Original Article

Oral versus single intravenous bolus dose antibiotic prophylaxis against postoperative surgical site infection in external dacryocystorhinostomy for primary acquired nasolacrimal duct obstruction – A randomized study

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Purpose: To compare the efficacy of a single perioperative bolus dose of intravenous antibiotic versus postoperative oral antibiotic prophylaxis for prevention of surgical site infection (SSI) in external dacryocystorhinostomy (DCR) for primary acquired nasolacrimal duct obstruction (PANDO).

Methods: This was a prospective randomized controlled study with a noninferiority design. Patients undergoing external DCR surgery were randomized into two groups A and B. Patients in group A received a single bolus dose of intravenous cefazolin 1 g at surgery, whereas those in group B received oral cephalxin 500 mg postoperatively twice a day for 5 days. Allocation concealment was ensured by sequentially numbered opaque sealed envelopes (SNOSEs). Both groups were advised identical postoperative local wound care regimens. Any clinical evidence of SSI at 4 weeks of follow-up in either group was the main outcome measure.

Results: In all, 338 patients randomized into two groups of 169 patients each participated in this study. At follow-up of 4 weeks, only one patient in group B developed postoperative SSI. None in group A developed postoperative SSI. Other potential risk factors for postoperative SSI were also analyzed by univariate and multivariate analyses but none achieved statistical significance in either group.

Conclusion: Our results demonstrate that a single bolus dose of perioperative intravenous antibiotic offers adequate prophylaxis against postoperative SSI and compares favorably with the more commonly used oral antibiotic prophylaxis in external DCR for PANDO in our population and our practice scenario.

Key words: Antibiotic prophylaxis, external dacryocystorhinostomy, surgical site infection

External dacryocystorhinostomy (DCR), first described by Toti in 1904,[1] has been a surgical procedure in widespread use for a very long time to address the problem of an obstructed nasolacrimal duct. Despite the advent of and the rapid increase in the use of endoscopic lacrimal surgery, a recently published survey shows that external DCR is preferred by a majority of ophthalmic plastic surgeons[2] and is considered the “gold standard” against which all other surgical techniques for DCR are compared. External DCR can be classified as a “Class II” or a “clean-contaminated” surgical procedure and the expected wound infection rate for such procedures is reported in the literature to be around 10%.[3] It is also reported that this may be lowered for Class II wounds by the use of prophylactic antibiotics.[4] Literature regarding surgical site infection (SSI) rates in external DCR surgery is very sparse. A wound infection rate of around 10% may be clinically considered to be a significantly high figure. This raises the question of the need for routine postoperative prophylactic antibiotic therapy in these cases especially when considering the diverse practice scenarios under which this surgery is performed in different geographical areas of the world. In the authors’ area of practice, use of postoperative oral prophylactic antibiotic therapy in external DCR surgery is the most commonly followed practice pattern.

Before planning this randomized study, the authors observed that perioperative intravenous prophylactic antibiotic administration appeared efficacious in preventing SSI in external DCR and was extremely convenient, cost-effective, and had no compliance issues.

This study was thus designed to investigate the comparative efficacy of postoperative oral antibiotic versus a single intravenous perioperative bolus dose antibiotic prophylaxis against postoperative SSI in external DCR in patients randomized into two groups.

Methods

This study was conducted at the authors’ institution between February 2014 and July 2015. A total of 338 patients were recruited for the study and were randomized into two groups of 169 each.

Adult patients (18 years of age or older) undergoing external DCR for primary acquired nasolacrimal duct obstruction (PANDO) were included in the study. Syringing of
the nasolacrimal system was performed to confirm the presence of PANDO. All patients had to complete at least 4 weeks of postoperative follow-up for inclusion in the study. Patients with secondary nasolacrimal duct obstruction (NLDO), congenital NLDO, known immunosuppression (cancer patients undergoing chemotherapy and those with HIV-positive status), and inability to complete a minimum of 4 weeks of postoperative follow-up were excluded. The purpose for excluding cases with secondary NLDO was to prevent inclusion of cases that could have a possible predisposition to postoperative SSI and thereby create a bias affecting the final outcome in the study groups.

