



Activity of temocillin and comparators against clinical isolates of *Vibrio cholerae* from Iran

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Dear Editor,

Acute diarrhoeal caused by *Vibrio cholerae* is a major public health problem with, according to the World Health Organization, up to 4.0 million cholera cases and 143,000 deaths occurring every year worldwide [1]. In conjunction to aggressive rehydration therapy that restores the circulating blood volume, it is recommended to use antibiotics for the most severe patients in order to reduce the severity of the symptoms and the treatment duration [2]. Concerns are now raised due to the increase resistance of *V. cholerae*. The objective of this study was to investigate the in vitro activity of temocillin, a narrow-spectrum penicillin stable to many beta-lactamases [3], against *V. cholerae* obtained from patients suffering of cholera and submitted to the national reference health laboratory of Iran. All isolates were collected consecutively and originated from 20 different provinces in Iran (Alborz, Busheher, Esfahan, Ghazvin, Gilan, Gonabad, Gorgan, Hormozgan, Jiroft, Kashmar, Kerman, Kermanshah, Khuzestan, Kordestan, Natanz, Qom, Semnan, Sistan, Tehran, West Azabaijan). Isolates were serotyped by O1 polyvalent and Ogawa/Inaba monospecific antisera (Becton Dickinson Co., USA). The minimal

inhibitory concentrations (MICs) of temocillin and six comparators available in Iran (ampicillin, cefixime, nalidixic acid, ciprofloxacin, erythromycin and tetracycline) were determined by E-test® (BioMérieux France) and interpreted according to CLSI breakpoints except for temocillin for which the systemic breakpoint of the BSAC was used ($S \leq 8$ mg/L) [4].

In total, 121 *V. cholerae* O1 isolates were tested, including 31 Ogawa and 90 Inaba serotypes. Seventy-five percent of the isolates were recovered from male. Patients ranged in age from 1 to 77 years old (mean and median of 29 and 23 years old, respectively). Table 1 displays the antibiotic MIC distributions of *V. cholerae* to each antibiotic. The less active drugs were tetracycline (susceptibility rate of 47%), erythromycin (33%) and nalidixic acid (9%). Multiresistant isolates were frequent; all isolates resistant to tetracycline were resistant to nalidixic acid, and 73% of them were non-susceptible to erythromycin. The most active drugs were temocillin and cefixime with susceptibility rate of 100%, followed by ampicillin and ciprofloxacin (99%). A reduced susceptibility to ciprofloxacin was observed in 15% of the isolates.

To our knowledge, this is the first report describing the activity of temocillin against clinical isolates of *V. cholerae*. Bier N. et al. previously reported the activity of temocillin against seven environmental isolates of *V. cholerae*, including four resistant to carbapenems. All of them were susceptible to temocillin with MIC ≤ 4 mg/L [5]. Over the past years, the susceptibility profile of *V. cholerae* has changed with now resistance or reduced susceptibility to various antibiotics among which tetracycline and quinolones [6]. The present study includes a significant number of multiresistant isolates; some of them have a reduced susceptibility to ciprofloxacin.

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Table 1 Distributions of antibiotic minimal inhibitory concentrations (MICs) against 121 isolates of *V. cholerae*

Antibiotics	Number of isolates with indicated MIC (mg/L)											Breakpoints	MIC ₅₀	MIC ₉₀	%S	%I	%R
	<0.5	0.5	1	2	4	8	16	32	64	128	256						
Temocillin	0	0	0	1	60	60	0	0	0	0	0	8/8	4	8	100	0	0
Ampicillin	0	0	1	16	62	41	0	0	0	0	1	8/32	4	8	99	0	1
Cefixime	120	1	0	0	0	0	0	0	0	0	0	1/4	0.125	0.25	100	0	0
Nalidixic acid	0	0	5	3	2	1	0	0	0	0	110	16/32	256	256	9	0	91
Ciprofloxacin	13	87	20	1	0	0	0	0	0	0	0	1/4	0.5	1	99	1	0
Erythromycin	0	0	1	39	67	13	0	0	0	0	1	2/16	4	8	33	66	1
Tetracycline	0	2	19	21	15	0	64	0	0	0	0	4/16	16	16	47	0	53

According to clinical practice, the choice of antibiotic should be informed by local antibiotic susceptibility patterns, and in this context, including temocillin would be of interest. Further clinical trials are warranted to evaluate whether temocillin offers an effective treatment for cholera.

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Compliance with ethical standards

Conflict of interest MR and MM have received sponsorship from Belpharma to attend scientific meetings. SVDV is an employee of Eumedica s.a. RS and MRF declare that they have no conflicts of interest.

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