Oral doxycycline in the treatment of adult chlamydial ophthalmia

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SUMMARY Ninety-three consecutive patients with adult chlamydial ophthalmia were treated with four different regimens of oral doxycycline. In patients treated with a single dose of 5 mg/kg of body weight (300 mg) of doxycycline the severity of clinical signs was reduced, and in half of the patients shedding of the infective agent was stopped. Treatment with a weekly dose of 300 mg of doxycycline for three weeks or a daily dose of 1.5 mg/kg of body weight (100 mg) for one week produced a clinical and microbiological cure in 100% of patients. However, in some of these patients mild to moderate papillary responses were present up to six months from completion of the treatment. The best results were obtained with a daily dose of 100 mg for two weeks, which produced rapid clinical and microbiological cure in all patients.

Adult chlamydial ophthalmia (ACO) or paratrachoma includes inclusion conjunctivitis, TRIC-agent punctate keratoconjunctivitis, and trachoma of sexually transmitted origin.¹ ACO is generally associated with a concurrent, but mainly asymptomatic, chlamydial genital infection in the patient and/or in the patient's consort(s).^{2,3} It is estimated that in the developed countries approximately 1% of the patients with a chlamydial genital infection may develop ACO (unpublished data). However, the prevalence of ACO is increasing because of the rising prevalence of chlamydial genital infections.⁴

ACO has been shown to respond well to topical treatment with tetracycline or rifampicin eye ointment when used for a minimum period of six weeks.^{5,6} However, the major setback in this method of therapy is the patient's poor compliance owing to difficulty with correct application of ointment and the long course of treatment. In addition the concurrent genital infection remains untreated, which may cause reinfection of the eye or other severe complications such as endometritis, pelvic inflammatory disease in women, and infertility in men and women.^{7,8} Oral therapy with systemic tetracycline has been shown to be effective against chlamydial genital infections⁹ and trachoma.^{1,10}

In this report we present the results of an open trial

of the efficacy of various regimens of therapy with oral doxycycline, a long-acting synthetic derivative of tetracycline, in the treatment of ACO.

Patients and methods

Patients. Patients attending the External Eye Diseases Clinic, Moorfields Eye Hospital, with a moderate or severe follicular conjunctivitis with or without keratitis and with a positive culture test for *Chlamydia trachomatis* were included. The patients were examined with a Haag-Streit 900 slit-lamp and the symptoms and signs observed in the whole of the conjunctiva (i.e., upper tarsus, upper fornix, and lower lid) and cornea were graded on a 0-3 scale following the method described earlier.⁵ Clinical scores were calculated by adding the individual scores for symptoms and signs from all areas of the conjunctiva and cornea. Patients were considered to be clinically cured when they had a clinical score of less than 10.

Chlamydial Isolation. Swabbings were collected from the whole conjunctiva and placed in plastic vials containing 2SP transport medium¹¹ with 3% fetal bovine serum. The methods of storage and transport of the conjunctival specimens and culture in irradiated McCoy cells are described elsewhere.¹²⁻¹⁴

Medication. Consecutive patients were treated with doxycycline on one of the following regimens: (a) a single dose of 300 mg (5 mg/kg body weight);

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(b) a weekly dose of 300 mg for three weeks; (c) an initial dose of 300 mg on the first day followed by a daily dose of 100 mg (1.5 mg/kg body weight) for one week; (d) an initial dose of 300 mg on the first day followed by a daily dose of 100 mg for two weeks. The patients were advised to take the drug after a meal.

Follow-up. Treatment was begun after the initial clinical and laboratory investigations. Follow-up clinical examinations and culture tests were carried out at weekly intervals for four weeks, then at six weeks, eight weeks, 12 weeks, six months and 12 months.

Results

Ninety-three consecutive patients with moderate to severe ACO and a positive culture for *C. trachomatis* were included in this study. The ages of the patients ranged from 16 years to 45 years, the majority being between 18 and 30 years old. There were 47 male and 46 female patients.

Single dose treatment. Eleven patients were treated with a single dose of doxycycline and followed up for eight weeks. Clinically no patient was cured (Table

1), but the intensity of inflammatory responses in all of these patients was substantially reduced (Table 2, Fig. 1). Microbiologically, four of the nine (44%) patients who attended regularly were culture negative at eight weeks (Table 2). However, because of the continuing presence of active clinical signs and/or positive culture tests, these patients were subsequently treated with 1% rifampicin eye ointment and were referred to our Genito-Urinary Medicine Clinic for investigation and management of probable chlamydial genital tract infection.

Weekly dose for three weeks. At 12 weeks 17 of the 22 patients treated on this regimen had completed their follow-up examinations. In all these patients clinical and microbiological cures were obtained (Table 1, Figs. 1 and 2). However, 5 of the 17 patients had persistent mild to moderate papillary responses up to six months after completion of treatment. These papillary responses resolved with no further treatment.

