CLINICAL SCIENCE

Longitudinal study of trachomatous trichiasis in the Gambia

R J C Bowman, H Faal, M Myatt, R Adegbola, A Foster, G J Johnson, R L Bailey

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See end of article for authors' affiliations

Correspondence to: Mr R J C Bowman, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK; richardbowman@iceh.freeserve.co.uk

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Aim: Investigation of the natural history of trachomatous trichiasis in the Gambia and of the outcome of self epilation and surgery for the condition.

Methods: A 1 year longitudinal study of 190 subjects with trichiasis was performed. Major trichiasis cases (five lashes or more) were referred for surgery and minor trichiasis cases were advised to epilate. Outcome measures included progression of trichiasis and corneal scarring; attendance for and results of surgery.

Results: 34 of 148 (23%, 95% CI 16 to 31) subjects with major trichiasis attended for surgery over the year. Progression from minor to major trichiasis occurred in 18 of 55 subjects (33%, 95% CI 21 to 47). Progression of corneal scarring occurred in 60 of 167 patients (36%, 95% CI 29 to 44). Clinically active trachoma and conjunctival bacterial isolation predicted progression of corneal opacity. Surgery was successful in 39 of 54 (72%) eyes.

Conclusions: Despite the overall decline in trachoma in the Gambia, patients with both minor and major trichiasis remain at risk of developing corneal opacity. Active trachomatous inflammation and additional infection with bacteria may accelerate this process. Antibiotic treatment for trichiasis patients (in addition to surgery) should be investigated. Surgery for minor trichiasis may be indicated. Regular audit of surgical results is necessary with retraining where needed.

Trachoma, a chronic conjunctivitis caused by *Chlamydia trachomatis*, has sight threatening complications such as trichiasis and corneal scarring. It remains the world's commonest form of preventable blindness, mainly affecting disadvantaged communities. The World Health Organization (WHO) estimates that 146 million children and adults have active inflammatory trachoma, and that 10 million people have trichiasis and need urgent surgery.[1]

The WHO is promoting the global elimination of trachoma as a public health problem by the year 2020 (GET 2020) and has adopted the SAFE strategy: *S*urgery for entropion and trichiasis, *A*ntibiotic treatment for active infection, and the promotion of both *F*acial cleanliness and *E*nvironmental improvement to reduce transmission, in order to achieve this goal.[2] Surgery is the one component of the SAFE strategy, which has been shown to prevent blindness,[3] in practice, however, acceptance of surgery in affected communities has been disappointingly low.[4 5] The need to investigate barriers to and improve uptake of trichiasis surgery was identified as a research priority by the WHO Alliance.[6]

Poor acceptance of surgery is known to be a problem in the Gambia but despite that there has been a decline in trachomatous blindness. Is it possible that trichiasis becomes less likely to result in corneal opacity and blindness when the community prevalence of active infection falls below a certain level? Reinfection has been shown to be important in development of the scarring complications of trachoma but its role in the pathway from trichiasis to blindness is not known. The importance of additional bacterial infection has been suggested but not investigated.[7] Very few longitudinal data are available on the scarring complications of trachoma and the path to blindness. In view of poor acceptance of surgery, information on the natural history of trichiasis may help national control programmes to predict future surgical loads and estimate the cost of low surgical coverage in terms of visual disability.

