Reducing the risk of postoperative trichiasis: lessons from a clinical trial

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Considerable efforts are ongoing across nearly 50 countries to eliminate trachoma—one of the leading causes of blindness worldwide—as a public health problem by 2020. The provision of high-quality surgery for people with trichiasis (end-stage trachoma) is crucial for the achievement of the WHO elimination targets. Estimates[1] suggest that more than 3 million individuals require trichiasis surgery to prevent blindness due to trichiatic eyelashes that scratch the surface of the eye. Previous trichiasis surgery programmes have reported poor surgical outcomes, with more than 40% of patients developing postoperative trichiasis in some settings.[2]

In the past 15 years, substantial research efforts have focused on the improvement of trichiasis surgery outcomes, and the study by Esmael Habtamu and colleagues[3] in this issue of *The Lancet Global Health* reinforces the fact that skilled trichiasis surgeons can reduce the risk of postoperative trichiasis. Habtamu and colleagues did a randomised, clinical trial to investigate whether a 28-day course of oral doxycycline could reduce the risk of postoperative trichiasis from 18% to 10%. 12 months after surgery, 12% of patients in both the doxycycline group and placebo group had developed postoperative trichiasis, which is perhaps the most important finding of the study.

Few previous studies have reported such a low incidence of postoperative trichiasis across the full spectrum of trichiasis severity, with the exception of one trial[4] that investigated the use of antibiotics at the time of surgery and one arm of a clinical trial[5] comparing two surgical procedures. One key similarity across these studies was that the most skilled surgeons were chosen to do the study-based surgeries, whereas in other well conducted trials[6,7] that have adopted programmatic approaches to surgical provision using all available surgeons, the proportion of patients with postoperative trichiasis was much higher, with substantial variation across surgeons.

These findings underscore the importance of limiting the provision of surgery to highly-skilled trichiasis surgeons who receive regular supportive supervision. Globally, the trichiasis community has made progress in this area by developing guidelines to improve training for trichiasis surgery and establishing recommendations that all patients are followed up between 6 weeks and 6 months after surgery.[8] However, work is still needed to ensure that only individuals with demonstrated skills are selected to train as trichiasis surgeons, and that these surgeons receive consistent support and regular supervision from qualified supervisors. Furthermore, the study highlights the value of having an external evaluator to assess new surgeons at the end of their training who can provide unbiased feedback and certification. In previous trials that have reported a low incidence of postoperative trichiasis, including the study by Habtamu and coworkers, an external evaluator selected the participating surgeons from a competitive pool, and selected only the most qualified individuals.

The trial by Habtamu and colleagues[3] investigated whether oral doxycycline once daily for 28 days after surgery would reduce the risk of postoperative trichiasis within 1 year compared with placebo. The scientific rationale for the use of doxycycline stems from a series of studies suggesting that doxycycline can inhibit matrix metalloproteinase enzymes and fibroblasts linked to the inflammation and scarring associated with recurrent corneal erosions[9,10] and trachoma.[11] However, the trial found that doxycycline had no effect on the risk of postoperative trichiasis.

A previous clinical trial[4] suggested that in addition to anti-microbial effects, antibiotics might have other benefits. The authors investigated the use of a single dose of oral azithromycin compared with 6 weeks of topical tetracycline to reduce the risk of repeat ocular chlamydial infection after trichiasis surgery, since ocular chlamydial infection is known to cause incident trichiasis. The proportion of patients with postoperative trichiasis was significantly lower in the azithromycin group than the tetracycline group;[4] however, few participants in either treatment group had ocular chlamydia at follow-up. It is possible that the anti-inflammatory properties of azithromycin were of benefit, but the study was not designed to investigate that hypothesis.

Considering the existing evidence, it is unclear whether other anti-inflammatory drugs can reduce the risk of postoperative trichiasis. Future studies

investigating the effect of reducing scarring on the incidence of postoperative trichiasis should assess drugs with stronger anti-inflammatory properties and should also consider comparing the study drug with oral azithromycin because it has demonstrated efficacy when given after surgery that was deemed to be of high quality.

Habtamu and colleagues concluded that doxycycline should not be integrated into standard care for trichiasis surgery. However, unfavourable outcomes were rare, which serves as a reminder to the trachoma community that attaining good surgical results is achievable.

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I declare no competing interests.

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1 WHO Alliance for the Global Elimination of Trachoma by 2020. Eliminating trachoma: accelerating towards 2020. 2016. http://www.trachomacoalition.org/sites/all/themes/report-2016/PDF/GET2020_2016_EN.pdf (accessed March 8, 2018).

2 Khandekar R, Mohammed AJ, Courtright P. Recurrence of trichiasis: a long-term follow-up study in the Sultanate of Oman. *Ophthalmic Epidemiol* 2001; **8:** 155–62.

3 Habtamu E, Wondie T, Aweke A, et al. Oral doxycycline for the prevention of postoperative trachomatous trichiasis in Ethiopia: a randomised, double-blind, placebo-controlled trial. *Lancet Glob Health* 2018; **6:** e579–92.

4 West SK, West ES, Alemayehu W, et al. Single-dose azithromycin prevents trichiasis recurrence following surgery: randomized trial in Ethiopia. *Arch Ophthalmol* 2006; **124:** 309–314.

5 Habtamu E, Wondie T, Aweke S, et al. Posterior lamellar versus bilamellar tarsal rotation surgery for trachomatous trichiasis in Ethiopia: a randomised controlled trial. *Lancet Glob Health* 2016; **4:** e175–84.

6 Burton MJ, Kinteh F, Jallow O, et al. A randomised controlled trial of azithromycin following surgery for trachomatous trichiasis in the Gambia. *Br J Ophthalmol* 2005; **89:** 1282–88.

7 Gower EW, West SK, Harding JC, et al. Trachomatous trichiasis clamp vs standard bilamellar tarsal rotation instrumentation for trichiasis surgery: results of a randomized clinical trial. *JAMA Ophthalmol* 2013; **131:** 294–301.

8 WHO. World Health Organization Alliance for Global Elimination of Trachoma by 2020: Second Global Scientific Meeting on Trachomatous Trichiasis. 2016. http://apps.who.int/iris/bitstream/10665/250571/1/WHO-HTM-NTD-2016.5-eng.pdf (accessed March 8, 2018).

9 Dursun D, Kim MC, Solomon A, Pflugfelder SC. Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9, doxycycline and corticosteroids. *Am J Ophthalmol* 2001; **132:** 8–13.

10 Wang L, Tsang H, Coroneo MT. Treatment of recurrent corneal erosion syndrome using the combination of oral doxycycline and topical corticosteroid. *Clin Exp Ophthalmol* 2008; **36:** 8–12.

11 Li H, Ezra DG, Burton MJ, Bailly M. Doxycycline prevents matrix remodeling and contraction by trichiasis-derived conjunctival fibroblasts. *Investig Ophthalmol Vis Sci* 2013; **54:** 4675–82.