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A Comparison of Treatment Approaches for Bilateral Congenital Nasolacrimal Duct Obstruction

Katherine A. Lee¹, Danielle L. Chandler², Michael X. Repka³, Michele Melia², Roy W. Beck², C. Gail Summers⁴, Kevin D. Frick⁵, Nicole C. Foster², Raymond T. Kraker², and Scott Atkinson⁶ on behalf of PEDIG^{*}

¹St. Lukes Children's Ophthalmology, Boise, ID

²Jaeb Center for Health Research, Tampa, FL

³Wilmer Ophthalmological Institute, Johns Hopkins University, Baltimore, MD

⁴University of Minnesota, Minneapolis, MN

⁵Johns Hopkins School of Public Health, Johns Hopkins University, Baltimore, MD

⁶St. John's Clinic - Eye Specialists, Springfield, MO

Abstract

Purpose—To compare clinical outcomes of two treatment approaches for bilateral nasolacrimal duct obstruction (NLDO) in infancy

Design—Multicenter, randomized clinical trial

Methods—Fifty-seven infants aged 6 to <10 months with bilateral NLDO were randomized to receive either 1) immediate office-based probing within two weeks (N=31) or 2) 6 months of observation/nonsurgical management followed by surgical facility-based probing for unresolved cases (N=26). Treatment success was defined as the absence of clinical signs of NLDO (epiphora, increased tear lake, mucous discharge) in both eyes on masked examination at 18 months of age.

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Corresponding author: Katherine A. Lee, MD, PhD; c/o Jaeb Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33647; Phone: (813) 975-8690, Fax: (813) 975-8761, pedignld3bil@jaeb.org.

^{*}A complete list of participating members of the Pediatric Eye Disease Investigator Group (PEDIG) can be found in a previous publication.¹

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Results—In the observation/deferred facility probing group, resolution without surgery occurred by 6 months after randomization in both eyes for 14 participants (56%), in one eye for 5 (20%), and in neither eye for 6 (24%). Eight observation/deferred facility probing group participants underwent facility probing (1 of whom later had a second facility probing). Four immediate office probing group participants later underwent an additional procedure, in a surgical facility. In the immediate office probing group, treatment success at 18 months of age occurred in both eyes for 19 of 29 (66%) participants and in one eye for 3 (10%); in the observation/deferred facility probing group, treatment success occurred in both eyes for 19 of 25 (76%) participants and in one eye for 3 (12%) (difference in success = -10%; 95% CI = -35% to 14%).

Conclusions—Both the immediate office probing approach and the observation/deferred facility probing approach are successful and reasonable treatment options for infants with bilateral NLDO.

Introduction

Congenital nasolacrimal duct obstruction (NLDO) occurs commonly in infants²⁻⁵ and often resolves without surgery.⁴⁻¹⁰ Treatment of infants with symptoms of NLDO persisting beyond 6 months of age generally follows one of two management approaches. One approach is to probe the nasolacrimal duct in the office setting using topical anesthesia and restraint. Another approach is to continue observation, prescribing non-surgical treatment with lacrimal sac massage and/or topical antibiotics,⁹⁻¹³ as prospective studies have shown that most cases of NLDO that persist to between 6 and <10 months of age (64% to 70%^{10, 11}) resolve within 6 months without surgery. If the NLDO persists, a probing is often performed under general anesthesia in a surgical facility because the now older infant would be more difficult to sufficiently restrain to safely complete probing in the office setting.

We recently conducted a randomized trial comparing the immediate office probing approach with the observation/deferred probing approach and previously reported results in participants with unilateral NLDO. Although the trial did not find a statistically significant difference between treatment groups, the trial showed that the immediate office-based probing approach was likely to be at least as successful as the observation/deferred probing approach for treating infants with unilateral NLDO.¹ Herein we report clinical outcomes for participants who had bilateral NLDO in the same randomized clinical trial.

Methods

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health, and was conducted by the Pediatric Eye Disease Investigator Group (PEDIG) at 22 academic and community-based pediatric ophthalmology practices. The protocol and Health Insurance Portability and Accountability Act (HIPAA) compliant informed consent forms were approved by institutional review boards, and a parent or guardian of each study patient gave written informed consent. The study is listed on www.clinicaltrials.gov (NCT00780741, accessed 3/1/13). Key aspects of the protocol have been published.¹ The full protocol is available on the PEDIG website (www.pedig.net, accessed 12/13/12) and is briefly described below.

