

NORFLOXACIN MONODOSE USE IN PATIENTS WITH CHOLERA IN SALTA, ARGENTINA

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SUMMARY

The use of monodose (800 mg) per os of Norfloxacin was evaluated in 32 patients with cholera at Salvador Mazza's Hospital, Salta, Argentina. It was considered the celerity in negativization of stool culture (100% of cases: 12 hours post administration), its efficiency along time (24/24 controlled patients were negative at 10th day) and MIC of isolated strains (100% of strains were sensitive: range 0.008 to 0.016 µg/ml). It was included oral administration of sorbitol 70% in peanut oil in order to study patients at 10th day's control. This method could be an alternative one in the study of asymptomatic carrier. Norfloxacin monodose shows good performance in early negativization of stool culture and it was also effective along the whole observation period, suggesting it could prevent carriage.

KEYWORDS: Cholera; Treatment; Norfloxacin; Carriage.

INTRODUCTION

Many antimicrobial agents have been used in the treatment of cholera for clinical and epidemiological purposes. During the last fifteen years many isolations of *Vibrio cholerae* with different patterns of antibiotic resistance were reported. In most of the cases these strains are an exception to the general behavior of the microorganisms involved in an area^{15,17}, but sometimes they may include most of the isolations^{12,16}. Although outbreak in our country began in 1992, 2% of resistant strains have already been reported⁶.

On measuring *Vibrio* excretion after antimicrobial administration different results have been found, specially when using drugs that have been recommended by the World Health Organization^{1,5,9,14}.

The difficulties in the recovery of *V. cholerae* from formed feces or rectal swab from carriers have also been reported^{4,7,10}.

Provided the importance of the use of monodose in this kind of disease a non-comparative study with Norfloxacin

was conducted in order to evaluate its bacteriological efficiency. A more sensitive procedure was included in order to enhance possibilities of pathogen's recovery at 10th day's culture.

Antimicrobial susceptibility tests were performed on isolated strains.

MATERIALS AND METHODS

32 patients, 19 (59.4%) male, 15 to 80 years old, who entered Salvador Mazza's Hospital (Province of Salta, Argentine Republic) with clinical and bacteriological cholera diagnosis, were studied. All isolated strains were El Tor, Ogawa. Those patients who have received previous antibiotic treatment were excluded. The protocol of study consisted in: 1) stool culture at admission; 2) 800 mg (2 tablets) per os of Norfloxacin as monodose, in absence of vomit; 3) stool culture at 12, 24, 48 and 72 hours post administration; 4) stool culture at 10th day after drug administration with patient under ambulatory assistance. As *V. cholerae* recovery from formed feces is considered very low^{4,7,10} and its persistence in gallbladder is already

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known¹⁰, the administration of sorbitol 70% in peanut oil (Boyden Radiological Test) was indicated on this case before stool culture.

Sorbitol 70% concentration was not inhibitory for *V. cholerae* development in previous laboratory assays. The sorbitol solution produced a liquid to semisolid evacuation within 3 hours of its administration, with a 500 ml approximated volume.

Sample was obtained with a rectal swab, transported in Cary Blair medium. Then it was enriched in Alkaline Peptone Water for 6 to 12 hours at 35°C and then plated on TCBS (tiosulfate-citrate-bile salts-sucrose) medium. Biochemical and serological tests according to standard procedures were developed on isolates¹³. Several antimicrobial agents were used in diffusion tests to measure susceptibility of *V. cholerae* strains. Minimum Inhibitory Concentration (MIC) for Norfloxacin was determined according to standard dilution method³.

RESULTS

12 hours after Norfloxacin administration stool culture was negative in all cases, and controls after 24, 48 and 72 hours showed the same results. At 10th day, 24 out of the 32 initial patients could be controlled, due to operational difficulties. All of them were negative.

All of the strains (n:32) were sensitive to Norfloxacin. MIC range was 0.008 to 0.016 µg/ml. One of the isolated strains was resistant to: Gentamicin, Nitrofurantoin, Amoxicilin, Amikacin, Piperacillin, Cephalotine and Ceftazidime but sensitive to Cotrimoxazol, Nalidixic Acid, Fleroxacin, Ciprofloxacin, Pefloxacin, Norfloxacin, Amoxicillin-Clavulanate, Ceftriaxone, Doxycycline and moderately sensitive to Netilmicine.

DISCUSSION

To make patients free of *V. cholerae* is an important event in order to cut epidemiological chain. In this study Norfloxacin showed 100% effectiveness in negativization of stool culture being specially remarkable its celerity. These results agree with those reported by BATTACHARYA et al.⁵. Similar evidences were found out when Docycycline 200 mg¹, Furazolidone¹⁴ and Cotrimoxazol or Tetraciclina in monodose were tested^{5, 14}.

However it has been pointed out that cessation of the diarrhea and/or negativization of stool culture before discharge does not mean eradication of the microorganism^{1, 14}. In that sense, GOTUZZO et al. in their study in Peru found better results when using Norfloxacin in

multiple dose⁹. In the present 10 days follow up the use of monodose of the drug was effective in the eradication of the carrier state after the disease.

The use of the sorbitol-peanut oil solution could be proposed as an alternative in the study of the asymptomatic carrier, provide it accelerates intestinal transit and stimulates bile secretion without inhibiting *V. cholerae* in laboratory tests. Norfloxacin administration produces an active and high concentration of the drug in the intestine as well as in the gallbladder² and its cost does not exceed those of Tetracycline, Cotrimoxazol and Furazolidone in multiple dose.

Finally, resistance to quinolones is possible under laboratory conditions, but it has not been observed in clinical experience¹¹, while resistance of some strains of *V. cholerae* to other antibiotics has been related with plasmid mediation^{8, 16, 17}. These considerations are important when an antimicrobial agent is used on numerous populations due to the cross antibiotic resistance it may induce.

RESUMEN

El uso de monodosis de norfloxacin en pacientes con colera en Salta, Argentina

Se evaluó el uso de monodosis (800 mg) per os de Norfloxacin en 32 pacientes con cólera en el Hospital de Salvador Mazza, Salta, Argentina. Se consideró la rapidez en la negativización del coprocultivo (100% de los casos = 12 horas post administración), su eficacia a través del tiempo (24/24 pacientes controlados fueron negativos al 10º día) y la CIM de las cepas aisladas (100% sensibles, rango 0.008 a 0.016 µg/ml). Para estudiar a los pacientes en el control del 10º día se incluyó la administración oral de sorbitol 70% en aceite de maní. Este método puede ser una alternativa en el estudio del portador asintomático. Norfloxacin en monodosis mostró buen desempeño en la pronta negativización del coprocultivo y fue también efectiva a lo largo de todo el período de observación sugiriendo que puede evitar la portación.

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