For the past 10 years, the Gambian national eye care programme has provided trichiasis surgery, predominantly performed by trained ophthalmic nurses, routinely at a number of rural health centres in addition to the two main hospitals. There is a charge of US$2.50 per eye. The standard surgical technique used in the Gambia is the modified tarsal rotation procedure. It is similar but not identical to the bilamellar tarsal rotation, which was found to be the best procedure among those tested in a randomised controlled trial.[3] Both techniques involve a transverse lid incision with eversion of the distal fragment. The difference is that in the modified tarsal rotation the transverse lid incision involves conjunctiva and tarsal plate sparing orbicularis and skin and there is some dissection between orbicularis and tarsal plate in the distal fragment, whereas in the bilamellar tarsal rotation the transverse lid incision is full thickness including orbicularis and skin with no dissection of the terminal fragment (like a Wies procedure to the upper lid). Although the bilamellar technique is recommended by the WHO as a result of the above trial, the modified tarsal rotation (not included in the trial) is widely used throughout Africa. It is thought by some to be easier to teach and has been reported by Bog and colleagues[8] as safe and effective when performed by a trained nurse in the community. Current Gambian practice is to refer only patients with major trichiasis (five or more lashes abrading the globe) for surgery and to treat minor trichiasis with repeated epilation. This classification has been previously reported as an indication for surgery[8] and is standard in the Gambia. Although outcomes have been reported for electroepilation,[3 9] the outcome of simple mechanical epilation (much more widely practised) for trichiasis has not previously been reported.

A study was designed to measure surgical uptake in the Gambia and the factors which influence it. This study is presented in a separate paper (*Invest Opthalmol Vis Sci*, in press) but it provided the opportunity also to study the factors influencing progression of trichiasis to corneal scarring and blindness in patients who refused surgery or were advised to epilate. It is these findings that are presented in this paper.

Table 1 World Health Organization classification of corneal opacity[10 11]

Detailed system[11]	Simple system[10]	Definition
0	0	No scarring
1	0	Minimal scarring or opacity but not involving the visual axis, and with clear central cornea
2	CO	Moderate scarring or opacity involving the visual axis, with the pupillary margin visible through the opacity
3	CO	Severe central scarring or opacity with the pupillary margin not visible through the opacity

METHODS

Ethical approval

The study was designed in accordance with the Declaration of Helsinki and the joint Gambia Government/Medical Research Council ethics committee approved the study and its procedures.

Recruitment

Three geographic divisions of the Gambia with the highest prevalence of trachoma in a 1996 national survey,[10] Western Division, North Bank Division, and Lower River Division, were chosen for village based recruitment of patients with unoperated trichiasis. Villages of varying size and ethnicity were chosen. The importance of lid surgery and the nature and aims of the study and the benefits of lid surgery were explained to village leaders during sensitisation visits. Subjects with past or present problems with lashes rubbing on the eye were invited to attend a central point in the village. Further community screening was not conducted. Subjects with trichiasis or signs of epilation were eligible for recruitment unless they had already had lid surgery and gave individual consent following further explanation in an appropriate local language. All subjects were offered immediate epilation and a tube of tetracycline ointment to apply twice a day. Subjects with minor trichiasis were treated by epilation and those with major trichiasis referred for surgery according to usual Gambian practice.

Clinical examination

Clinical examination was performed by an ophthalmologist (RJCB) at each visit included grading of active trachoma (using the standard WHO grading[11]—TF or trachoma follicular: five or more lymphoid follicles on the central area of the upper tarsal conjunctiva; and TI or trachoma intense: diffuse inflammation of the tarsal conjunctiva which obscures 50% or more of the deep tarsal vessels), degree of trichiasis (major or minor), and corneal scarring (using a more detailed WHO grading,[12] see Table 1) with a torchlight and 2.5× magnification loupe. Trichiasis in an eye was classified as major trichiasis if five or more lashes were abrading the globe or as minor trichiasis if four or fewer lashes were abrading the globe, and subjects were classified according to their worse eye. In cases where lashes had been epilated, the classification of major or minor was based on the extent of epilation estimated by the number of bare lash follicles present. Visual acuities were measured in daylight with a standard tumbling E Snellen chart. The standard WHO definitions of visual impairment (visual acuity worse than 6/18 in better eye) and blindness (visual acuity worse than 3/60 in better eye) were used.

Microbiology

Conjunctival swabs (dry) for bacterial culture were taken only from patients living in regions where same day access to a microbiology laboratory was possible. Swabs were plated onto blood agar, transported in a candle jar, and incubated in 5% carbon dioxide at 37°C.