The trial enrolled 57 participants aged 6 to <10 months with bilateral NLDO, onset of NLDO symptoms before 6 months of age, no prior nasolacrimal duct surgery, and no Down syndrome or craniofacial anomalies. Bilateral NLDO was defined as presence of epiphora, increased tear lake, and/or mucous discharge in both eyes; a dye disappearance test was not required. Each participant was randomly assigned to receive either 1) bilateral probing in the office setting with topical anesthesia and gentle restraint (often including use of a papoose board), within two weeks of study entry or 2) 6 months of observation/nonsurgical management followed by probing in a surgical facility for unresolved eyes. During the 6-

month observation period, lacrimal massage was to be performed when discharge was present and antibiotic eye drops were to be used when discharge was purulent. Participants' parents were contacted by phone 3 months (± 2 weeks) after randomization to determine whether NLDO symptoms were present. Participants had follow-up visits 6 months (± 2 weeks) after randomization and a masked primary outcome examination at 18 months of age (± 4 weeks). At the 6-month post-randomization visit, observation/deferred group participants who had one or more clinical signs of NLDO were to undergo probing in a surgical facility within 4 weeks. After the initial treatment approach of immediate office probing of both eyes or 6 months of observation followed by deferred probing for unresolved eyes, further treatment (including reoperation) was at investigator discretion.

The primary efficacy outcome was success of the treatment approach, defined as the absence of all clinical signs of NLDO (epiphora, increased tear lake, and mucous discharge) in both eyes as assessed by a masked examiner at a visit at 18 months of age, and regardless of whether the patient received any probing procedures. A secondary outcome was months of NLDO symptoms in one or both eyes between randomization and 18 months of age. For participants who did not complete the primary outcome visit, we attempted to contact parents by phone to ask whether their child had NLDO symptoms.

The analysis followed the intent to treat principle. The treatment group difference in the proportion of eyes with success and a 95% confidence interval (CI) were calculated using binomial regression with generalized estimating equations to adjust for the correlation between the two eyes from each participant.¹⁴ The treatment group difference in the proportion of participants who had success in both eyes and a 95% CI were calculated using binomial regression. Participant-level treatment group differences in months of symptoms and a 95% confidence interval were estimated using an independent samples t test.

All analyses were conducted using SAS version 9.3. (SAS Institute Inc. Cary, NC).

Results

Between November 2008 and September 2010, 57 participants with bilateral NLDO were enrolled as part of a larger randomized trial that included both unilateral and bilateral NLDO.¹ Of the children with bilateral NLDO, 31 and 26 participants were randomized to immediate office probing and observation/deferred facility probing groups, respectively (Table 1). The participants were an average of 7.7 (± 1.3) months of age, 24 (42%) were female, and 40 (70%) were white. Fifty-one (89%) had been treated previously with antibiotics and/or lacrimal massage.

In the immediate office probing group, 30 of 31 patients (97%) underwent bilateral office probing. The remaining patient did not have surgery, although parents later reported by phone that the NLDO had resolved. Four immediate office probing group patients (13%) underwent a second surgical procedure at investigator discretion before 18 months of age (1 had bilateral probing and 3 had bilateral nasolacrimal intubations, all performed in a hospital outpatient operating room under general anesthesia). No surgical complications were reported.

In the observation/deferred probing group, resolution without surgery occurred by six months after randomization in both eyes for 14 participants (56%, 95% CI = 37% to 74%), one eye for 5 (20%), and neither eye for 6 (24%). Of the 11 participants whose NLDO did not resolve by 6 months of observation, 7 underwent bilateral facility probing (1 of whom later underwent a second procedure, a bilateral nasolacrimal intubation), 1 underwent unilateral facility probing, and 3 did not undergo surgery. All 9 surgeries were performed

under general anesthesia, 6 (67%) in a hospital outpatient operating room and 3 (33%) in an ambulatory surgery center. No surgical complications were reported.

Of the 31 participants in the immediate office probing group, 25 (81%) completed the 18-month visit, 4 (13%) did not complete the visit but were included in the analysis because outcome data were reported by parents via phone contact (NLDO signs were absent in 3 of the 4 patients), and 2 (6%) participants were not included because they did not complete the visit and phone contact with their parents was unsuccessful (Figure 1). Of the 26 participants in the observation/deferred group, 25 (96%) completed the 18-month visit, and 1 participant was not included because the visit was not completed and phone contact with his/her parents was unsuccessful.

