

CONTROLLED CLINICAL TRIAL OF DOXYCYCLINE IN CHOLERA

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Introduction and Rationale

Tetracycline is the antibiotic of choice in reducing the duration of diarrhoea in cholera. However, this antibiotic has to be administered six-hourly which takes up a considerable part of the nursing time in a large outbreak. Acute renal failure following prolonged shock is not an uncommon complication in cholera where use of ordinary tetracycline is contraindicated as it may produce a toxic serum level. Doxycycline, a long acting tetracycline with a long serum half life, is administered once daily and may be used safely in renal failure, offers certain advantages for use in cholera. A clinical trial was carried out during the 1974 epidemic to compare the efficacy of doxycycline with the ordinary tetracycline.

Materials and Methods

Patients admitted with history suggesting uncomplicated cholera and who had not been treated outside with antibiotic were selected for the study. Only those who had at least one litre of liquid stool in 8-hours after admission were included. A total of 60 patients were studied but 9 were found to be subsequently negative for cholera and were excluded from this analysis. Selection of patients were made by picking up a card arranged in strict order.

Doxycycline in 100 mg doses and a placebo was supplied as similar looking coded capsules, the code being unknown to any of the investigators. Tetracycline hydrochloride as 250 mg capsules was used as a positive control. The dose of doxycycline given was approximately 2 mg./kg. as a start dose followed by another dose at 12 hours and repeated at 0-hours daily for four days. Tetracycline capsule was given six hourly for 4 days also.

Results

The number of patients in each group, their ages, heights and weights are shown in Table 1. All the groups

were comparable. Stool passed and I.V. fluid given prior to the start of the therapy are shown and found to be comparable.

Stool volume passed and I.V. required in the placebo, doxycycline and tetracycline groups are shown in Figure 1. The results point out the clear superiority of both doxycycline and tetracycline in reducing the volumes of liquid stool and I.V. required in comparison to placebo. Table 2 shows this in actual numbers. Duration of diarrhoea also followed a similar trend. The difference between the doxycycline and placebo and tetracycline and placebo were statistically significant. Rectal swabs were found to be persistently positive for the duration of hospital stay in the placebo group compared to the groups receiving antibiotics. Doxycycline administered once daily had positive swabs for three days, compared to two days in the group on tetracycline hydrochloride given six hourly.

Discussion

Results show that doxycycline administered less frequently has efficacy similar to tetracycline. This may become a distinct advantage in treating cholera epidemic in areas where the number of nursing personnel may be few. As doxycycline is considered to be a safe medicine to be used in renal failure, many cases of suspected renal failure following cholera may be treated without waiting for full kidney function to return.

Doxycycline is an expensive antibiotic and its advantages have to be weighed against its cost. However, cost of antibiotic is only a fraction of the total cost of patient care in cholera where personnel and I.V. fluid are the most expensive items.

Conclusion

Doxycycline tried against ordinary tetracycline and a placebo was found to be an effective antibiotic in reducing the duration of diarrhoea and the requirement of I.V. fluid.

FIGURE 1.