Study approval was obtained from the institutional ethics committee and the study adhered to the tenets of the Declaration of Helsinki. The study had a noninferiority design and the patients were randomly assigned to two groups designated as A and B. Randomization was performed by use of a computer-generated sequence of random number series, and allocation into groups was done preoperatively by the sequentially numbered opaque sealed envelope (SNOSE) technique. The operating surgeon had no role in the allocation of the patients, and the allocation status of the patient was kept concealed from the surgeon. Group A consisted of patients receiving a single intravenous perioperative bolus dose of 1 g of cefazolin (a first-generation cephalosporin) within 15 min before surgical incision. The antibiotic was administered to the patient before the surgeon entered the operating room. For patients known to be allergic to penicillins and/or cephalosporins, 1 g of vancomycin was considered as an alternative to be administered as an intravenous infusion. Group B consisted of patients receiving postoperative oral antibiotic prophylaxis – 500 mg of cefalexin (also a first-generation cephalosporin) twice daily for 5 days. For patients known to be allergic to penicillins and/or cephalosporins, 500 mg of azithromycin was considered as an alternative to be administered orally once daily for 5 days. However, none of the patients in the study had known drug allergy to cephalosporins, and hence there was no need to administer these alternative drugs. External DCR surgery was performed in a standard fashion as described elsewhere in the literature. In all, 24 patients (7.1%) were documented to have mucoceles/mucopyoceles with either frank pus or mucus with pus evident upon sac incision during surgery. Thirteen of these were in group A and 11 were in group B. Bicanalicular intubation was not performed as a routine in all of our patients. We used an absorbable 6-0 coated polyglyactin 910 suture with a spatulated needle to suture the incisional wound. The wound was sutured in two separate layers (deeper sutures for the orbicularis muscle and superficial sutures for the skin) with interrupted sutures. Postoperative wound care (local wound toilet with application of 5% povidone iodine followed by local application of a combination of polymyxin-B sulfate and chloramphenicol eye ointment twice daily to the sutured wound for the first postoperative week) was identical for both groups. Oral nonsteroidal anti-inflammatory drugs were used for postoperative pain relief as required. The patients underwent removal of the skin sutures at the first week postoperative visit and were finally assessed for wound healing at the end of the fourth postoperative week. In an attempt to reduce possible bias, evaluation at each postoperative visit was performed by an assessor other than the operating surgeon for most but not all visits. It was not possible to maintain this uniformity for a sample size of more than 300 patients due to logistical difficulties as patient assessment was sometimes made on routine outpatient postoperative visits.

Patients were seen twice during the postoperative period – at 1 week and at 4 weeks after surgery – and were assessed for the presence of SSI as the primary outcome measure. SSI was diagnosed in the presence of frank purulent discharge from the wound or in the presence of serous/nonpurulent discharge from the wound with clear signs of associated cellulitis. The secondary outcome measures noted at 4 weeks of follow-up were early failure of DCR surgery (failure was defined by nonpatency to lacrimal syringing), occurrence of any episode of secondary hemorrhage, and scar prominence as subjectively reported by the patients.

Being a noninferiority study design, the assumed difference between the true mean response rates in the two groups was taken to be zero. For a study power of 80% with an alpha error of 0.05 and a noninferiority margin of 0.02, the total sample size was calculated to be 308. A 10% addition was made to the total sample size as a buffer against possible loss to follow-up. The final sample size was 338 with 169 patients being allocated to each arm of the study. Descriptive statistics were used to analyze the demographic parameters, and univariate and multivariate regression analyses were carried out to assess the factors that could possibly influence the final primary outcome measure.

Results

A total of 400 consecutive patients were assessed for eligibility during the study period and 338 patients were recruited as per the inclusion criteria and necessary sample size. The sample was equally divided into 169 patients each in two groups A and B. All patients in both groups received the planned intervention as per the study protocol. A total of 27 patients (14 in group A and 13 in group B) were excluded from the final analysis due to loss to follow-up. The final analysis was performed with 155 patients in group A and 156 patients in group B.

