WORLD VIEW

Impact of oral azithromycin on recurrence of trachomatous trichiasis in Nepal over 1 year

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Background: Recently, a significant association between *Chlamydia trachomatis* infection and post-operative trachomatous trichiasis (TT) recurrence was shown. The current study evaluated whether azithromycin treatment at the time of surgery could reduce recurrence.

Methods: As part of Nepal's national trachoma control programme, patients received azithromycin (53 patients) or placebo (56 patients) at surgery. Conjunctivae were graded for trachoma and swabbed to detect chlamydiae preoperatively and postoperatively up to 12 months. Logistic regression was performed for associations of treatment option with recurrence, infection, and active trachoma (by eye and by patient).

Results: TT recurrence was 28.9% at 12 months. Recurrence was significantly lower for those with major TT at baseline in the azithromycin group at 12 months ($p=0.03$); incident recurrence was also significantly lower at 6 months (OR, 0.056; 95% CI, 0 to 0.423; $p=0.004$). There was a trend for increased recurrence among those with minor TT at baseline and for reduction of active trachoma and infection in the azithromycin group but not the placebo group.

Conclusion: These data suggest that azithromycin treatment at the time of surgery may be warranted for patients with major TT. However, treatment should be investigated further for minor TT, for efficacy at subsequent time intervals and in other trachoma endemic settings.

Trachoma is a chronic ocular infection caused by *Chlamydia trachomatis*. Trachomatous trichiasis (TT; $\geq$ one eyelash touching the eye)¹ is a sequela of trachoma that occurs years to decades following infection. In hyperendemic areas where clinical disease and infection rates are high (30–50%), 8–17.5% of the population have TT.^{2–5} The World Health Organization (WHO) initiated the global elimination of blinding trachoma strategy, which calls for implementation of the SAFE programme⁶: Surgery (for TT), Antibiotics (for active trachoma), Facial cleanliness, and Environmental improvement for reducing transmission.

The surgery component⁷ of SAFE is effective in preventing progressive vision loss and blindness. However, TT recurrence rates regardless of surgical procedure are high, up to 75% in some countries.^{2–8–11} Few studies have prospectively evaluated potential risk factors for recurrence. One study found that conjunctival scarring and suture adjustment were associated with recurrence in Vietnam.¹² We recently showed that *C. trachomatis* infection at the time of surgery and at follow up was a significant risk factor for postoperative TT recurrence in Nepal.¹³ While the WHO recommends oral or topical treatment (topical tetracycline twice daily for 6 weeks or five consecutive days a month for 6 months) for active trachoma (follicular trachoma (TF) and/or inflammatory trachoma (TI)),¹⁴ there is no recommended antibiotic treatment for TT surgery. Treatment may reduce infection rates and disease severity in the short term, but in endemic areas, infection usually returns to pretreatment levels within a year or two.^{15–16} Also, topical treatment is not effective against extraocular reservoirs such as the nasopharynx, oropharynx, and rectum^{17–19} that could be a source for re-infection, and is not given to individuals without signs of active trachoma who may harbour chlamydiae,^{13–15} although mass treatment with azithromycin has been given regardless of clinical signs.

Treatment trials in Gambia, Egypt, and Saudi Arabia showed that oral azithromycin was as effective as topical tetracycline for the treatment of active trachoma.^{15–20–22} The

ease of oral dosing and efficacy for ocular and extraocular infections contribute to high rates of compliance and community acceptance.²³ The focus of this study was to evaluate whether azithromycin treatment at the time of TT surgery could significantly reduce the rate of postoperative recurrence over the course of 1 year in Nepal.

METHODS

Study population

This community intervention study was approved by Nepal Netra Jhoti Sangh (Nepali Prevention of Blindness Program) and Children's Hospital Oakland Research Institute institutional review board. Informed consent was obtained from all patients. A survey, which was similar to a previous survey conducted in a more remote district of Nepal,¹³ was conducted in a trachoma endemic district of Lumbini Zone to enumerate and grade for trachoma each household member according to the modified grading scale.²⁴

Trichiasis surgery and conjunctival sample collection

Bilamellar tarsal rotation surgery (BTRS) was offered to all TT patients with minor ($\leq$ five lashes touching globe) and major ($>$ five lashes touching globe) TT as recommended by WHO⁶ and performed by a Nepali ophthalmologist as part of the Nepali SAFE Program. Patients with evidence of self epilation (defined as eyelids with entropion but no lashes touching the globe) were also offered BTRS. None of the patients had undergone previous surgery, and no patient was re-operated during the 12 month study.