Follow up

Examinations were repeated at 6 and 12 months and all patients with major trichiasis at any visit were referred for surgery.

Data handling and analysis

Data were entered and analysed with EPI-INFO software, version 6. Possible predictors of disease progression (including age, sex, demographic and socioeconomic parameters (including income sources, type of dwelling, livestock ownership, educational level), severity of trichiasis at baseline, presence of clinically active trachoma, conjunctival bacterial isolation, epilation practices, and undergoing surgery) were tested for significance using χ^2 tests with continuity corrections. Possible factors influencing surgical success including the above factors and location of surgery and the level of experience of the operating surgeon were similarly investigated.

RESULTS

Major trichiasis patients (mean age 55 years, SD 14, range 11–80) were older (t = 3.4, p <0.001) than minor trichiasis patients (mean age 47 years, SD 16, range 9–78). A demographic profile of study subjects by trichiasis status is

Table 2 Profile of study subjects (n=190)

	Major trichiasis (n=135)	Minor trichiasis (n=55)
Female sex	100 (74%)	44 (80%)
Western Division	69 (51%)	36 (65%)
Gambian citizens	122 (91%)	53 (96%)
Mandinka ethnic group*	109 (81%)	32 (58%)
Muslim religion	131 (97%)	49 (89%)
Attended Koranic school	30 (22%)	9 (16%)
Attended Western school	4 (3%)	5 (9%)
Bilateral trichiasis*	119 (88%) (84 bilateral major + 35 minor in 2nd eye)	25 (45%)

*Significant difference in proportion (p<0.05).

Table 3 Treatment practices with epilation

Perception	Frequency out of 190 (%)
Epilate	161 (85%)
Weekly or more frequently	68 (36%)
By:	
Self	54 (28%)
Friend or family member	98 (52%)
Health worker	9 (5%)
Using:	
Locally made forceps	89 (47%)
Fingers	54 (28%)
Sharp blade	7 (4%)
Hot ash as adjunct	42 (22%)
Other treatments:	
Traditional eye medicine	40 (21%)

Table 4 Progression rates of trichiasis and corneal opacity over 12 months

	Proportion	%	95% Confidence interval
Minor trichiasis to major trichiasis (either eye)	18/55	33	21 to 47
Unilateral to bilateral trichiasis	21/46	46	31 to 61
Incident/progressive corneal scarring (any worsening of WHO grade, Incidence of sight threatening corneal opacity (grades 0 or 1 at baseline and 2 or 3 at 12 months, either eye)	10/104	10	5 to 17

Table 5 Progressive corneal scarring and visual status improvement over 1 year in surgical attenders and non-attenders (major trichiasis only)

	Surgical proportion (%)	Non-surgical proportion (%)	Relative risk value (95% CI)	p Value
Progressive corneal scarring	14/32 (44%)	33/96 (34%)	1.3 (0.8 to 2.1)	0.46
Visual status improvement	8/31 (26%)	11/85 (13%)	2.0 (0.88 to 4.94)	0.17

shown in Table 2 and epilation practices are indicated in Table 3. None of the demographic variables tested had a significant influence on the laterality (unilaterality versus bilaterality) of trichiasis or on epilation practices.

All 135 patients with major trichiasis were referred for surgery at baseline, and all non-attenders as well as a further 13 patients (who had progressed from minor to major) were referred at 6 months. Of the 148 subjects thus referred a total of 34 patients attended for surgery (attendance rate = 23%, 95% CI 16.5 to 30.6) in the 12 month period, including two of the 13 referred because they had progressed at 6 months. In 20 subjects both eyelids were operated on and in 14 surgery was unilateral: 54 eyelids were operated on in all.

