Peer Review File

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Reviewer A

I am sending my comments about your article.
General comments:
This article explores a very important subject – the need for lacrimal surgery if there is nasolacrimal obstruction concurrent with cataract and other intraocular pathologies.
Due to the possibility of endophthalmitis after intraocular surgery in a patient with concomitant nasolacrimal obstruction, it seems reasonable that the lacrimal obstruction should be detected and treated before the intraocular surgery to reduce the risk of postoperative endophthalmitis. The better integration of intraocular surgeons with oculoplastic specialists, as well as implementation of training in education programs could reduce the occurrence of endophthalmitis after intraocular surgeries, a devastating condition with the possibility of resulting in significant visual impairment in most cases.
Specific comments:

ABSTRACT
Comment 1: Page 1
Line 24 – The authors start talking about bacteria resistance after the chronic use of topical antibiotics. However, there are patients who do not perform surgery to have the lacrimal system re-opened before cataract surgery. It is necessary to talk about this also.
However, I suggest starting background in Line 28: "This study aimed to determine the appropriate interval for intraocular surgery in patients with previous EN-DCR for chronic 30 dacryocystitis…"
Reply 1: We agree with the reviewer's suggestion and start background with "This study aimed to determine the appropriate interval for intraocular surgery in patients with previous EN-DCR for chronic dacryocystitis. "
Changes in the text: Page3 Line50-52

Comment 2: Line 31 – Methods
"Methods: The medical files of all patients who underwent intraocular surgery after 32 EN-DCR surgery in our hospital from 2016 to 2019 were reviewed…"
The exclusion criteria involved patients who underwent EN-DCR and evolve with obstruction?
Reply 2: Thanks for your comment. All the patients who underwent EN-DCR did not evolve with obstruction
Changes in the text: No changes in the text

Page 2
INTRODUCTION

Comment 3: Line 52 - "…the discharge of mucous urine from the punctum…"
Urine???
Reply 3: Thanks for your comment. We have corrected the typos error.
Changes in the text:Page4 Lines 77-79

Comment 4: Line 64: "It should be noted that patients with dacryocystitis usually applied antibiotic eye drops for a long time, ranges from months to years, which may develop drug-resistant bacteria."
This is unusual. I suggest removing this sentence because there is no reason to treat chronic or acute dacryocystitis with topical antibiotics for long periods.
Reply 4: Thanks for your comment. We have removed this sentence. Patients use antibiotic eye drops by themselves.
Changes in the text:Page5 Lines91-93

Comment 5: Line 68: "Moreover, it has been indicated that even one year after EN-DCR, conjunctival bacterial isolation rate increased compared with the normal fellow eyes,…"There are different reasons to have the level of bacteria elevated after any surgery…
Reply 5: Thanks for your comment. The quoted study indicated that DCR may be considered as a local risk factor for developing postoperative endophthalmitis.
Changes in the text: No changes in the text

Comment 6: Line 77:" in different periods after EN-DCR for dacryocystitis…"
Acute or chronic dacryocystitis was considered?
Reply 6: Thanks for your comment. We have revised the statement as "in different periods after EN-DCR for chronic dacryocystitis"
Changes in the text: Page5 Line104

METHODS
Comment 7: How many surgeons performed the intraocular surgeries?
The authors in previous paragraphs pointed long surgeries were more likely to develop endophthalmitis.
However, here they do not explain if the surgeons had good training or no.
Did the authors check if the lacrimal system was pervious after END-DCR?
Reply7: Thanks for your comment. The intraocular surgeries were performed by surgeons with good training.
Changes in the text: Page6 Line116

Comment 8: Line 92: about inclusion and exclusion criteria:
Inclusion criteria – patients predisposing to infectious diseases were all included? Systemic diseases as diabetes were also included?
The exclusion criteria involved patients who underwent EN-DCR and evolve with obstruction?
The adopted study protocol was not presented here in Methods. There is no information about how to detect or confirm the endophthalmitis diagnosis.
Relpy8: We agree with the reviewer's suggestion and add the "Inclusion criteria—All the

patients have evaluate preoperative examination before EN-DCR, they were all not predisposing to infectious diseases. Preoperative diabetes aim to keep a target glucose range for the perioperative period of 80 to 180 mg/dL (4.4 to 10 mmol/L)
The lacrimal passage is flushed smoothly without secretion after EN-DCR in all the patients.
The exclusion criteria involved patients who underwent EN-DCR and evolve with obstruction. Endophthalmitis was diagnosised as described previously[Clin Microbiol Rev. 2017 Jul;30(3):597-613. doi: 10.1128/CMR.00113-16.]. Nearly all endophthalmitis patients present with decreased vision, and some also have eye pain. Eye examination usually reveals a hypopyon and intraocular inflammation. Diagnosis is clinical, supported by cultures of the vitreous and/or aqueous or by blood cultures in some endogenous cases. Molecular diagnostic techniques have been used in research laboratories for pathogen identification in endophthalmitis and offer the possibility of rapid diagnosis, including in culture-negative cases."
A detailed description was added in the section of Methods (Page6-7 Lines 117-138) in the revised version.
Changes in the text: Page6-7 Lines 117-138

