1.1. Type of the Paper (Article)

**A Meta-analysis on the management options of Idiopathic Inflammatory Punctal Stenosis**

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**Abstract**

**Introduction:** Punctal obstruction is the narrowing or complete blocking of the external opening of the lacrimal canaliculus. Acquired punctal obstruction with profuse epiphora is a rather common illness, with a prevalence ranging from 8.3% to 54.3%.

**Aim of the study:** Aim of the study: To perform a meta-analysis on the management options for idiopathic inflammatory pyloric stenosis.

**Subjects and Methods:** This meta-analysis follows the PRISMA flow diagram. We searched PubMed, Cochrane, Web of Science, Embase, and local databases for relevant clinical trials evaluating the management of idiopathic inflammatory punctal stenosis. The analysis was performed using the risk ratio (RR) for dichotomous data and the mean difference (MD) for continuous data, in addition to the 95% confidence interval (CI). The data were considered homogenous if the I2 was 50% and heterogenous if the I2 was > 50%.

**Results:** Results showed significantly improved punctal staging in groups (I) and (III) compared to baseline, \( P = 0.007 \) and \( 0.017 \), respectively). However, no significant improvement was observed in group II. The relative risk (RR) across all groups was 1.68 (95% CI: 1.03, 2.75, \( P = 0.04 \)), indicating a significant improvement in the treatment at the assessment time. The analysis of individual stages showed that the treatment effect varied across stages, with a significant improvement observed in stage 3. The study also found a substantial increase in Outer Punctal Diameter (OPD) in the groups (I) and (III) immediately after the treatment compared to baseline, with a pooled effect size of -58.22 (95% CI: -108.50, -7.93, \( P = 0.02 \)).

**Conclusions:** Dexamethasone (0.1% non-preserved, 0.4% non-preserved) showed an effective, symptom-relieving, and outer punctal diameter (OPD) improvement as compared with the 0.1% preserved dexamethasone; on the other hand, the 0.4% non-preserved dexamethasone carried more risk of increasing the intra-ocular pressure (IOP).

**Keywords:** Idiopathic; Punctal Obstruction; Epiphora; AS-OCT; Outer Punctal Diameter.

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1. Introduction

Based on clinical staging and AS-OCT findings, we evaluate the efficacy of different concentrations of dexamethasone in addition to non-preserved artificial tears in this study, intending to determine the most effective concentration of
dexamethasone for the treatment of idiopathic inflammatory pyloric obstruction. Non-preserved Dexamethasone 0.1% and non-preserved Dexamethasone 0.4% eye drops were compared to preserved Dexamethasone 0.1% eye drops and non-preserved artificial tears for the treatment of idiopathic inflammatory punctal blockage.

2. Subjects and methods

This meta-analysis follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram and the guidelines of the Cochrane Handbook.

2.1. Information Sources

Up to September 2022, we looked through the databases in PubMed, Scopus, Web of Science, and Cochrane Central for papers that met our inclusion criteria.

2.2. Search and Study Selection

The included articles were reviewed in three stages. The initial stage involved utilizing EndNote software to import the findings from electronic databases onto a Microsoft Excel sheet. The second step involved two independent authors assessing the article titles and abstracts that were entered into the Excel sheet. The included citations from step 2 were subjected to full-text screening in the third stage. In addition, we manually checked the included publications' references for any potential overlooked investigations were done.

2.3. Data Collection

We gathered information on the participants' initial demographics, the SPI was measured five minutes after the incision and ten minutes prior to recovery as outcome endpoints and information for assessing the risk of bias was included in the third category. Data gathering was carried out using Microsoft Excel.

2.4. Risk of bias assessment

Using Cochrane's risk of bias methodology for meta-analyses, two writers evaluated the risk of bias among the included papers. Through seven domains, the instrument evaluates patient randomization, allocation concealment, and sufficient blinding. Each domain is assigned a risk of bias rating of "low," "unclear," or "high."

2.5. Analysis

With the use of Review Manager software, we conducted the meta-analysis for this study. Both continuous and binary outcomes were included in our study. We used mean difference (MD) and 95% confidence interval (CI) to analyze continuous data and risk ratio (RR) and 95% CI to evaluate dichotomous data. When the data were homogenous, the fixed-effects model was employed; when the data were heterogeneous, the random-effects model was utilized. We used the I2 and p-value of the Chi-square tests to assess the degree of consistency between the studies.
3. Results

The following is a PRISMA flow chart for our search

![PRISMA flow chart]

