

IN VITRO SUSCEPTIBILITY OF ENTEROBACTERIACEAE TOWARDS SEVEN CEPHALOSPORIN ANTIBIOTICS

VKE LIM MBBS. MRCPATH*
AND
JAM TAY**

Summary

The sensitivities of 226 clinical isolates of *Enterobacteriaceae* towards seven cephalosporin antibiotics were determined using an agar dilution method for establishing m.i.c. (minimum inhibitory concentration). The cephalosporins tested were cephaloridine, cephalothin, cephalixin, cefoxitin, cephadrine, cefuroxime and cefotaxime. Cefotaxime showed the highest anti-bacterial activity among the cephalosporins tested. The other cephalosporins also had good antibacterial activity against *Enterobacteriaceae* with the notable exceptions of *Enterobacter* sp. and indole-positive *Proteus* sp. Only slightly over 50% of *E. coli* were found sensitive to cephaloridine and cephalothin.

INTRODUCTION

The cephalosporins are a family of beta-lactam antibiotics which are widely used in the treatment of infections today. This study seeks to establish the susceptibilities of clinical isolates of *Enterobacteriaceae* towards some of the cephalosporins currently available in Malaysia.

MATERIALS AND METHODS

The cephalosporins which were tested were as follows: cephaloridine, cephalothin, cephalixin, cefoxitin, cephadrine, cefuroxime and cefotaxime. 226 clinical isolates of *Enterobacteriaceae* from patients in the Kuala Lumpur General Hospital were tested for their susceptibilities towards the abovementioned cephalosporins. The m.i.c.s (minimum inhibitory concentrations) of the cephalosporins towards these bacterial isolates were determined by an agar dilution method.

The 226 bacterial isolates comprised of 49 isolates of *E. coli*, 44 isolates of *Klebsiella* sp, 15 isolates of *Salmonella typhi*, 34 isolates of *Salmonella* sp, 14 isolates of indole-positive *Proteus* sp and 35 isolates of *Enterobacter* sp. These isolates were derived from 89 wound swabs, 49 stool specimens, 44 blood cultures, 27 urine specimens, 17 respiratory specimens and 6 vaginal swabs.

RESULTS

The antibacterial activity of the seven cephalosporins are shown in Table 1. The results

are expressed in terms of m.i.c.₅₀ and m.i.c.₉₀ i.e. the m.i.c.s that inhibit 50% and 90% of strains tested respectively. The m.i.c.s are expressed in units of mg per litre.

Taking an m.i.c. of greater than 16 mg/litre as denoting resistance to the cephalosporin,² the percentages of the strains sensitive to the various cephalosporins tested are shown in Table 2.

DISCUSSION

The cephalosporins are a family of beta-lactam antibiotics originally derived from *Cephalosporium acremonium*, a mould first isolated from sewage in Sardinia.³ From this mould, a compound named Cephalosporin C was isolated. Cephalosporin C was found to have a broad spectrum of activity against both Gram-positive as well as Gram-negative bacteria. Most of the cephalosporins in use today are semi-synthetic derivatives of Cephalosporin C. Cefoxitin is a notable exception. It is a cephamycin and is derived from *Streptomyces lactamdurans*.

Of the seven cephalosporins tested, cefotaxime showed the highest overall antibacterial activity. The m.i.c. values obtained in this study are similar to those reported by other workers.⁴⁻⁶ Its high antibacterial activity against *Enterobacter* sp and indole-positive *Proteus* sp is worthy of note as these bacteria are generally resistant to most cephalosporins. The m.i.c.s obtained with cefotaxime were extremely low when compared with the other cephalosporins. Weight for weight, cefotaxime was between 50-100 times more active, than the

* Lecturer, Department of Microbiology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur (Address reprint requests).

** Medical Laboratory Technologist. Department of Microbiology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur.

TABLE I
ANTIBACTERIAL ACTIVITY OF SEVEN CEPHALOSPORINS AGAINST
226 CLINICAL ISOLATES OF *ENTEROBACTERIACEAE*

	Organism						
	<i>Klebsiella</i> sp	<i>Salmonella typhi</i>	<i>Salmonella</i> sp	<i>Proteus</i> sp (indole-negative)	<i>Proteus</i> sp (indole-positive)	<i>Enterobacter</i> sp	<i>E. coli</i>
Total No.	44	15	34	35	14	35	49
Cephalosporin							
Cephaloridine	4 / > 64	2 / 2	4 / 64	8 / > 64	> 64 / > 64	> 64 / > 64	16 / 64
Cephalothin	4 / 64	2 / 2	4 / 32	8 / 64	> 64 / > 64	> 64 / > 64	16 / 64
Cephalexin	4 / 8	2 / 4	4 / 16	16 / 32	64 / > 64	64 / > 64	8 / 16
Cefoxitin	4 / 4	2 / 4	4 / 16	4 / 4	16 / > 64	> 64 / > 64	4 / 8
Cephradine	8 / 16	8 / 8	8 / 16	32 / 64	64 / > 64	32 / > 64	16 / 16
Cefuroxime	2 / 8	4 / 8	4 / 8	2 / 4	32 / > 64	8 / 32	4 / 8
Cefotaxime	0.03 / 0.12	0.06 / 0.06	0.12 / 0.25	0.03 / 0.03	0.06 / 0.12	0.12 / 0.5	0.06 / 0.12

Note: the upper and lower figures for each cephalosporin refer to the m.i.c.₅₀ and m.i.c.₉₀ respectively expressed in mg/l

other cephalosporins against *E. coli*, *Klebsiella* sp, *Salmonella* sp and indole-negative *Proteus* sp. Against *Enterobacter* sp and indole-positive *Proteus* sp, cefotaxime was found to be 250-1000 times more active than the other cephalosporins. These low m.i.c.s may have an important bearing on *in-vivo* effectiveness of cefotaxime as there is a correlation between m.i.c. and ED₅₀ (effective dose 50). Drugs with low m.i.c.s are more effective if similar doses are administered. Cefuroxime also showed high antibacterial activity against the strains of *Enterobacteriaceae* tested including *Enterobacter* sp. However, its activity against indole-positive *Proteus* sp was rather poor. This is in contrast to that reported by Eykyn from the United

Kingdom.' This highlights the important fact that antibiotic resistance pattern differs from region to region and from time to time. Cefoxitin, cephalexin and cephradine were generally quite active against *E. coli*, *Klebsiella* sp, *Salmonella* sp and indole-negative *Proteus* sp. However, their activity against indole-positive *Proteus* sp and *Enterobacter* sp were not unexpectedly rather disappointing. It is also interesting to note that only slightly over 50% of *E. coli* were still sensitive to cephaloridine and cephalothin. This probably reflects the long and widespread use of these antibiotics in this country which has given rise to the emergence of resistant strains.

TABLE 2.
PERCENTAGES OF STRAINS OF *ENTEROBACTERIACEAE* SENSITIVE
TOWARDS SEVEN CEPHALOSPORINS

Cephalosporin	Organism						
	<i>E. coli</i>	<i>Klebsiella</i> sp	<i>Salmonella typhi</i>	<i>Salmonella</i> sp	<i>Proteus</i> (indole - ve)	<i>Proteus</i> (indole + ve)	<i>Enterobacter</i> sp
Cephaloridine	51	70	100	77	69	7	11
Cephalothin	55	70	100	85	80	7	6
Cephalexin	94	96	100	97	80	7	17
Cefoxitin	96	96	100	91	98	50	11
Cephradine	94	96	100	94	3	7	26
Cefuroxirne	100	98	94	97	100	29	89
Cefotaxime	100	100	100	100	100	100	97

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