Table 1 provides the comparison of demographic data of the two groups showing they were well matched with respect to the parameters considered for analysis. With respect to the primary outcome measure, at 4 weeks postoperative follow-up, none of the patients in group A (those receiving

| Parameter                              | Group A | Group B | P value |
|----------------------------------------|---------|---------|---------|
| Mean age (years)                       | 50.17   | 52.18   | 0.15    |
| Males                                  | 74      | 60      | 0.14    |
| Females                                | 95      | 109     | 0.15    |
| Comorbidity – DM                       | 3       | 8       | 0.22    |
| Comorbidity – HTN                      | 9       | 11      | 0.82    |
| Mean duration of symptoms (months)     | 14.52   | 16.30   | 0.12    |
| Acute dacryocystitis                   | 10      | 10      | 1.00    |
| Regurgitation on pressure over the sac | 116     | 106     | 0.30    |
| Mean duration of surgery (min)         | 51.29   | 47.42   | 0.54    |

DM: Diabetes mellitus; HTN: Hypertension
a single perioperative intravenous bolus dose of antibiotic] showed any evidence of SSI, whereas only one patient in group B (those receiving 5 days of postoperative oral antibiotic) developed an SSI which was successfully managed medically. This difference in primary outcome was well below the noninferiority margin of 0.02 considered during the sample size calculation and was thus both statistically and clinically insignificant. A study was also made of the risk factors that could possibly have influenced the primary outcome measure. Six independent potential risk factors (age, duration of symptoms, acute dacryocystitis, duration of surgery, surgery done by fellow versus consultant, and diabetes mellitus as a comorbidity) were analyzed by univariate and multivariate regression analyses and none of them was seen to achieve statistical significance in either of the two groups. However, both in univariate and in multivariate analyses, the odds ratios for SSI were slightly higher for patients with diabetes mellitus as a comorbidity.

The secondary outcome measures studied were as follows. At 4 weeks follow-up, 3 of 155 patients in group A and 6 of 156 patients in group B had a failed external DCR giving short-term success rates of around 98% and 96%, respectively. The difference between the groups was not statistically significant. Within the follow-up period of the first 4 postoperative weeks, five patients from group A and two patients from group B developed an episode of secondary hemorrhage. All were managed successfully by conservative measures. Four patients in each group subjectively reported noticing a conspicuous scar at the incision wound site.

Discussion

Use of routine postoperative antibiotic prophylaxis in external DCR surgery has been an area of some debate, and diverse practices are followed in different practice scenarios across the world. A survey of the members of the American Society of Ophthalmic and Reconstructive Surgery (ASOPRS) showed an almost even split of opinion where 48% were in favor of and 50.3% were against the use of routine antibiotic prophylaxis in DCR surgery with many respondents specifying that the decision to use prophylactic antibiotics depended on the degree of preoperative inflammation present.[5] However, the questionnaire used for this ASOPRS survey did not include an option to assess the degree of preoperative inflammation present. On the other hand, studies from the United Kingdom have shown higher rates of postoperative cellulitis in open lacrimal surgery in the absence of prophylactic antibiotic use.[6] In a retrospective study, Walland and Rose reported soft-tissue infection in 7.9% of their patients who underwent open lacrimal surgery and did not receive postoperative prophylactic antibiotics as against 1.6% of patients who did receive postoperative prophylactic antibiotics. The difference they noted between the groups was statistically significant (P < 0.02).[6]