At the last available follow up, 39 of the 54 (72%) eyes operated on were completely free of trichiasis, five (9%) had major trichiasis and nine (19%) had minor trichiasis (one loss to follow up). In five operated eyes, which were free of trichiasis at 6 months, trichiasis had recurred by 12 months. No significant predictors of surgical failure were identified. Complications, noted in eight (24%) subjects, included five suture granulomas requiring excision, two cases of slight lid notching, and one case of a 2 mm ptosis with reduced levator function.

A total of 173 of 190 (91%) subjects were seen at 6 months, and 169 of 190 (89%) at 12 months; 183 (96%) subjects were seen at either 6 or 12 months. Eight (4%) subjects died during the 12 months and two refused to be re-interviewed or examined at the follow up visit. The remainder of those lost to follow up had moved to an unknown location. Ten patients who had moved within the Gambia were successfully traced: 74 of 190 (39%, 95% CI 32 to 46) patients were found to have signs of active trachoma at least one of the three visits (age range 24–80). This was commoner in subjects with major trichiasis (relative risk (RR)=1.60 (1.00 to 2.57) p=0.05). It was also associated with the presence of pannus in one or both eyes at baseline (RR=1.65 (1.01 to 2.69) p=0.04). The association between active disease and major trichiasis was independent of age and pannus.

In 22 of 97 (23%) subjects, bacteria were isolated from conjunctival swabs at either 6 or 12 months. *Staphylococcus aureus* was isolated in nine cases, *Streptococcus pneumoniae* in five cases, *Haemophilus influenza* (non type B) in four cases, *Streptococcus* group C in two cases, *Moraxella catarrhalis* in two cases, *Klebsiella* species in two cases, non-specific Gram negative species in one case, and *Haemophilus parainfluenza* in one case. Four subjects had mixed infections.

Progression rates from minor to major and unilateral to bilateral are illustrated in Table 4. The use of ash as an aid to epilation was associated with transition from unilateral to bilateral trichiasis (RR 2.48 95% CI 1.37 to 4.47, p = 0.015). The presence of baseline pannus was predictive of transition from minor to major trichiasis (RR = 1.99, 95% CI 1.02 to 3.89, p = 0.05).

At 6 months, seven of 139 unoperated subjects (5%) no longer had trichiasis and three of these remained trichiasis free at 12 months. At 12 months nine of 135 (7%) unoperated subjects no longer had signs of trichiasis. Subjects with minor trichiasis at baseline were more likely (RR 1.20, 95% CI 1.05 to 1.38, p = 0.003) to be free of signs of trichiasis at 6 or 12 months.

Ninety nine (52%) subjects had corneal opacity in at least one eye at baseline, and in 58 (31%) this was sight threatening (WHO grades 2 and 3 or CO). Rates of progression are shown in Table 4. The rate of progression was similar for left and right eyes. Risk factors for progression of corneal scarring in either eye included the presence of clinically active trachoma on at least one occasion (RR = 1.66, 95% CI 1.10 to 2.51, p = 0.03) and bacterial growth from a conjunctival swab on at least one occasion (RR = 1.91, 95% CI 1.23 to 2.97, p = 0.02). Degree of baseline trichiasis did not significantly affect progression of corneal scarring (42/116=36% of major trichiasis experienced progression versus 18/51=35% minor trichiasis). Subjects who experienced progressive corneal scarring were more likely to complain that symptoms interfered with work (RR = 1.71, 95% CI = 1.10 to 2.66, p = 0.02). There was no significant difference in the progression of corneal scarring in subjects accepting surgery compared with those who did not (see Table 5) and no difference in the risk factors for progression between compliers and non-compliers (even if only successful operations were considered).

Of 171 subjects tested at baseline 93 (54%) had normal visual acuity at baseline, 65 (38%) had visual impairment, and 13 (7%) were blind. The distribution was similar at 1 year: of 167 subjects tested 101 (60%) had normal vision, 56 (34%) were visually impaired, and 10 (6%) were blind. The incidence of visual impairment and blindness was 8/88 = 9% (95% CI 4 to 17) over the 12 months. Against this, 21 patients (14%, 95% CI 9 to 20) improved their visual status (that is, from blind to visually impaired or visually impaired to normal) over the year. Undergoing surgery (even if only successful operations were considered), degree of baseline trichiasis, or progressive corneal scarring were not significantly correlated with changes in visual acuity. There was, however, a trend which suggested that major trichiasis at baseline (9/104=9%) as opposed to minor trichiasis (2/47=4%) was associated (RR=2.1, 95% CI 0.48 to 9.45) with visual status deterioration.

