

Effect of doxycycline on transmission of *Vibrio cholerae* infection among family contacts of cholera patients in Calcutta*

P. G. SEN GUPTA,¹ B. K. SIRCAR,² S. MONDAL,³ S. P. DE,⁴
D. SEN,¹ S. N. SIKDER,⁵ B. C. DEB,⁶ & S. C. PAL⁷

Doxycycline was used among the family contacts of hospitalized cholera patients in Calcutta to determine its effectiveness in controlling transmission of V. cholerae infection. A total of 137 such contacts were given a single oral dose of doxycycline in graded doses according to age. A similar group of 139 contacts received a single dose of multivitamins as placebo. All 276 contacts were examined bacteriologically daily for 10 days for the presence of V. cholerae in their stools. The results showed that doxycycline was effective in significantly reducing the load of V. cholerae infection for up to 5 days following treatment.

The seventh cholera pandemic due to the *eltor* biotype of *V. cholerae*, involving a large number of countries in three continents, brought to light the possible role of cholera carriers in the spread of this disease. The inability of the cholera vaccines currently in use to afford significant protection against cholera for a long period as well as to control carriers has led various workers to consider chemoprophylaxis for the control of transmission of cholera infection.

De et al. (1) recently used doxycycline in the treatment of cholera patients. Of three dosage schedules used by these workers, a 300-mg single oral dose of doxycycline was found to be almost as effective as a 6-hourly, 2-day schedule of tetracycline.

The objective of the present study was to determine whether a single dose of doxycycline would also be effective in reducing the load of *V. cholerae* infection

among contacts of cholera patients and, if so, the duration of its effectiveness.

MATERIALS AND METHODS

Between April and August 1976, stool samples or rectal swabs of 276 family contacts of 59 cholera index cases (bacteriologically established) were collected daily for 10 consecutive days and processed as described earlier (2). After the samples had been collected on the first day, the family contacts of index cases were given either doxycycline or multivitamins (placebo). A graded dosage schedule was used for doxycycline: adults over 15 years of age received a single oral dose of 300 mg; those under 15 years of age were given 6 mg of doxycycline per kg of body weight. Age-specific weights were calculated on the basis of an Indian Council of Medical Research report (3). Biscuits were given before administration of the medicines to prevent possible gastric irritation. Infants under 3 months of age were excluded from the study. The age and sex distribution of the 276 contacts are shown in Table 1, and it can be seen that there was a fair degree of similarity between the two treatment groups. Of the expected total of 2760 samples from 276 contacts, 2672 (96.8%) were collected.

RESULTS

The results of sampling the 276 contacts in the two groups on all 10 days are shown in Table 2. It

* From the Cholera Research Centre, 3 Kyd Street, Calcutta-700016, India. These studies were carried out under the joint auspices of the Indian Council of Medical Research, the Health Department of the Government of West Bengal, and the World Health Organization.

¹ Research Officer.

² Senior Research Officer.

³ Research Fellow.

⁴ Assistant Director.

⁵ Assistant Statistician.

⁶ Deputy Director.

⁷ Director.

Table 1. Distribution of the study population by age and sex

Age group (years)	No. of persons								Total	
	Doxycycline				Placebo				No.	%
	Male	Female	Total	%	Male	Female	Total	%		
≤ 4	9	8	17	12.4	6	12	18	12.9	35	12.7
5-9	6	15	21	15.3	11	9	20	14.4	41	14.9
10-14	17	8	25	18.2	12	11	23	16.5	48	17.4
≥ 15	38	36	74	54.0	40	38	78	56.1	152	55.1
All ages	70	67	137	100.0	69	70	139	100.0	276	100.0

Table 2. Sampling of 276 contacts in two groups on different days of follow-up and isolation of *V. cholerae* from them

Days of follow-up	Treatment groups				Sampling coverage %
	Doxycycline		Placebo		
	Number sampled	Number positive	Number sampled	Number positive	
1	137	5	135	4	98.6
2	135	2 ^a	136	10	98.2
3	134	nil ^a	135	6	97.5
4	136	nil ^a	135	6	98.2
5	132	1 ^b	133	7	96.0
6	131	4	136	6	96.7
7	131	4	136	4	96.7
8	131	2	136	3	96.7
9	132	2	132	2	95.7
10	128	3	131	4	93.8

^a Significantly different from placebo group ($P < 0.5$).

^b Difference near significance.

is seen that doxycycline was effective immediately after administration in reducing the load of infection among family contacts, compared with the control group. This effectiveness was maintained until the fifth day, after which no difference was observed between the two groups. Although the difference between the results on the fifth day was not statistically significant, it was very close to significance.

The distribution of 12 carriers who excreted *V. cholerae* more than once is shown in Table 3. None of the carriers in the doxycycline group excreted *V. cholerae* more than twice, whereas in

the placebo group two carriers excreted *V. cholerae* 5 times, two 4 times and two 3 times during the 10-day period of follow-up. Moreover, no excretion of *V. cholerae* was detected in the doxycycline group during the first 5 days after treatment, whereas in the placebo group excretion was detected in eight carriers.

