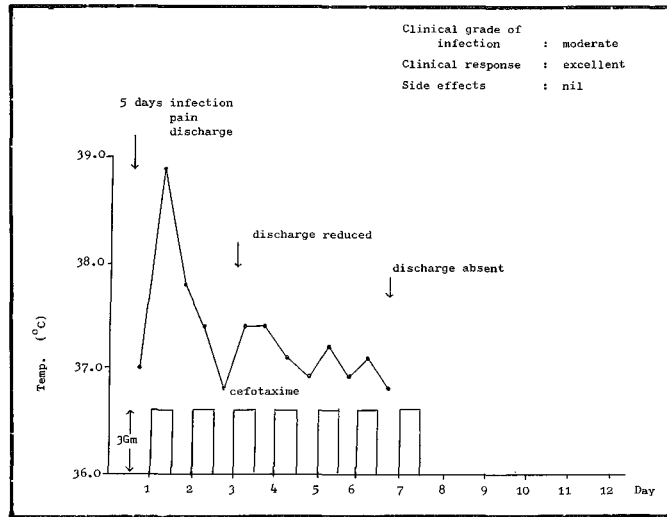


Fig. 1: Response in Patient with Post-appendectomy Infection Caused by Pseudomonal organisms and Treated with Cefotaxime.

TABLE I: CHARACTERISTICS OF PATIENT AND RESPONSE TO CEFOTAXIME TREATMENT

Code	Patient	Race	Sex	Age	Diagnosis	Duration of infection (days)	Grade of infection	Response to Treatment	Side-effects
S1	MD	M	F	38	Breast abscess	14	Moderate	Good	Nil
S2	SM	I	M	42	Post-appendectomy infection	5	Moderate	Excellent	Nil
S3*	CNY	Ch	M	56	Perforated gastric ulcer with septicaemia	3	Moderate	Good	Nil
S4*	NH	Ch	M	62	Ascending Cholangitis	3	Moderate	Excellent	Nil
S5*	TPY	Ch	F	32	Perforated Appendicitis	3	Severe	Excellent	Nil
S6	RK	M	M	69	Hepatoma with Septicaemia	—	Moderate	Poor	Nil
S7	SHH	M	M	63	Hepato-biliary disease	—	Moderate	Good	Nil
S8	V	I	M	55	Pyogenic liver abscess	4	—	Good	Nil
S9	LSK	Ch	F	58	Acute cholecystitis	5	Severe	Good	Nil
S10*	NSH	Ch	F	63	Ascending cholangitis	—	—	Good	Nil
S11	MS	I	M	56	Ascending cholangitis	25	Moderate	Good	Nil

*patients who failed to other antibiotics before cefotaxime treatment.

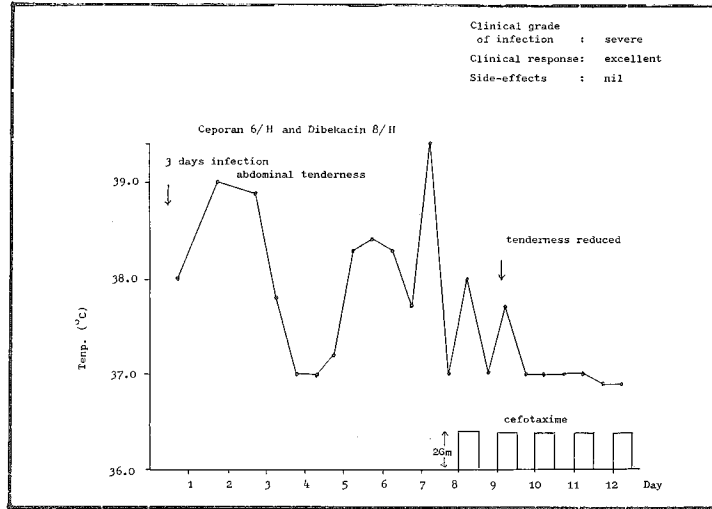


Fig. 2: Perforated Appendix with Localised Abscess. Response to Cefotaxime after Failure to Other Antibiotics.