None of the demographic variables tested had a significant influence on any of the indices of disease progression.

DISCUSSION

Because of the poor attendance for surgery reported here (the subject of a separate paper) and elsewhere, the natural history of trichiasis and the outcomes of epilation are important information for eye care planners and are previously unreported. This study reveals that despite the decline in active trachoma in the Gambia,[12] trichiasis is a progressive disease with 46% unilateral cases becoming bilateral, 33% of minor trichiasis cases becoming major, and 36% cases experiencing incident or progressive corneal scarring within 1 year. Because there are infrequent opportunities for eye examination in a rural setting it may be appropriate to consider recommending surgery for minor trichiasis cases (previously shown to be of anatomical but not visual benefit compared to cryotherapy and electrolysis[3]) and for asymptomatic fellow eyes. It is possible that epilation resulted in some true major trichiasis cases being misclassified as minor, hence exaggerating the subsequent progression rates. This would be another reason for abandoning the distinction and offering surgery to all trichiasis cases. Since attendance is related to symptom severity, however, uptake of surgery for minor trichiasis and fellow eyes would be expected to be low.

This population practised epilation more frequently than reported in Tanzania[10] and, except where hot ash was used as an adjunct, this did not have a measurable beneficial or adverse effect on progression of disease. The use of hot ash as an aid to epilation by trichiasis patients has not, to our knowledge, been previously reported and probably contributes to progressive trichiasis by causing further conjunctival scarring. This practice should be discouraged through health education programmes though changing cultural traditions such as this can be difficult.

Thirty nine per cent of subjects were observed to have active trachoma at some point during the study, much higher than might be expected from the national prevalence estimate for this age group (0.9–1.6%),[10] even allowing for observation on three occasions. Microbiological confirmation of active trachoma was not possible owing to technical problems with polymerase chain reaction (PCR) but the clinical grading was made by an ophthalmologist experienced in trachoma and the clinical appearance was very suggestive of TI. Furthermore, the diagnosis was supported by an association with baseline corneal pannus known to be associated with active trachoma. Other possible explanations for the appearance could include viral or bacterial conjunctivitis (though there was no association between the appearance and bacterial conjunctival isolation) or even persistent mechanical trauma from lashes directed subtarsally or eye rubbing induced by the discomfort of trichiasis. Assuming that this appearance did represent active trachoma, it could be that scarring and trichiasis develop in people who are inherently more prone to recurrent infection, or that trichiasis itself predisposes to reinfection through mechanical damage to the ocular surface. Previous work in the Gambia found that cell mediated immune responses to chlamydial antigens (which are important in resolving disease episodes) were reduced in scarred subjects compared to non-scarred controls from similar communities.[13] Our study provides some evidence that episodes of conjunctival infection may drive the progression of visually threatening lesions. Both active trachoma and infection with other bacteria were associated with progressive corneal scarring in our study, and the presence of pannus (usually associated with chlamydial infection) predicted progression of trichiasis. Repeated chlamydial infection has been shown to produce progressive scarring in studies in animals[14] and has been implicated in epidemiological studies[15] of scarred subjects. These observations suggest a possible benefit from targeting trichiasis patients and their families with antibiotic therapy as an adjunct to surgery. This illustrates the importance of an integrated SAFE strategy, which addresses active infection and transmission as well as trichiasis.

