Background: Although endonasal laser dacryocystorhinostomy (ELDCR) offers many advantages compared with conventional techniques, postoperative scarring leading to occlusion of the rhinostomy is more common with ELDCR.

Objective: To investigate whether fluorouracil applied to the rhinostomy site intraoperatively has an effect on the outcome.

Participants: We randomly allocated 155 consecutive patients (201 procedures) to a control group and a fluorouracil group. Patients and investigators were masked to the choice of treatment.

Methods: All patients underwent ELDCR. A pledget soaked in isotonic sodium chloride solution or 0.5-mg/mL fluorouracil, randomly allocated by the pharmacy, was applied to the rhinostomy site for 5 minutes at the time of surgery. Patients were followed up for 12 months and their symptoms were assessed at each visit.

Results: Among patients followed up for 12 months or longer, ELDCR procedures performed with topical application of fluorouracil to the rhinostomy site were successful in 65 (76%), compared with 52 (63%) for the control group. This was not statistically significant when patients who failed to attend follow-up at or after 12 months were not counted as successfully treated ($P = .21, \chi^2$ test). Even if those who failed to attend for follow-up were counted as successes, the effect of fluorouracil did not reach significance at the .05 level ($P = .08, \chi^2$ test).

Conclusion: The topical application of fluorouracil failed to increase the patency rates in ELDCR.


A N EXTERNAL dacryocystorhinostomy (DCR) is widely accepted as the gold standard in the treatment of acquired distal nasolacrimal duct obstruction. The conventional approach described by Toti1 in 1904 has been modified, and the reported success rates are high, ranging from 80% to 99%.2 This external approach has the disadvantage of leaving the patient with a facial scar and a greater than 3% risk for postoperative bleeding.

Endonasal laser DCR (ELDCR) has recently been gaining popularity as an alternative approach. The endonasal laser-assisted approach has all the advantages associated with outpatient surgery under local anesthesia. It also requires a shorter operating time.3 In addition, no externally visible facial scars result. Our group previously reported our results of 97 procedures using the holmium:YAG laser to fashion the rhinostomy. This procedure resulted in an initial success rate of 78% at 3 months, with a further failure rate of 19% at 12 months.4

Unlike conventional DCR, in which the aim is to obtain an edge-to-edge anastomosis of the lacrimal sac and nasal mucosa is used to keep the rhinostomy patent, ELDCR relies on secondary-intention healing to create a fistula. Scarring of the nasal mucosa is the primary cause of failure of the procedure. Endonasal DCR performed using conventional instruments has a good success rate, but it is less feasible as an outpatient procedure, and it cannot be performed while patients are undergoing anticoagulation. Endoscopic DCR allows wide exposure of the sac and the approximation of mucosa from the sac to nasal mucosa.5

We believe that because of the many benefits afforded by ELDCR compared with conventional DCR, modifications to this technique aimed at increasing long-term patency rates merit further investigation. Many agents have been shown to reduce the process of healing and scarring after surgery. Fluorouracil is a pyrimidine analogue that is known to inhibit fibroblast proliferation by inhibition of thymidylate synthase necessary for DNA synthesis.

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synthesis. The use of fluorouracil and mitomycin is now well established in the prevention of postoperative conjunctival scarring in high-risk patients undergoing glaucoma surgery.6 Similarly, such antimetabolites may have a role in the reduction of scar formation of the nasal and lacrimal mucosa due to lacrimal surgery. We conducted a double-masked, randomized, controlled trial to investigate whether fluorouracil applied to the rhinostomy site during ELDCR affects the outcome of this procedure. Herein we report the outcome of this trial.

METHODS

We randomly allocated 155 consecutive patients with evidence of primary nasolacrimal obstruction (eg, epiphora, mucocele, dacyrocystitis) and symptoms severe enough to require surgery to one of 2 groups. Randomization was performed in the pharmacy department using isotonic sodium chloride solution in the control group. This study was approved by the ethics committee of the University Hospital, Nottingham, England, and patients were all given an information sheet before informed consent was obtained. Age, sex, and indications for surgery were recorded for all patients, and all procedures were performed by the same team of an ophthalmologist (R.D.) and a rhinologist (N.S.J.). The ELDCR was performed on all patients using a holmium:YAG laser, and nasolacrimal intubation was performed with silicone stents. Most surgery was performed with the patient under local anesthesia, and the method of surgery was unchanged from that of previous reports from our group.7 A cotton pledget soaked in isotonic sodium chloride solution or fluorouracil (0.5 mg/mL) was applied to the nasal ostium under direct visualization for 5 minutes after the rhinostomy had been created. The ostium was then washed through with isotonic sodium chloride solution in both groups. Surgeons and patients remained masked to the choice of treatment until the study and follow-up had been completed.

Postoperative treatment consisted of a 1-month course of topical nasal steroid (betamethasone dipropionate). Silicone stents were used in all patients and were routinely removed 3 months after surgery under direct visualization with the nasal endoscope; an additional 1-month course of topical steroids was then administered. Preoperative and perioperative evidence of nasolacrimal mucosal scarring was also noted.

The patients’ symptoms were assessed and recorded at each postoperative visit for the presence of epiphora. The state of the nasal mucosa and the nasal ostium was assessed with a rigid 30°, 2.7-mm nasal endoscope, and nasolacrimal syringing was performed. Follow-up was defined as the time from surgery.

RESULTS

One hundred fifty-five patients underwent 201 ELDCR procedures. Forty-six patients had bilateral surgery; 57 underwent the procedure on the right side; and 52 underwent the procedure on the left side. Patients included 101 women and 54 men, and the mean age of all patients was 66 years. We randomized 54% of the men and 49% of the women to the treatment arm. One patient opted for general anesthesia, whereas 154 patients underwent local anesthesia. One hundred fifty-four patients were treated as outpatients, and 1 patient required hospital admission.