Postoperative cellulitis is believed to be a significant risk factor for the failure of open lacrimal surgery,[8] and studies by Walland and Rose[6] and Vardy and Rose[9] have shown that the use of oral or intravenous postoperative antibiotic prophylaxis reduces the rate of soft-tissue infection. In a prospective, nonrandomized, comparative trial of three separate methods used for the prevention of postoperative infection in open lacrimal surgery, Vardy and Rose demonstrated that intraoperative and postoperative antibiotic prophylaxis are equally efficacious in preventing postoperative cellulitis in open lacrimal surgery.[5] Prevention of postoperative infection has been reported to be more effective in preventing failure of DCR than treating postoperative infection once it has occurred.[9] In their retrospective study, Yazici and Meyer have advocated selective antibiotic use for prevention of postoperative wound infection after external DCR.[9] In their series, they used intraoperative intravenous antibiotics for patients who had inflammatory signs at the medial canthal region or for those who had purulent collection within the sac at surgery. Oral antibiotics were administered to patients with persistent external medial canthal inflammation before and after surgery. They concluded that for patients undergoing external DCR, selective use of antibiotics in those demonstrating signs of lacrimal sac inflammation was likely to be sufficient for prevention of postoperative infection. Dulk et al.[10] also noted that in 6% of their patients with mucoceles and purulent material noted at surgery, there was no occurrence of SSI. They also reported an infection rate of 1.2% with a 95% confidence interval (CI) of 0.3%–6.6%. Considering the lower limit of the CI, the number needed to treat (NNT) to prevent one case of postoperative SSI was calculated to be 104, but considering the upper limit of the CI, the NNT was calculated to be 19. That indicated a fairly wide range of NNT. They stated that successful treatment of preexisting infection before surgery yields infection rates that are significantly lower than previously estimated even without routine systemic antibiotic prophylaxis. All their patients did not receive any oral or intravenous antibiotic but did receive topical antibiotics for 1 week postoperatively. All their cases with acute dacryocystitis and mucocele were treated till the inflammatory signs settled before surgery was performed which was identical to the practice followed by the authors of this study. Their number of mucoceles with purulent material noted at surgery were 6% of the cases and did not demonstrate any occurrence of postoperative SSI but were too small to make any significant statistical analysis. They concluded that routine use of systemic antibiotic prophylaxis in external DCR may not be justified. In their retrospective analysis of a fairly large sample of patients, Pinar-Suiero et al. reported similar outcomes and recommended prophylactic antibiotics for external DCR in patients with prior episodes of mucocele, mucopyocele, or acute dacryocystitis.[10] In this study, the authors had 7.1% of patients with pus or mucopus noted on sac incision at surgery. None of these patients had any evidence of postoperative SSI. In addition, the presence of preoperative infection in the form of acute dacryocystitis was not found to be a statistically significant risk factor for postoperative SSI either by univariate or multivariate analysis.

In their article discussing bacteremia during DCR surgery in 52 cases, Ali et al.[11] reported that they did not find any intraoperative bacteremia and none of the patients had wound infection irrespective of postoperative prophylaxis. All their patients (100%) received an intraoperative single bolus dose of cefuroxime immediately after withdrawal of blood. Clean cases of PANDO without any sac discharge on marsupialization (22% of the total cases) were not prescribed any postoperative prophylactic antibiotics, whereas all the other patients (78%) received postoperative oral antibiotics for 5 days. Thus, 22% of their patients received intraoperative bolus dose of an antibiotic
and 78% received both an intraoperative bolus dose and oral postoperative prophylactic antibiotic coverage. There were no patients who did not receive any form of antibiotic at all. They mentioned that the practice of postoperative prophylactic antibiotic administration after DCR surgery continues to be widely prevalent in the developing world and based on their finding of absence of intraoperative bacteremia suggested that routine use of such prophylaxis may not be justified.[11]

The opinion on whether routine postoperative antibiotic prophylaxis is necessary in external DCR still remains a slightly contentious one with very little in the literature to recommend any preferred practice pattern guidelines. The older literature would appear to recommend its use,[6-8] while others recommend usage in selected cases,[5,10] and still others suggest that routine use may not be justified.[9,11] In this study, we found that in our practice scenario, the use of a single intravenous bolus dose of antibiotic is as efficacious for prophylaxis against postoperative SSI in external DCR as the more commonly used 5-day oral antibiotic regimen. The strength of this study lies in the fact that it was randomized and the sample size in both groups was fairly large. We also found that there was better patient compliance to and decreased cost of medication with intravenous prophylactic antibiotic use when compared with oral antibiotic prophylaxis although the study was not designed to formally evaluate these outcomes. Improved compliance may potentially have some contribution in the prevention of development of antibiotic resistance out in the community. The limitations of the study were that logistical issues precluded us from conducting a completely masked study and that there was no separate control arm consisting of patients who did not receive any postoperative prophylactic antibiotic coverage.

**Conclusion**

In conclusion, we believe that a single perioperative intravenous bolus dose of antibiotic is effective prophylaxis against postoperative SSI in external DCR and may be recommended as the method of choice where antibiotic prophylaxis for postoperative SSI is being considered in external DCR surgery.

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