RESULTS
Comment 9: Line 101: please add the reason for the exclusion of some patients.
Relpy 9: Thanks for your comment. The others underwent external eye surgery after EN-DCR,
Changes in the text: Page7 Lines138-139

Comment 10: Line 107 – 37 had a smears culture but just 18 had a positive culture. Why???
Even when we collect material for culture from the could-sac and the patient has no conjunctivitis or dacryocystitis the result can be positive due to the normal flora.
Is there a relation between the positive culture and the endophthalmitis cases?
Are there no endophthalmitis cases in this study???
Reply 10: Thanks for your comment. The culture-positive rates were low because patients with dacryocystitis usually applied antibiotic eye drops for a long time by themselves before they come to the doctor, which may There are no endophthalmitis cases in this study. We explain that in the discussion section.(Page9 Lines 184-186)
Changes in the text: Page9 Lines 184-186

DISCUSSION
Comment 11: Line 127: which condition? Dacryocystitis? Endophthalmitis???
Reply 11: Thanks for your comment. We have revised the statement as "Previous study has reported that dacryocystitis often affects adults above 30 years old".
Changes in the text: Page8 Line161

Comment 12: Line 130: Why talk about the quality of life. Is this your subject?
Reply 12: We agree with the reviewer's suggestion and remove the statement.
Changes in the text: Page8 Lines 164-166

Comment 13: Line 140: not related to this paper
Reply 13: We agree with the reviewer's suggestion and remove the statement, add the statement

" It is found that most surgeons prefer to perform a DCR in cases of NLDO and wait for 4 weeks before intraocular surgery in the Indian survey on practice patterns of lacrimal & eyelid disorders"
Changes in the text: Page8 Lines 173-175, Page8 Lines 179-181

Comment 14: Line 146: "In the present study, 7 eyes were examined by conjunctival 147 sacs bacterial culture…"
Information not provided in RESULTS.
Reply 14: Thanks for your comment. We made a mistake. It should be "In the present study, 37 eyes were examined by conjunctival 147 sacs bacterial culture…" as present in the table2.
Changes in the text: Page9 Line 181

Comment 15: Line 148: "The culture-positive rates were not high, owing to the 149 use of antibiotic eye drops before patients come for the EN-DCR routinely."
Wrong information. How many days do the authors agree it is necessary to have the commensal flora regrowing?
Reply 15: Thanks for your comment. We have revised the statement as "The culture-positive rates were not high, because patients had been using antibiotics before they came to see the doctor."
Changes in the text: Page9 Lines 184-186

Comment 16: Line 152: "In our study, we found that although the interval between intraocular surgery and EN-DCR was different, there was no change in the incidence of endophthalmitis after intraocular surgery"
Where may I find the incidence of endophthalmitis in the present paper??? Another wrong information in this sentence.
Reply 16: Thanks for your comment. We have revised the statement as "we found that although the interval between intraocular surgery and EN-DCR was different, there was no endophthalmitis after intraocular surgery."
Changes in the text: Page9 Line 190

Comment 17: Line 165: the comment is speculative.
Reply 17: We agree with the reviewer's comment. This is what we're going to do next.
Changes in the text: Page10 Lines 206-208

Comment 18: Line 179 – I agree with this CONCLUSION. However, this can not be the conclusion of the present study…
Reply 18: We agree with the reviewer's suggestion and revised the statement as "We speculate that the interval between intraocular surgery and ED-DCR did not increase the risk of endophthalmitis after intraocular surgery as long as the patients had patency

on lacrimal passage irrigation and no secretions, but the results need to be confirmed by future larger studies."

Changes in the text: Page10 Lines 214-218

Reviewer B

Comment 1: The English and writing style need to be enhanced, some terms are unusual:
ν line 52 'urine'
ν Line 70-71, fresh retinal detachment, drugs-uncontrollable glaucoma
ν Line 180-181, lacrimal passage is flushed smoothly without secretion
ν Table 1 'Retinal reattachment surgery'

Reply 1: Thank you for your comments. The manuscript has carefully proofed for typos, grammar, spelling, and punctuation.

Changes in the text: Page4 Line79
Page5 Lines 97-98
Page10 Lines 206-207

Comment 2: Retrospective case series only, selection biased, some case underwent EnDCR may have surgeries in other places.
Reply 2: We agree with the reviewer's comment. We can't get information about patients who have surgery in other places.
Changes in the text: No changes in the text.