We isolated a number of other pathogenic micro-organisms from the conjunctivae of these trichiasis patients, and their presence was associated with progressive corneal opacity. Others have speculated on the relative contribution of infections with *Chlamydia trachomatis* and other bacteria in the pathogenesis of chlamydial disease[7] but this remains unknown. Azithromycin has been found to be as effective in one single oral dose as 6 weeks of topical tetracycline for active trachoma,[16] and has been donated by its manufacturers to the International Trachoma Initiative for trachoma control programmes in selected countries. It is preferentially localised to inflamed tissues[17] and would have effectively treated many of the bacterial conjunctival infections in our study.[18] Whether repeated azithromycin treatment of subjects with trichiasis will effectively reduce the rate of disease progression could be investigated in countries receiving donated drug.

Caution should be exercised in the generalisation of the progression indices to the whole population since active disease, shown to be a factor, is known to cluster geographically. A randomly selected population based sample might have provided more accurate data but would have been difficult because of time and logistical constraints and the need for repeated visits. The case finding technique used resulted in most patients coming from Western Division and hence an over-representation of Mandinkas (comprising approximately 40% of the national population but 75% of the study sample and further over-representation in minor cases compared to the major), who predominate in this region. The effect of this on the results is uncertain. Ethnicity is not an obvious marker for geography or socioeconomic status in the Gambia though cultural practices do vary. The Mandinkas are the largest ethnic group in the Gambia and are scattered throughout the country. They might be thought to be at less risk of trachoma than smaller more marginalised groups. A previous study of ours, however,[19] found that Mandinka ethnicity was associated with progression from TS (trachomatous scarring without trichiasis) to TT (trachomatous trichiasis). In this study, however, no ethnic predisposition to progression of trichiasis was seen. The small sample size limited the power of the study to detect weaker risk factors for disease progression —for example, a risk factor occurring in 50% of the population would have had to increase the risk by about 80% (RR 1.8) to be detected in this study with 80% power and 95% confidence intervals.

Although 80% of surgical patients reported themselves pleased with the results and the surgery worth the expenditure, surgical success rate was only 72% after at most 1 year. This is worse than comparable reports of 77% success at 21 months[3] and 81% at 24 months.[7] More experienced surgeons had a tendency towards better results but numbers were small and health centre records were sometimes inadequate to ascertain who had performed the surgery. Community surgery programmes entail larger numbers of surgeons being trained and it is important that accurate records are kept and follow up performed to allow audit and retraining where necessary.

No statistically significant benefit from surgery in terms of corneal scarring or visual acuity was demonstrated in this study, but the short follow up, although minimising losses, limited the power of the study to detect changes in visual acuity. Most of the subjects had not previously performed a Snellen visual acuity test and some learning curve is inevitable, accounting for some of the patients who improved their visual status over the year. This may have masked both deterioration in acuity because of slowly progressive disease and improvements after surgery. There was however a trend between undergoing surgery and improved visual status (Table 5)

which did not reach statistical significance because of low acceptance but which supports a previous study from Oman with demonstrated visual benefit for surgery for major trichiasis compared to non-operated fellow eyes.[3] In that study follow up was longer (21 months) and the severity of disease was greater and visual impairment probably more quickly progressive in the control (fellow) eyes. The use of fellow eyes as controls is more likely to demonstrate a visual benefit from surgery because patients who attend for surgery are more likely to have severe disease.[5 10] It is possible that progressive corneal scarring may have motivated some subjects to attend for surgery, and that the surgery was consequently too late to be of optimal visual benefit. Because subjects were examined infrequently and the information available on timing of the surgery was incomplete, we do not know whether this was the case. Further follow up studies of trichiasis surgery may clarify these issues, and long term follow up of our cohort would be valuable.

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Authors' affiliations

R J C Bowman, M Myatt, G J Johnson, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK
R J C Bowman, H Faal, National Eye Care Program of the Gambia, PO Box 950 Banjul, Gambia
A Foster, R L Bailey, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK
R Adegbola, R L Bailey, Medical Research Council Laboratories, Fajara, PO Box 273, Banjul, Gambia

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