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Antibacterial Activity of Ciprofloxacin against Clinical Strains of *Vibrio cholerae* O139 recently Isolated from India

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We determined the *in vitro* antibacterial activity of ciprofloxacin against *Vibrio cholerae* O139 recently isolated from cholera patients in India. Ciprofloxacin showed excellent antibacterial activity against the O139 strains, and ciprofloxacin-resistant O139 strains were not observed. The lack of incidence of ciprofloxacin resistance in O139 strains may be because O139 strains appeared comparatively recently and have not been extensively treated with antibacterial agents including fluoroquinolones.

Key words——antibacterial activity; ciprofloxacin; *Vibrio cholerae* O139

Vibrio cholerae O1 and O139 produce cholera toxin and are the causative agents for human cholera disease. To date, seven pandemics of cholera caused by *V. cholerae* O1 have been recorded since 1817; and the ongoing seventh pandemic started in 1961 in Indonesia and has spread rapidly throughout the world.[1] *V. cholerae* O139 is a new causative strain of cholera that first emerged in 1992 in the south Indian coastal city of Madras;[2] and then the strain spread rapidly to different areas of India and neighboring countries. Cholera caused by *V. cholerae* O139 is an emerging infectious disease. Currently, *V. cholerae* O1 and O139 both cause epidemics of cholera alternatively or simultaneously in India and Bangladesh.[1]

Fluoroquinolones (FQs) exhibit potent antibacterial activity against *V. cholerae* O1 and O139 strains[3] and, among FQs, ciprofloxacin (CPFX) is frequently used in the treatment of cholera. Yamamoto et al. previously reported that FQs including CPFX showed excellent antibacterial activity against *V. cholerae* O1 and O139 strains isolated during or before 1994 in Asian countries such as India and Bangladesh (MICs, $\leqq$0.06 μg/ml for FQs including CPFX); and FQs-resistant strains were not found among the O1 and O139 strains.[3] However, we have recently described a high incidence of FQs-resistance including CPFX-resistance among *V. cholerae* O1 strains isolated during 1995 to 1998.[4] This high incidence of FQs-resistance among the O1 strains is a serious problem in the treatment of cholera with FQs. Therefore, in this study, we determined the *in vitro* antibacterial activity of CPFX against *V. cholerae* O139 strains that were isolated during 1995 to 1998 in India.

CPFX used in this study was synthesized at Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan. The 16 *V. cholerae* O139 strains used in this study were isolated during 1995 to 1998 from cholera patients admitted to the Infectious Diseases Hospital in Calcutta, India. The MICs were determined using the standard agar dilution method with Mueller-Hinton agar recommended by the Clinical and Laboratory Standards Institute (formerly the National Committee for Clinical Laboratory) Standards.[5] Using the MICs, the MIC range, MIC_{50}, and MIC_{90} were estimated. We used the agar dilution breakpoints adopted by the Centers for Disease Control and Prevention (Atlanta, GA): *i.e.* MICs$\geqq$1.0 μg/ml for CPFX were deemed CPFX-resistant strains.[6]

The 16 *V. cholerae* O139 strains tested were highly susceptible to CPFX and CPFX-resistant strains were not detected among the O139 strains; the MIC range, MIC_{50}, and MIC_{90} of CPFX against O139 strains were$\leqq$0.002–0.008, 0.004, and 0.008 μg/ml, respectively.

The decreased susceptibility of *V. cholerae* O1

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strains shown in our previous study[4] to CPFX with a high incidence of CPFX-resistance may be due to the frequent use of FQs in the treatment of cholera instead of using tetracycline (TC) (the sensitivity of the O1 strains to TC has decreased and TC-resistant O1 strains have increased by the frequent use of TC). Conversely, the lack of incidence of CPFX resistance in the O139 strains may be because O139 strains appeared recently in 1992 and have not been treated as extensively with antibacterial agents including CPFX. Garg et al. previously described a low incidence of CPFX-resistance among *V. cholerae* O139 strains isolated during or after 1995 when the susceptibility testing of these strains was performed using the simple E-test strip (AB Biodisk, Solna, Sweden).[7] Our present results conducted by using the standard agar dilution method were in close agreement with the observations reported by Garg et al.[7]

Using the data here and previous observations reported by Garg et al.[7] show the *V. cholerae* O139 strains isolated before about 2000 had excellent susceptibility to CPFX and exhibit the low incidence of CPFX resistance. However, it will be necessary to carry out antimicrobial susceptibility surveillance of more recently isolated *V. cholerae* O139 strains. Further, hereafter, the vigilant and appropriate use of antibacterial agents including FQs in the treatment of cholera caused by *V. cholerae* O139 will be required to avoid resistance.

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