Trachoma was graded just before surgery (baseline) and postoperatively at 3, 6, and 12 months.²⁴ Upper tarsal conjunctival swabs were collected at baseline from the

Abbreviations: BTRS, bilamellar tarsal rotation surgery; OD, optical density; PCR, polymerase chain reaction; SES, socioeconomic status; TF, follicular trachoma; TI, inflammatory trachoma; TT, trachomatous trichiasis

Table 1 Baseline characteristics of trichomatous trichiasis (TT) patients in the treatment and placebo groups

	Total (%)	Treatment group (%)	Placebo group (%)	p Value
Sex*				NS (0.410)
Male	29 (26.6)	16 (30.2)	13 (23.2)	
Female	80 (73.4)	37 (69.8)	43 (76.8)	
Total	109 (100)	53 (48.6)	56 (51.4)	
Age (years)*				NS (0.188)
<40	20 (18.3)	9 (17.0)	11 (19.6)	
40–49	17 (15.6)	7 (13.2)	10 (17.9)	
50–59	31 (28.4)	15 (28.3)	16 (28.6)	
60–69	26 (23.9)	10 (18.9)	16 (28.6)	
70–79	15 (13.8)	12 (22.6)	3 (5.4)	
Total	109 (100)	53 (48.6)	56 (51.4)	
TT at surgery†				NS (0.300)
epilated (no eyelashes)‡	40 (27.0)	21 (29.2)	19 (25.0)	
≤ 5 eyelashes (minor)	67 (45.3)	28 (38.9)	39 (51.3)	
> 5 eyelashes (major)	41 (27.7)	23 (31.9)	18 (23.7)	
Total	148 (100)	72 (48.7)	76 (51.4)	
Active trachoma†				NS (0.813)
TF or TI or both	88/148 (59.5)	41/72 (56.9)	47/76 (61.8)	
Infection‡§				NS (0.993)
<i>C trachomatis</i> PCR+	13/144 (9.0)	7/69 (10.1)	6/75 (8.0)	

*Based on the number of patients.

†Based on the number of eyelids; no previous lid surgery for any study subject; TT defined as ≥one inturned eyelash (es) touching the globe of the eye.

‡Epilated cases defined as eyelids that had entropion but no eyelashes touching the globe, not included in the minor or major categories.

§Denominator differed from the number of eyelids at baseline (148) because of loss of four conjunctival samples.

operated eye and at 3, 6, and 12 months to detect chlamydiae as described.¹³ For ethical reasons, every patient with active trachoma (TF) and/or (TI) at baseline and each follow up was treated with tetracycline ointment according to WHO.¹⁴

Only one patient was in the operating room at a time. Immediately after surgery in the operating room, the patient received azithromycin or placebo (similarly coloured, shaped and sized tablet stored out of view of study subjects), in an alternating fashion and recorded as patient ID No/treatment type by the OR assistant who was blinded as to all examinations, data, and data analyses. Each patient was re-examined postoperatively at 24 hours. Follow up examinations at 3, 6, and 12 months were performed by the same two ophthalmic assistants masked as to previous examination, treatment group, and data analysis. No additional azithromycin or placebo was given at any time.

Detection of *Chlamydia trachomatis*

Conjunctival samples were tested for chlamydiae by Amplicor-PCR (Roche Diagnostics Corp, Indianapolis, IN,

USA) as described.¹³ Samples with an optical density (OD) <0.2 were considered negative while samples >0.8 were considered positive^{13–25}; samples with an OD of 0.2–0.8 were considered equivocal and screened by in-house polymerase chain reaction (PCR) as previously described.^{13–25} In-house PCR products of the correct molecular weight size on 2% agarose gels were considered positive if the negative control was negative, and negative, if there was no band, and positive and negative PCR controls were positive and negative, respectively.¹³

Data analysis

The outcome variables were active trachoma (defined above), chlamydial infection as measured by Amplicor and in-house PCR and incident and cumulative incident TT recurrence, defined as ≥one lash touching the globe or evidence of epilation, at 3, 6, and 12 months following BLTR surgery. Surgical failure was defined as ≥5 lashes touching the globe at the lateral margins of the surgical incision (instead of centrally) at 3 months. Surgical failures were excluded from