Ten out of 137 contacts (7.3%), although they were given biscuits immediately before the administration of doxycycline, complained of nausea. Similarly, four (2.9%) of the same group suffered from mild vomiting. However, these minor reactions

Table 3. Distribution of 12 carriers,^a with dates of excretion of *V. cholerae*, in the two groups

Treatment group	No.	Days of follow-up on which <i>V. cholerae</i> excreted
doxycycline	1	1st, ^b 7th
	2	6th, 7th
	3	6th, 9th
placebo	1	1st, ^b 2nd
	2	1st, ^b 2nd, 3rd
	3	1st, ^b 3rd, 4th
	4	2nd, 3rd, 5th, 6th
	5	2nd, 3rd, 5th, 6th
	6	2nd, 6th
	7	4th, 5th, 6th, 8th, 10th
	8	4th, 10th
	9	6th, 7th, 8th, 9th, 10th

^a These carriers (23.1 % of the total) excreted *V. cholerae* on more than one occasion.

^b Treatment was given after collection of stool samples on the first day.

did not result in any lack of cooperation by the families during the subsequent 9 days of follow-up.

DISCUSSION

Previous chemoprophylaxis trials, although effective in various degrees in reducing the number of

contact cholera carriers, revealed the limitations of the different drugs used. None could be recommended for single oral dose therapy in cholera chemoprophylaxis. Tetracycline, although effective, requires repeated administration for 3-5 days and is consequently not ideal for routine purposes. As a result, sulfadoxine was tested in Calcutta (4). This drug, when given as a single oral dose, was effective for the same length of time as tetracycline but was sluggish in its action during the initial period. This time-lag was considered vital since some of the carriers, though treated with sulfadoxine, might pass on the infection during the first 24 hours. The present trial, on the other hand, showed that doxycycline given as a single oral dose could effectively reduce the number of cholera carriers almost immediately. Furthermore, it has been observed (2) that the number of carriers among those treated with tetracycline remained significantly low for only 2 days after the last dose had been administered on the third day, whereas in the present trial, the effect of doxycycline was still evident for 4 days following treatment.

The minor reactions observed with a single dose of doxycycline might have been further reduced if the drug had been administered after a large meal.

Doxycycline, therefore, appears to be a safe, long acting, and effective prophylactic when given in a single oral dose. Moreover, these trials were conducted in a hyperendemic area where the chance of reinfection is greater; in a nonendemic area doxycycline might be even more effective.

ACKNOWLEDGEMENTS

The authors are thankful to Dr D. Barua, World Health Organization, Geneva for his helpful cooperation and comments on the results of this study. The Vibramycin brand of doxycycline used in the present trial was supplied by the Pfizer Chemical Co. The authors also thank the authorities of the Health Department of the Government of West Bengal for their continued cooperation. Finally, the excellent assistance provided by the field and laboratory workers of the Cholera Research Centre is gratefully acknowledged.

RÉSUMÉ

EFFET DE LA DOXYCYCLINE SUR LA TRANSMISSION DE L'INFECTION À *VIBRIO CHOLERAE* PARMIS LES CONTACTS FAMILIAUX DES PERSONNES ATTEINTES DE CHOLÉRA À CALCUTTA

La doxycycline, antibiotique à effet rémanent, a été employée à Calcutta chez un certain nombre de contacts familiaux de malades souffrant de choléra pour déter-

miner si elle permettait d'empêcher la transmission de l'infection cholérique. Une seule dose orale de doxycycline, plus ou moins forte selon l'âge des intéressés,

a été administrée à un total de 137 contacts. Un autre groupe de contacts, au nombre de 139, a reçu une dose unique de placebo sous forme de multivitamines. L'ensemble de ces 276 contacts ont été soumis à un examen bactériologique quotidien pendant 10 jours en vue de déceler la présence de *V. cholerae* dans leurs selles. Les résultats ont montré que la doxycycline permettait de

réduire de manière significative l'excrétion de *V. cholerae* pendant une période de 5 jours au maximum après le traitement. La doxycycline a donc été jugée constituer un instrument prophylactique de choix dans une région non endémique où risque de se produire une nouvelle poussée de choléra.

REFERENCES

1. DE, S. ET AL. *Bulletin of the World Health Organization*, **54**: 177-179 (1976).
2. JOINT ICMR-GWB-WHO CHOLERA STUDY GROUP, CALCUTTA. *Bulletin of the World Health Organization*, **45**: 451-455 (1971).
3. INDIAN COUNCIL OF MEDICAL RESEARCH, STATISTICS DIVISION. *Studies on growth and physical development of Indian infants and children. Part 1A—all India*. New Delhi, ICMR, vol. 2, 1968.
4. DEB, B. C. ET AL. *Bulletin of the World Health Organization*, **54**: 171-175 (1976).

ERRATA

Vol. 55, No. 1

Évaluation simplifiée sur le terrain de l'état nutritionnel des jeunes enfants: suggestions pratiques pour les pays en développement

Résumé

Page 85, 2^e colonne, 13^e ligne: au lieu de « poids pour l'âge » lire « poids pour la taille »