Treatment success at 18 months of age occurred in 41 (71%) of 58 eyes in the immediate office probing group compared with 41 (82%) of 50 eyes in the observation/deferred probing group. The difference in the proportion of eyes with success (immediate office probing group minus observation/deferred probing group) was -11% (95% CI = -32% to 9%). In the immediate office probing group, treatment success at 18 months of age occurred in both eyes for 19 of 29 (66%) participants, and in one eye for 3 (10%) participants; in the observation/deferred probing group, treatment success at 18 months of age occurred in both eyes for 19 of 25 (76%) participants, and in one eye for 3 (12%) participants (Table 2). The difference in the proportion of participants with success in both eyes was -10% (95% CI = -35% to 14%).

Between randomization and 18 months of age, participants in the immediate office probing group had symptoms for an average of 4.2 months compared with 6.2 months in the observation/deferred group participants (difference = -2.0; 95% CI = -4.1 to 0.1) (Table 3).

Discussion

We conducted a randomized treatment trial of infants 6 to <10 months of age with NLDO comparing immediate office probing with observation for 6 months followed by probing in a surgical facility if necessary. In this report, we provide an analysis of data from the cohort of infants with bilateral NLDO. We found the likelihood of treatment success to be high with either approach. When we consider the outcome for participants at age 18 months, treatment success was found in 66% of the immediate office probing group and 76% of the observation/deferred facility probing. For each eye considered alone the likelihood of treatment success was 71% in the immediate office probing group and 82% in the observation/deferred facility probing. Not unexpectedly, the immediate office probing group may have had slightly fewer months of symptoms than the observation/deferred group.

We are not aware of other randomized trials that compare these two treatment approaches. Comparing our data on bilateral NLDO with those data from infants with unilateral NLDO participating in the same randomized trial,¹ we found that the observation/deferred facility probing approach had similar success rates in eyes from participants with bilateral and unilateral NLDO (82% versus 83%) while the immediate office probing approach had a lower success rate in eyes from participants with bilateral NLDO compared with unilateral NLDO (67% vs. 92%, $p = 0.01$). The finding that the immediate office probing approach had a lower success rate among bilateral NLDO is consistent with an earlier PEDIG study which reported the success rate of office probing in patients 6 to <15 months of age to be 59% (58 of 98) in eyes from bilateral NLDO participants compared with 78% (106 of 136) of eyes from unilateral NLDO participants.¹⁵ Potential reasons for the lower success rate with bilateral office probings could be that in a conscious child, the increased time required to probe both eyes might lead to a more hurried procedure, or that a child's physical

resistance to probing the first eye may make probing the second eye more difficult. We did not collect data on which eye was probed first so are unable investigate whether success is related to operative order.

Several factors may influence the choice of treatment approach. Both approaches have only a minimal risk of complications. However, compared with the observation/deferred facility probing approach, the immediate office approach may have slightly faster resolution of symptoms, may potentially reduce the burden on caregivers, is more convenient, and generally avoids the use of general anesthesia. Conversely, parents may be concerned about discomfort from office probing despite the use of a topical anesthetic and about the potential for negative psychological effects from the use of restraint, or may view the procedure as unnecessary given the high rate of resolution of symptoms without surgery.

This study has important limitations. First, few participants with bilateral NLDO were recruited into the randomized trial. The small sample produces wide confidence intervals on the treatment group differences which preclude definitive conclusions about success rates and months of symptoms. Second, loss to follow up was higher in the immediate office probing group compared with the observation/deferred group (19% vs. 4%), although we were able to obtain parent-reported outcome on 4 of the 6 immediate office probing group participants who did not complete the outcome visit. We included these 4 patients with parent-reported outcomes in the analysis to help minimize the potential bias resulting from higher loss to follow up in the immediate office probing group. Third, potential misclassification of outcome can occur based on the presence or absence of signs at a single outcome visit.