Table 2 Comparison between treatment and placebo groups for active trachoma and infection at 3, 6, and 12 months following TT surgery by multivariate analysis controlling for age, sex, and bilateral lid surgery

	Total* (%)	Treatment group (%)	Placebo group (%)	p Value†
Active trachoma (TF/TI)‡				
Baseline	88/148 (59.5)	41/72 (56.9)	47/76 (61.8)	NS (0.813)
3 month follow up	14/128 (10.9)	5/64 (7.8)	9/64 (14.1)	NS (0.911)
6 month follow up	17/114 (14.9)	6/56 (10.7)	11/58 (20.0)	NS (0.238)
12 month follow up	17/116 (14.7)	8/57 (14.0)	9/59 (15.3)	NS (0.891)
<i>C trachomatis</i> infection§				
Baseline	13/144 (9.0)	7/69 (10.1)	6/75 (8.0)	NS (0.993)
3 month follow up	4/118 (3.4)	2/60 (3.3)	2/58 (3.5)	NS (0.888)
6 month follow up	3/126 (2.4)	1/62 (1.6)	2/64 (3.1)	NS (0.967)
12 month follow up	5/118 (4.2)	2/60 (3.3)	3/58 (5.2)	NS (0.325)

TF, follicular trachoma inflammation; TI, intense trachoma inflammation; NS, not significant.

*Denominator is based on number of eyelids; survival analysis over the 12 month time period was performed using a Kaplan-Meier analysis with log rank test; results were similar to regression analysis.

†Multiple logistic regression controlling for age, sex, and bilateral lid surgery; statistical significance ($p \leq 0.05$).

‡Denominator differs from the number of eyelids at baseline because of loss of trachoma grading information and loss to follow up (table 3).

§Denominator differs from the number of eyelids at baseline because of loss of conjunctival samples and loss to follow up (table 3).

study analyses. Surgical complications were defined as haemorrhage, haematoma formation, and postoperative wound infection.

The explanatory variable was a single oral dose of azithromycin (1 g) versus a single oral dose of placebo given at baseline only. Univariate and multivariate analyses were performed using Stata (version 7.0; Stata Corp, College Station, TX, USA) to examine the associations of azithromycin treatment and placebo with active trachoma, infection, baseline TT severity, and postoperative TT recurrence. We controlled for age, sex, bilateral surgery, and tetracycline when performing multiple logistic regression. We performed the χ^2 test comparing TT recurrence in those who had unilateral surgery versus those who had bilateral surgery; we also performed the Huber-White sandwich estimators to adjust for two operated eyes from the same individual. Contingency table analysis was performed to examine crude associations. The χ^2 test or Fisher's exact test (when numbers were small) was used to determine significance ($p \leq 0.05$). Multiple logistic regressions were performed where the change in the β coefficient was $\geq 10\%$. A multiple comparison correction was performed for the subanalyses.

Survival analysis was performed using a Kaplan-Meier analysis with log rank test for the 12 month period of the study to estimate surgical cases at risk at the beginning of each time interval; we also examined the incidence in each interval and tested for the differences between treatment and placebo groups.

RESULTS

Characteristics of treatment and placebo groups

A total of 109 individuals participated in one of the Nepali trachoma control field camps and formed the basis for our analyses; 56 patients (76 eyelids) received placebo while 55 patients (72 eyelids) received azithromycin; two patients who were operated and received azithromycin died before the 3 month follow up, decreasing the number to 53. An additional 26 surveyed individuals with TT were away from their village on business at the time of the camp and could not be operated. There were no significant differences between those patients who consented to surgery versus those who were unavailable. Azithromycin and placebo groups had similar baseline characteristics (table 1).

Patient follow up

The treatment and placebo groups were well balanced as confirmed by a lack of significant differences (tables 1 and 2).

Patients were lost to follow up because they died from natural causes ($n = 3$) or were in another district. However, these patients were seen at two of three follow up time points (Table 3). Among those lost to follow up, there were no statistically significant differences between azithromycin and placebo groups.