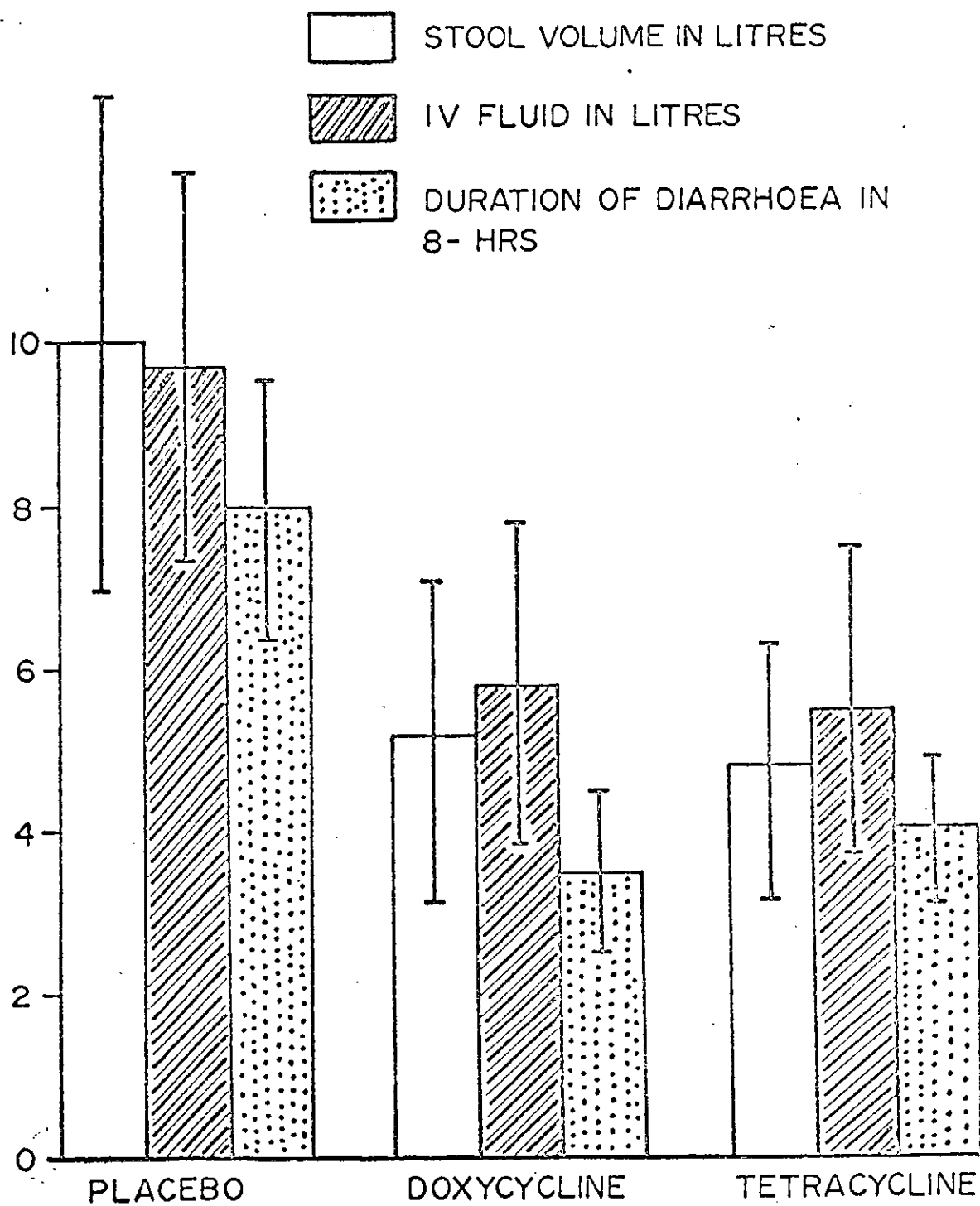


TABLE II

	Placebo		Doxycycline		Tetracycline	
	Mean	SD	Mean	SD	Mean	SD
Stool volume(l)	10.0	6.0	5.2	4.0	4.8	3.1
I.V.required(l)	9.7	4.8	5.7	4.9	5.5	3.9
Duration of diarrhoea (in 8 hour period)	8.0	3.2	3.5	2.1	4.1	2.1
Rectal swab positive (days)	4.8	0.9	2.6	0.7	1.8	0.8

TABLE I

	Placebo		Doxycycline		Tetracycline	
	Mean	SD	Mean	SD	Mean	SD
Number	19		17		15	
Age (yrs)	23.2	17.6	18.2	13.5	21.5	16.3
Height (cm)	147	24	130	25	138	28
Weight (kg)	33	13	25	11	30	13
Stool volume before Therapy (l)	2.0	1.1	2.1	1.7	2.0	1.7
I.V. fluid given (l)	5.2	2.0	4.4	2.3	4.2	2.2

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