CONTROL GROUP

We performed 98 ELDCR procedures (in 76 patients) with the intraoperative application of isotonic sodium chlo-

FLUOROURACIL GROUP

One hundred three ELDCR procedures were performed on 82 patients with intraoperative application of 0.5-mg/mL fluorouracil to the rhinostomy site. Follow-up time ranged from 2 to 48 months, and 85 cases (83%) were assessed at 12 months or later. Of those, 65 (76%) were free of epiphora at their last visit. Postoperative systemic levels of fluorouracil were undetectable (<0.625 µmol/L) in all patients. The invariable cause of treatment failure was stenosis of the rhinostomy site at the nasal mucosa that was visible. Stenosis was palpable by means of gentle probing, and the mucosa could be seen to bulge with syringing.

COMMENT

Massaro et al3 first reported the technique of ELDCR, and it was soon recognized as a promising alternative to the conventional external approach. This procedure had the potential to change DCR into an elegant, minimally invasive operation. The advantages mentioned in the literature include limitation of tissue injury to a discrete rhinostomy site, avoidance of an externally visible scar, excellent hemostasis, the ability to perform lacrimal surgery on an outpatient basis, quicker rehabilitation, decreased overall expense, and patient preference.

However, the aims of a DCR are to leave the patient with a patent, unscarred rhinostomy, to bypass primary nasolacrimal obstruction, and to relieve the patient of the presenting symptoms, regardless of the technique used. Unfortunately, the success rates of external DCR have not been reproduced using the endonasal laser-assisted approach.

A review of 169 external DCRs quoted a long-term success rate of 92%,8 and many other series have reported similar outcomes. Success rates for ELDCR have been lower. Boush et al9 reported a 70% success in primary surgery, which increased to 80% with a revision ELDCR. Similar success rates have been reported by Woog et al10 (82%), Seppa et al11 (83%), and Metson et al12 (85%). However, few studies have compared the 2 techniques within the same unit. Hartikainen et al13 performed a prospective, randomized comparison of external DCR and ELDCR, and reported success rates of 91% and 63%, respectively.

Most cases of failed DCR are due to postoperative scarring in which a submucous membrane or scar tissue can be seen to occlude the ostium. In ELDCR, the decreased amount of surgical trauma to the adjacent tissues might be anticipated to produce a more limited inflammatory response. Modulation of this postoperative healing response may be a key factor in maintaining the ostium patency in external DCR and ELDCR techniques, and could increase the overall success rate of the procedures. The fibroblast is the key player in the formation of scarring in response to tissue damage.14 Stages that have been commonly identified include stimulation of fibroblasts and migration to the site of injury, me-
diated by chemotactic factors; cell division and proliferation; contraction of the granulation tissue; and synthesis of an extracellular matrix. The pharmacological control of scarring can target any of these stages; however, drugs that control fibroblast proliferation have been the most popular. Mitomycin has been shown experimentally and clinically to have a useful effect on scarring. Hu et al have shown that proliferation of cultured human nasal fibroblasts is inhibited by brief exposure to mitomycin, and Liao et al have used intraoperative mitomycin administration successfully in external DCR to limit the extent of scarring at the ostium. Camara et al recently reported a retrospective, single-masked case-control study in which mitomycin was used intraperoperatively in a series of 123 consecutive endoscopic laser-assisted DCRs; they achieved an overall success rate of greater than 99% compared with 89% for a group of 48 patients in whom mitomycin was not used. No obvious explanation exists for the discrepancy between the good results of the ELDCR control group in the latter report compared with those in this study or those reported in the literature.8-12

To our knowledge, the use of fluorouracil has not previously been reported in ELDCR. Fluorouracil is a synthetic pyrimidine that inhibits the formation of thymidine and so has its maximal influence on DNA synthesis. Fluorouracil also affects cell protein synthesis by binding to RNA as a secondary mode of action. No published studies have investigated the effect of fluorouracil on nasal fibroblasts in vitro. However, in vitro studies have shown that fluorouracil inhibits the proliferation of conjunctival fibroblasts, and clinically it has been used successfully in controlling scar formation after aqueous drainage surgery for glaucoma, providing a rationale for a probable role in reducing endonasal and lacrimal scarring.

Our success rate for ELDCR with intraoperative fluorouracil administration was 76%, compared with 63% for the standard ELDCR procedure in patients who underwent a minimum follow-up of 12 months. Statistical analysis of these results using the χ² test with the Yates continuity correction suggests that this difference is not statistically significant (P = .21). Fifty patients attended follow-up appointments for less than 1 year (25% of procedures). This figure may partly reflect a subgroup of patients who did not attend because their symptoms had been relieved. However, per our study protocol, these patients were excluded from the statistical analysis. Many reported studies regard nonattendance at follow-up as an indicator of success. We do not believe this to be good practice. However, even if an optimistic scenario were envisaged and these nonattenders were considered to have undergone successful treatment, no significant difference would be found between the 2 groups (fluorouracil group, 81% [n=83]; control group, 69% [n=68]; χ² test, P = .08).

**CONCLUSIONS**

Endonasal laser DCR avoids an external scar when compared with external DCR; it allows surgery to be performed in a shorter operating time and it also makes an outpatient procedure more viable. The success rates of ELDCR are worse than those for external and endoscopic DCR due to scar formation at the rhinostomy site. This study sought to determine whether the application of topical fluorouracil reduced scar formation and improved patency rates.

This prospective, randomized controlled study showed no improvement in patency rates with the application of fluorouracil (P = .21). The success rates of surgery in the study are not as good as those for external DCR or endonasal DCR using mucosal flaps.

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**REFERENCES**


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