C *trachomatis* infection rates and active trachoma

All conjunctival samples tested by Amplicor-PCR fell within the OD range of <0.2 or >0.8 , and, therefore, did not meet

the criteria for in-house PCR.²⁵ Table 2 provides the infection rates for treatment and placebo groups at each time point. There was no association between infection and TT severity at baseline.

Over 60% of the eyelids in both azithromycin and placebo groups had active trachoma while baseline infection rates were low, 8–10% (table 2). Since patients with active trachoma were given tetracycline ointment, the rate of active trachoma also reflects the numbers of patients who were treated with tetracycline (table 2; 56.9% (41/72) azithromycin versus 61.8% (47/76) placebo at baseline). At 3, 6, and 12 months, few patients in both groups had active trachoma and, thus, few were treated with tetracycline. There was no significant difference between the two groups in terms of tetracycline treatment for any time point (table 2). There was a trend for decreased active trachoma and infection at each follow up in the treatment versus placebo group.

Surgical failure

The rate of surgical failure overall was 5.6% (7/126 eyelids) at the 3 month follow up. Surgical failure was defined as ≥ 5 lashes touching the eye at the lateral margins of the surgical incision (instead of centrally located) occurring at 3 months. There was no significant difference between the failure rates for treatment and placebo groups (6.3% (4/63 eyelids) and 4.8% (3/63 eyelids), respectively). Individuals who epilated or had major TT at baseline had higher rates of surgical failure in both the treatment (10.5% (2/19) and 10.5% (2/19), respectively) and placebo (5.9% (1/17) and 15.4% (3/63), respectively) groups at 3 months; there were no surgical failures in either group for those with minor TT at baseline.

Association of baseline TT severity with postoperative TT recurrence

Surgical failure was excluded from all analyses. Patients with major TT had severe conjunctival scarring while those with minor TT had mild to moderate scarring at baseline (data not shown). Table 4 presents the incidence of TT recurrence for each time point; for example, the 12 month follow up incidence rate reflects TT recurrence compared with baseline, excluding TT recurrences that occurred at the 3 month and 6 month follow up. This provides an indicator of new incident cases for each time point to determine at which time point the highest number of recurrences are occurring. There was no significant association between TT severity at baseline with postoperative TT recurrence at 3 months, excluding those with surgical failure, between treatment and placebo groups (tables 4 and 5). At 6 months, there was a significant decrease in the incidence of recurrence in the azithromycin group compared with the placebo group for those who had major TT at baseline ($p = 0.004$) (table 4). The odds ratio (OR) of incident recurrence for the treatment group compared with the placebo group at 6 months was only significant for those eyelids with major TT at baseline: 0.056 (95% CI, 0 to 0.423, $p = 0.005$); for epilated cases and minor TT cases at baseline for the 6 months follow up, the OR was 0.525 (95% CI, 0.116 to 2.411; $p = 0.693$) and 3.429 (95%

Table 3 Follow up rates by eyelids* at each time point

	3 months (%)†	6 months (%)†	12 months (%)†
Treatment	64/72 (88.9)	62/72 (86.1)	63/71 (88.7)§
Placebo	64/76 (84.2)	65/74 (87.8)‡	60/73 (82.2)§

*Loss of follow up mainly because of patients being away from village at the time of examination.

†Four individuals in the treatment group and three in the placebo group had surgical failure at 3 months and were not included in the numerator for any time point.

‡Two lids (one patient) died of natural causes.

§One lid (one patient) died due to natural causes.

Table 4 Comparison of treatment versus placebo groups for the association of trachomatous trichiasis (TT) severity at baseline with the incidence of postoperative recurrence at 3, 6, and 12 months

TT severity at baseline	3 month TT incident recurrence*			6 month TT incident recurrence*			12 month TT incident recurrence*		
	Treatment group (%)	Placebo group (%)	p Value†	Treatment group (%)	Placebo group (%)	p Value†	Treatment group (%)	Placebo group (%)	p Value†
Epi-lated‡ (no eyelashes)	1/17 (5.9)	0/16 (0)	NS (1.000)	3/15 (20.0)	5/14 (35.7)	NS (0.427)	2/12 (16.6)	0/9 (0)	NS (0.872)
Minor TT (<5 eyelashes)	1/25 (4.0)	0/33 (0)	NS (0.431)	6/22 (27.3)	3/30 (10.0)	NS (0.144)	0/15 (0)	0/27 (0)	NS
Major TT (>5 eyelashes)	2/17 (11.8)	0/11 (0)	NS (0.505)	1/16 (6.3)	8/14 (57.1)	0.004	1/16 (6.3)	0/5 (0)	NS (1.000)
Total	4/59 (6.8)	0/60 (0)	NS (0.057)	10/53 (18.9)	16/58 (27.6)	NS (0.279)	3/43 (7.0)	0/41 (0)	NS (0.241)

NS, not significant.