Although a larger randomized trial would be needed to determine whether one treatment approach has a higher success rate, both immediate office probing and observation/delayed facility probing are reasonable treatment approaches for infants aged 6 to <10 months with bilateral nasolacrimal duct obstruction. Implementing 6 months of conservative management would avoid a probing procedure in 37% to 74% of infants; however, probings for cases of persistent NLDO would generally need to be performed under general anesthesia due to difficulties of safely restraining older infants in the office setting. Alternatively, implementing the immediate office probing approach results in probing some infants who would have resolved with 6 months of nonsurgical treatment, but largely avoids the need for general anesthesia.

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A complete list of participating members of the Pediatric Eye Disease Investigator Group (PEDIG) can be found in a previous publication.¹

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Figure 1. Flow Chart of Patients with Bilateral Congenital Nasolacrimal Duct Obstruction

*Of the 6 immediate office group patients who withdrew from the study before the primary outcome visit at 18 months of age, the parents were able to be contacted by phone in 4 cases and therefore these 4 patients were included in the analysis.

Table 1

Baseline Characteristics in Patients with Bilateral Congenital Nasolacrimal Duct Obstruction

	Immediate Office Probing Group	Observation/Deferred Facility Probing Group
PARTICIPANT-LEVEL CHARACTERISTICS	(N = 31)	(N = 26)
Female gender, n (%)	13 (42)	11 (42)
Race/ethnicity, n (%)		
White	19 (61)	21 (81)
Hispanic	7 (23)	5 (19)
African American	4 (13)	0 (0)
Other	1 (3)	0 (0)
Age at enrollment, n (%)		
6 to <7 months	12 (39)	11 (42)
7 to <8 months	3 (10)	7 (27)
8 to <9 months	8 (26)	4 (15)
9 to <10 months	8 (26)	4 (15)
Mean (SD) months	7.8 (1.4)	7.5 (1.2)
EYE-LEVEL CHARACTERISTICS	(N = 62)	(N = 52)
Previous treatment, n (%)		
Lacrimal massage and/or topical antibiotics	36 (58)	30 (58)
Lacrimal massage only	9 (15)	12 (23)
Topical antibiotics only	6 (10)	8 (15)
None	9 (15)	2 (4)
Epiphora present, n (%)	46 (74)	38 (73)
Increased tear film present, n (%)	62 (100)	48 (92)
Mucous discharge present, n (%)	36 (58)	35 (67)

Table 2

Treatment Outcome at 18 Months of Age in Patients with Bilateral Congenital Nasolacrimal Duct Obstruction^{a,b}

Eyes with Treatment Success at 18 Months of Age, n (%)/ Number of Surgeries by 18 Months of Age, n	Immediate Office Probing Group ^c (N=29)	Observation/Deferred Facility Probing Group ^d (N=25)
Both eyes successful	19 (66)	19 (76)
No surgeries	1	13
Initial surgery	17	6
Reoperation	1	0
One eye successful	3 (10)	3 (12)
No surgeries	0	1
Initial surgery	3	1
Reoperation	0	1
Neither eye successful	7 (24)	3 (12)
No surgeries	0	3
Initial surgery	4	0
Reoperation	3	0

^aTreatment success for a given eye defined as the absence of all clinical signs of NLDO (epiphora, increased tear lake, and mucous discharge) as assessed by a masked examiner at a visit at 18 months of age.

^bFour participants in the immediate group did not complete the 18 months of age visit but had outcome data provided by the parents by phone.

^cIn the immediate probing group, all initial surgeries were bilateral office probings. All three reoperations were bilateral (one facility probing and two nasolacrimal intubations).

^dIn the observation/deferred probing group, all initial surgeries were facility probings (7 bilateral, 1 unilateral). The single reoperation was bilateral nasolacrimal intubation.

Table 3

Months of Symptoms between Randomization and 18 Months of Age in Patients with Bilateral Congenital Nasolacrimal Duct Obstruction

Months of Symptoms between Randomization and 18 Months of Age, n (%)	Immediate Office Probing Group ^a (N=29)	Observation/Deferred Facility Probing Group (N=25)
<1	15 (52)	0 (0)
1 to <3	0 (0)	4 (16)
3 to <6	2 (7)	10 (40)
6 to <9	6 (21)	7 (28)
9 to 12	6 (21)	4 (16)
Mean	4.2	6.2
Range	0.0 to 11.6	1.5 to 11.8

^aFour participants in the immediate office probing group did not complete the 18 months of age visit but had outcome data provided by the parents by phone.