TABLE II: DETAILS OF ANTIBIOTICS GIVEN TO CASES WHICH FAILED TO RESPOND BEFORE INITIATION OF CEFOTAXIME TREATMENT

Case =	Antibiotics/Chemotherapy	Duration of treatment (days)
SI 3	Garamycin 80mg/8hr	7
SI 4	Tobramycin and i.v. Flagyl	7
SI 5	Ceporan/6hr and Dibekacin 8hr	7
SI 10	Dalacin C 900mg/day Tobramycin 80mg b.i.d.	5

Response in Cases Failing to Other Antibiotics

We have separated these out for special consideration as they probably reflect the usefulness of cefotaxime in these problem cases. 4 patients were in this category and details of their previous antimicrobial treatment is given in Table II. The response seen in these cases were gratifyingly dramatic in contrast to the lack of response to the previously used antibiotics (Fig.2)

Response Pattern

Rapid remission of symptoms was seen following successful treatment with cefotaxime. Fever returned to normal within a day of initiating

cefotaxime treatment in 5 instances and within 2 days in 3 other instances. In addition, other clinical symptoms specifically associated with the infection were clinically ameliorated in the mean period of $1.63 \pm \text{S.D. } 0.92$ days (range 1 - 3 days) and were absent after a mean of $3.63 \pm \text{S.D. } 1.51$ days (range 1 - 5 days) in the 10 cases successfully treated.

Dose Used and Duration of Treatment

The dose used in the cases which responded to treatment is given in Table III. The dose used for successful cases on the first day was a mean of $4.18 \pm \text{S.D. } 1.47\text{Gm}$ and on the subsequent days it was approximately 3.0Gm . All cases were

treated for 4 days. The longest period of treatment was 9 days. The mean total amount of drug given per treatment was 20.00 + S.D. 6.26Gm. In the only case of failure to treatment, the patient was given a total of 92Gm of cefotaxime over the 12 days of treatment but did not show remission of his illness. Cefotaxime was the sole antibiotic used in 9 cases, whilst in two instances metronidazole was given as well and in one case clindamycin was used in the first two days of antibiotic treatment.

sion of cases of infection which were previously refractory to antibiotic treatment to a certain degree reflects some form of comparison.

The clinical results of treatment with cefotaxime were most satisfactory as seen by the predictable and rapid clinical response to treatment. This would be all the more important in serious infection where a reliable antibiotic is mandatory to deal with prolonged morbidity and possibly mortality. The lack of renal toxicity

TABLE III: DOSE OF CEFOTAXIME USED (GM)

Day	1	2	3	4	5	6	7	8	9
Range	2-6	2-4	2-4	2-4	2-4	3-4	1-4	3	3
Mean	4.18	3.09	3.09	3.09	3.00	3.17	2.80	3.00	3.00
S.D.	1.47	0.54	0.54	0.54	0.50	0.41	1.10	—	—
n	11*	11*	11*	11*	9	6	5	2	2

*including one case with second treatment because of recurrence of infection

Tolerance

Cefotaxime was well tolerated and no untoward clinical effects or laboratory abnormalities were reported during the study.

Organisms isolated

Only in three instances were bacteriological investigations positive. Organisms isolated in these cases were *Staph. aureus*, *Ps. pyocyaneous* and *Esch. coli*. The rest of the cases had no positive bacteriological findings.

DISCUSSION

This study has the well-known limitation of methodology in the sense that it was an open study. However in the clinical situation of the study, methodological precision has to give way to ethical considerations. Nevertheless the inclu-

means that its use in patients with renal disease (Clumeck, 1979) has the advantage that tedious and sometimes unavailable monitoring of serum levels of the antibiotic is not a clinical prerequisite as is with a nephrotoxic aminoglycoside such as gentamicin (Regazzi Bonora, 1980).

Considering the extremely low m.i.c.s reported against the Enterobacteriaceae (Hamilton-Miller 1978) and the reported peak plasma levels of cefotaxime achievable especially after i.v. injection, it is possible that lower doses of the drug could have just been as effective. However until more definite dose studies in comparable situations have been done, it is felt that in the specific situation of serious or problem infection, the dosage which was used would be a good guide to achieving the therapeutic objectives.

Of special note is the situation of infection not responding to previous treatment with aminogly-

cosides and cephalosporins. Although the number of cases are relatively few, the experience seems to bear out Clumeck's (1979) report of efficacy of cefotaxime in antibiotic resistant infection. The *in vitro* studies of Sosna *et al.* (1978) showed that while the m.i.c.s of organisms resistant to cephalothin, cefoxitin and cefamandole were also raised against cefotaxime when compared to sensitive organisms, these raised m.i.c.s were well within the plasma levels achieved by therapeutic doses of cefotaxime. The useful antipseudomonal action of cefotaxime could be attributable to the plasma levels achieved in relation to the m.i.c.s of the organisms involved.

It could be that the availability of cefotaxime would make the earlier cephalosporins redundant and would seriously question the role of the more toxic aminoglycoside group except perhaps in resistant pseudomonas infection.

CONCLUSIONS.

Cefotaxime has been found to be very effective in treatment of serious and problem surgical infections. No untoward effects have been observed in treatment. Cefotaxime may find a role as an antibiotic of choice in serious infection especially those suspected of being or due to the Gram-negative organisms.

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