*Denominator reflects number of eyelids; TT incident recurrence compared with baseline; Surgical failures were excluded from this table; surgical failure was defined as ≥ 5 lashes at the lateral margins of the surgical incision (instead of centrally located) and touching the globe of the eye at the 3 month follow up; TT recurrence was defined as ≥ 1 lash touching the globe of the eye following TT surgery, excluding surgical failures.† χ^2 test; p values reflected the differences in incidence rates between treatment and placebo groups according to TT status at baseline, after excluding surgical failures; statistical significance ($p \leq 0.05$).

‡Epi-lated cases defined as eyelids that had entropion but no lashes touching the globe, not included in the minor or major categories.

CI, 0.837 to 13.843; $p = 0.144$), respectively. ORs could not be calculated for 3 month or 12 month follow up time points as there were zero values in the numerator. At 12 months, there was no significant difference in incidence rates between the treatment and placebo groups because of the small number of TT recurrences (table 4). The greatest number of TT recurrences were at the 6 month follow up.

For cumulative incidence rates (table 5), there were fewer recurrences in the azithromycin group (3/16) compared with the placebo group (8/14) at 6 months for those with major TT at baseline. However, the numbers did not quite reach statistical significance ($p = 0.057$). At 12 months, there were significantly fewer TT recurrences in the treatment group (4/19) compared to the placebo group (8/13) for those with major TT at baseline ($p = 0.030$). Of note is that there was a trend for minor TT cases at baseline to have a greater number of TT recurrences at 6 months and 12 months in the azithromycin group compared with the placebo group, although the numbers did not reach statistical significance (table 5). However, for the placebo group at 6 months and 12 months, there was a significantly higher number of recurrences associated with those who had major TT at baseline (8/14 and 8/13, respectively) compared to those who had minor TT at baseline (3/30 and 3/30, respectively) ($p = 0.003$).

The above results remained the same after controlling for topical tetracycline treatment in our multivariate model. There was also no significant difference in TT recurrence among those patients who had bilateral eye surgery compared with those with unilateral eye surgery.

Survival analysis using Kaplan-Meier estimates found that there was no difference in TT recurrence among the placebo versus the treatment group.

DISCUSSION

We previously demonstrated that chlamydial infection at the time of TT surgery and at follow up was a significant risk factor for recurrence in a trachoma endemic district in Nepal.¹³ In the current community intervention study, we found a significant reduction in the incidence of TT recurrence for the azithromycin group compared with the placebo group at 6 months for those who had major TT at baseline. While the cumulative incidence at 6 months did not quite reach statistical significance, the p value of 0.057 (table 5) is supportive of the incidence data. For those individuals with minor TT at baseline, there was a greater number of TT recurrences in the azithromycin treatment group compared with placebo, although the numbers did not reach statistical significance. Importantly, the placebo group at 6 months and 12 months had a significantly higher number of recurrences for patients with major TT and severe scarring at baseline compared to those who had minor TT at baseline (tables 4 and 5; $p = 0.003$). This would be expected given that severe scarring has been associated with TT recurrence.¹² The cumulative incidence at 12 months showed a significant reduction in recurrence for those with major TT at baseline in the azithromycin group, which would be expected based on the 6 month findings. Thus, our data collectively support the notion that azithromycin treatment appears to be effective in preventing postoperative TT recurrence up to 12 months for patients with major TT at baseline.