Comment 3: What was the outcome measure? Was it post op endophthalmitis? Or any form or post operative infection?
Reply 3: Thank you for your comments. All patients (100%) who had previously undergone EN-DCR did not develop endophthalmitis infection after intraocular surgery at a follow-up of 12 months. The outcome is endophthalmitis.
Changes in the text: Page3 Lines61-62

Comment 4: What was post op regime for these patients? Was this the same as compared with those cases without dacryocystitis/ EnDCR? Was there any additional usage of stronger topical +/- systemic antibiotics?
Reply 4: Thank you for your comments. Post operation regime for these patients was the same as compared with those cases without dacryocystitis/ EnDCR.
Changes in the text: Page6 Lines118-120

Comment 5: The authors mentioned that 'It should be noted that patients with dacryocystitis usually applied antibiotic eye drops for a long time', was there any data in this cohort about this?

Reply 5: Thank you for your comments. We have removed the sentence. We found that most of the patients came to the doctor because the antibiotic eye drops failed to treat the chronic dacryocystitis, but we didn't have the exact number of days.
Changes in the text: Page5 Lines91-93

Comment 6: Of the 116 surgical eyes, only 37 eyes were examined by conjunctival sac bacterial culture. The postulation that after the presence of drug resistance bacteria after repeated topical antibiotic usage in chronic dacryocystitis even after EnDCR cannot be ascertained.
Reply 6: Thank you for your comments. The use of antibiotics may reduce the concentration of conjunctival sac bacteria, leading to the failure of culture. And it is a consensus that long-term use of antibiotics will induce drug-resistant bacteria.
Changes in the text: No change in the text.

Comment 7: When the Microbial culture results obtained from the conjunctival sac of patients was positive, what precautions or pre op measures have the authors performed before proceed to intraocular surgeries? What about those cases without Microbial culture results?

Reply 7: Thank you for your comments. Microbial culture was performed before EN-DCR. All the patients had the patency on lacrimal passage irrigation before proceed to intraocular surgeries for excluding dacryocystitis. In addition, all patients will use topical antibiotic eye drops for three days before internal eye surgery. Bacterial culture is not necessary, but of course it's better if it can be done.
Changes in the text: Page10 Lines214-217

Comment 8: In table 2, was there any drug resistance organism (as mentioned in the introduction by the authors)?
Reply 8: Thank you for your comments. There was no drug resistance organism in the study.
Changes in the text: No change in the text.

Comment 9: For table 2, what is the meaning of 'overall' and 'within the group'? Please define more clearly.
Reply 9: Thank you for your comments. Overall means percentage of all the positive for bacterial growth. Within group means percentage of the Gram positive/ Gram-negative group. We have added the definition in table 2.
Changes in the text: Table 2

Comment 10: There is a patient age 6, what was the intraocular surgery performed for him?
Reply 10: Thank you for your comments. Glaucoma surgery was performed for him.
Changes in the text: No changes in the text.

Comment 11: Was there any failed EnDCR cases? If so, what have the authors done before proceed to intraocular surgery?
Reply 11: Thank you for your comments. There was no failed EnDCR cases in this study. All the patients had the patency on lacrimal passage irrigation before proceed to intraocular surgeries. Mild tearing but no eye discharge, this condition is acceptable.
Changes in the text: No changes in the text.

Comment 12: There are 23 cases of retinal detachment surgeries after EnDCR, did the authors purposely defer the retinal detachment surgery till after EnDCR were performed? Was it because the authors want to reduce the chance of post op infection? What was the mean time interval for between diagnosis and time of surgery? Suggest to supplement the time interval instead of just number in table 3.
Reply 12: Thank you for your comments. Some of the retinal detachment surgery were purposely deferred till after EnDCR were performed, because the doctors want to reduce the chance of post op infection. This study aimed to determine the appropriate interval for intraocular surgery in patients with previous EN-DCR for chronic dacryocystitis. The interval between EN-DCR and retinal detachment surgery varied from 7-249 days. We agree with the reviewer's comment and supplement the time interval in table 3.
Changes in the text: Table 3

Comment 13: The authors stated that 'However, some disease such as acute glaucoma, retinal detachment, which will damage the visual function seriously, intraocular surgery is urgently needed, we proposed that intraocular surgery could be performed as soon as possible after EN-DCR. But in table 3, there was still a significant time interval between EnDCR and glaucoma and retinal detachment surgery, especially in selected cases.
Reply 13: Thank you for your comments.
Changes in the text: Some of the retinal detachment surgery were purposely deferred till after EnDCR were performed, because the doctors want to reduce the chance of post op infection. We all hope to have retinal surgery as soon as possible, but some patients will postpone the internal eye surgery due to reasons other than dacryocystitis (such as economic reasons, family reasons), so some patients have long intervals. This study aimed to determine the appropriate interval for intraocular surgery in patients with previous EN-DCR for chronic dacryocystitis from the real world. And We speculate that the interval between intraocular surgery and ED-DCR did not affect the outcome of intraocular surgery as long as the patients had patency on lacrimal passage irrigation,
Changes in the text: Page10 Lines214-217