Daily dose for one week. All the 12 patients who were followed up at 12 weeks were microbiologically and clinically cured (Table 2; Figs. 1 and 2). Clinically three of the 12 patients showed papillary

Table 1 Number of patients cured following treatment with oral doxycycline

Treatment regimen	No. of patients	Four weeks clinical	culture*	Eight weeks clinical	culture†	12 Weeks clinical	culture‡
Single dose (300 mg)	11	0/11	5/11 (45%)	0/11	4/9 (44%)	Not done	Not done
Three weekly doses (300 mg)	22	14/22 (64%)	22/22 (100%)	14/22 (64%)	20/22 (91%)	17/17 (100%)	17/17 (100%)
One week (100 mg daily)	15	12/15 (80%)	15/15 (100%)	13/15 (87%)	13/13 (100%)	12/12 (100%)	12/12 (100%)
Two weeks (100 mg daily)	45	43/45 (96%)	45/45 (100%)	45/45 (100%)	43/43 (100%)	39/39 (100%)	39/39 (100%)

*Four weeks after beginning of treatment.

†Eight weeks after beginning of treatment.

‡Twelve weeks after beginning of treatment.

Table 2 Effect of different treatment regimens on clinical scores and isolation of *C. trachomatis*

Treatment Regimen	Number of patients	Time after commencement of treatment											
		Before		1 Week after		2 Weeks after		4 Weeks after		8 Weeks after		12 Weeks after	
		Aver. clin. score	No. of positives	Aver. clin. score	No. of positives	Aver. clin. score	No. of positives	Aver. clin. score	No. of positives	Aver. clin. score	No. of positives	Aver. clin. score	No. of positives
Single dose (300 mg)	11	42	11/11 (100%)	26	3/11 (27%)	22	8/11 (73%)	26	5/11 (45%)	22	4/9 (44%)		
Three weekly doses (300 mg)	22	42	22/22 (100%)	26	2/22 (9%)	18	2/22 (9%)	16	0/22	12	2/22 (9%)	9	0/17
One week (100 mg daily)	15	39	15/15 (100%)	21	1/15 (7%)	18	0/15	13	0/15	10	0/13	4	0/12
Two weeks (100 mg daily)	45	46	45/45 (100%)	20	2/45 (4%)	16	0/43	10	0/45	4	0/43	2	0/39

Clinical scores ≤10 trivial; 11–20 mild; 21–30 moderate; 31–40 severe.

Fig. 1 Clinical response to treatment on various regimens of oral doxycycline.

responses for up to six months after completion of treatment. These papillary responses resolved with no further treatment.

Daily dose for two weeks. All of the 39 patients who were followed up at 12 weeks were clinically and microbiologically cured.

Further follow-up. Further follow-up showed clinical and microbiological cure in those patients who did not attend regularly during the first three months of the study and were not included in the Tables 1 and 2.

Adverse reactions. Two of the 22 patients on

Fig. 2 Microbiological response to treatment on various regimens of oral doxycycline.

weekly doses for three weeks and three patients who received daily treatment for two weeks complained of nausea or epigastric burning.

Discussion

This open treatment trial was designed to find the optimal regimen of treatment with doxycycline for patients with ACO. The results showed that a single dose of 300 mg doxycycline reduces the severity of clinical signs and stops the shedding of *C. trachomatis* in about half of the patients. Treatments with a weekly dose for three weeks or a daily dose for one week were equally effective in producing clinical and microbiological cure in all the patients. However, some of these patients showed persistent papillary responses up to six months after completion of treatment, which resolved with no further treatment. The best result, however, was obtained with a daily dose of 100 mg for two weeks, when a rapid resolution of clinical signs was achieved. This finding is consistent with our previous study of treatment of trachoma with doxycycline in a village in Iran.¹¹

The advantages of therapy with doxycycline over other tetracyclines are that it requires minimal daily dose schedules, which greatly enhance patient compliance; it is better absorbed from the gut; and absorption is not affected by diet.

In this study we did not investigate the patients for the presence of chlamydial genital infections before the start of treatment. Three months after starting it 56 patients who had been treated with weekly or daily doses of doxycycline attended our Genito-Urinary Medicine Clinic. *C. trachomatis* was not isolated from specimens taken from the genital tract of any of these patients. In previous studies it had been shown that in untreated women and men with ACO 90% and 48% respectively had concomitant microbiologically proved genital chlamydial infections. The failure to isolate *C. trachomatis* from the genital tract of treated patients in this study suggests that oral doxycycline therapy can simultaneously cure both ocular and genital chlamydial infections.

The results of this study indicate that one weekly dose of doxycycline for three weeks, or a daily dose for one week, or a daily dose for two weeks are effective in the treatment of ACO and its associated genital infections. However, treatment with a daily

dose of doxycycline for two weeks produced a faster clinical recovery than the other two regimens.

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