Variation in surgical outcome for TT has been reported in previous studies where recurrence rates were 8–12.1% at 3 months,^{26, 27} 6.2–11.1% at 6 months,^{13, 27} and 9–25% at approximately 1 year.^{11, 13} Only one surgeon operated during the present study to eliminate inter-surgeon variation as a confounding factor. Yet, we noted seven cases of surgical

Table 5 Comparison of treatment versus placebo groups for the cumulative incidence of postoperative trachomatous trichiasis (TT) at 6 and 12 months with the severity of TT at baseline by multiple logistic regression controlling for age, sex, and bilateral lid surgery

TT severity at baseline	6 month TT cumulative incident recurrence*			12 month TT cumulative incident recurrence*		
	Treatment group (%)	Placebo group (%)	p Value†	Treatment group (%)	Placebo group (%)	p Value†
Epilated‡ (no eyelashes)	4/15 (26.7)	5/14 (35.7)	NS (0.700)	5/16 (31.3)	5/14 (35.7)	NS (0.796)
Minor TT (<5 eyelashes)	7/22 (31.8)	3/30 (10.0)	NS (0.075)	7/22 (36.4)	3/30 (10.0)	NS (0.075)
Major TT (>5 eyelashes)	3/16 (18.8)	8/14 (57.1)	NS (0.057)	4/19 (21.1)	8/13 (61.5)	0.030
Total	14/53 (26.4)	16/58 (27.6)	NS (0.911)	17/57 (29.8)	16/57 (28.1)	NS (0.955)

*Denominator reflects number of eyelids; surgical failures were excluded from this table; surgical failure was defined as ≥ 5 lashes at the lateral margins of the surgical incision (instead of centrally located) and touching the globe of the eye at the 3 month follow up; TT recurrence was defined as ≥ 1 lash touching the globe of the eye following TT surgery.

†Multiple logistic regression; statistical significance ($p \leq 0.05$).

‡Epilated cases defined as eyelids that had entropion but no lashes touching the globe, not included in the minor or major categories.

failure at 3 months. These cases were excluded from the data analyses since they would confound the effect of treatment.

We also found a high rate of active trachoma at the time of surgery. Patients were consistently graded by two ophthalmic assistants who had worked on previous trachoma studies where the concordance of active trachoma and infection was high.¹³ However, conjunctival inflammation might be due to infection with bacteria other than *C. trachomatis*. In many trachoma endemic countries including Nepal, there can be seasonal or non-seasonal outbreaks of conjunctivitis from multiple bacterial species, including *Haemophilus influenzae*, *Haemophilus aegyptius*, and *Streptococcus pneumoniae*.¹ Consequently, co-infection may promote inflammation,¹ which may have contributed to the higher number of individuals who were graded with active trachoma at baseline in our study.

Chlamydial infection was 9.0% at baseline while the infection rate in our previous study in Nepal was $\geq 27.8\%$.¹³ Chlamydial infection was determined by the same commercial test in both studies. The current study was conducted near the East-West highway while the previous study was conducted in a more remote district with difficult access. Proximity to roads often correlates with environmental and sanitation improvement and higher socioeconomic status (SES), which has historically been linked to a substantial reduction or elimination of trachoma in countries undergoing some industrial development.¹⁰ This effect likely contributed to the lower rates of infection in the current study. The true rates of chlamydial infection may also be underestimated as there is recent evidence that the organism may persist in the conjunctiva of trachoma patients²⁰ as well as the cervix.¹⁹ Persistent chlamydiae may evade detection by residing in subepithelial tissues that would not be accessible to current swabbing techniques.

We also evaluated whether topical tetracycline may have contributed to the low infection rates. At baseline, 56.9% and 61.8% of the azithromycin and placebo groups, respectively, received topical tetracycline for active trachoma. This should not affect the outcome because there was no significant difference between the azithromycin and placebo groups for tetracycline treatment. Furthermore, there were no significant differences at subsequent follow up time points where numbers of active trachoma cases were very small and thus few patients received tetracycline (table 2). While topical tetracycline would be expected to decrease infection rates after the baseline treatment, this response would be unlikely to be sustained for 6 months¹⁶ and, thus, unlikely to impact TT recurrence at 6 or 12 months. In fact, if it did, we would expect fewer recurrences in both azithromycin and placebo groups, which was not the case.

In conclusion, azithromycin treatment significantly improved the rate of TT recurrence compared with placebo up to 12 months for patients with major TT at the time of surgery, although there was a trend for increased TT recurrence in the azithromycin treatment group among those with minor TT at baseline. Larger studies, including randomised clinical trials, would help to elucidate whether azithromycin treatment will decrease the risk of TT recurrence among those with minor TT and in other endemic populations. Research in trachoma areas with higher chlamydial infection rates will also be important to determine the duration of treatment efficacy.

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There are no competing interests.

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