Figure 1: shows a PRISMA flow diagram of our literature search
3.1. AS-OCT

The overall meta-analysis of mean difference of OPD effect was significant. It was also in favor of pre-treatment -58.22 [(-108.5 to -7.93), (P = 0.02)]. Results of subgroup analysis were non-significant for group (I) and group (II) (P=0.36), Only group (III) was significant in favor of experimental group (P<0.01), Figure 2.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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<td>IV, Fixed, 95% CI</td>
<td>IV, Fixed, 95% CI</td>
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<td>3.1. AS-OCT ASSESSMENT</td>
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<tr>
<td>Group I</td>
<td>360.29</td>
<td>139.62</td>
<td>14</td>
<td>401.21</td>
<td>113.79</td>
<td>14</td>
<td>26.8%</td>
<td>-40.82 [138.49, 58.65]</td>
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<tr>
<td>Group II</td>
<td>454</td>
<td>112.23</td>
<td>15</td>
<td>487.4</td>
<td>119.36</td>
<td>15</td>
<td>36.8%</td>
<td>-23.40 [106.32, 59.52]</td>
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<tr>
<td>Group III</td>
<td>352</td>
<td>103.46</td>
<td>13</td>
<td>457.67</td>
<td>112.4</td>
<td>13</td>
<td>36.7%</td>
<td>-105.67 [168.71, -22.63]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>42</td>
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<td></td>
<td>42</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>-58.22 [-108.50, -7.93]</td>
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<tr>
<td>Heterogeneity: Chi² = 2.65, df = 2 (P = 0.38); I² = 3%</td>
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<td>Test for overall effect: Z = 2.27 (P = 0.02)</td>
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<tr>
<td>Test for subgroup differences: Not applicable</td>
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Figure 2: Analysis of AS-OCT outcome.

3.2.2. Recurrence rate

The overall results showed risk ratio (RR) favors the recurrent group (RR=0.56 [0.35,0.88], P=0.01), showing that all groups were all non-significant (P=0.95), Figure 3.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Recurrent Events</th>
<th>Non-Recurrent Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
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<tr>
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<td>MH, Fixed, 95% CI</td>
<td>MH, Fixed, 95% CI</td>
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<tr>
<td>Group I</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>22.2%</td>
<td>0.50 [0.10, 1.40]</td>
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<tr>
<td>Group II</td>
<td>2</td>
<td>6</td>
<td>8</td>
<td>14.8%</td>
<td>0.60 [0.14, 1.77]</td>
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<tr>
<td>Group III</td>
<td>10</td>
<td>27</td>
<td>37</td>
<td>63.0%</td>
<td>0.66 [0.33, 1.10]</td>
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<tr>
<td>Total (95% CI)</td>
<td>42</td>
<td>42</td>
<td>84</td>
<td>100.0%</td>
<td>0.56 [0.35, 0.88]</td>
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<tr>
<td>Total events</td>
<td>15</td>
<td>27</td>
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<tr>
<td>Heterogeneity: Chi² = 0.11, df = 2 (P = 0.95), I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 2.48 (P = 0.01)</td>
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Figure 3: Analysis of recurrence rate
4. Discussion

Many conditions and medications have been associated with acquired punctal obstruction. These include infectious causes, such as Actinomyces; autoimmune and inflammatory conditions, such as chronic blepharitis, ectropion, and graft-versus-host disease; and both topical and systemic medications, such as taxanes and topical glaucoma medications [7].

A cause can typically be determined in patients with acquired lacrimal punctal blockage. Nonetheless, there is still a subset called "idiopathic" in which no clear etiology can be identified [8]. Research on idiopathic lacrimal punctal blockage is scant at best. All stenotic puncta were found to have subepithelial and subconjunctival fibrosis, according to histological and electro-microscopic examinations, but there was also significant inflammation and high immunoreactivity [9]. The current study aimed to explore medical therapy for treating idiopathic, non-infectious acquired punctal inflammation, which has not been extensively studied. Patients received treatment based on the size of the puncta, were examined under a slit lamp and high-resolution anterior segment optical coherence tomography, and comprised 49 patients with a mean age of 59.22 ± 11.23 years, similar to other studies with a higher prevalence in individuals 40 years of age and beyond [10]. Most of the publications that have been published discuss punctal blockage in primarily female patients (63–71%) [2]. The fact that our present study only included patients with idiopathic inflammatory disease may be the reason why we were unable to detect any gender differences in the examined cohort [male:female ratio = 1.2:1].

In the current study, the efficacy of non-preserved Dexamethasone 0.1%, preserved clinical Dexamethasone 0.1%, and non-preserved Dexamethasone 0.4% eye drops for idiopathic inflammatory punctal blockage was examined.

In this study, it was discovered that using AS-OCT characteristics was an effective way to track and gauge how well medical care was working to relieve punctal blockage. AS-OCT has been employed in earlier investigations to characterize puncta in both healthy individuals and patients with punctal stenosis [11]. The study found that the outer punctal diameter (OPD) measured by AS-OCT was significantly improved in groups I and III after treatment compared to before, with the greatest improvement rate in group III. Elshorbagy et al. (2020) findings on the effectiveness of preservative-free methylprednisolone 5% eye drops were consistent with the symptomatic improvement observed in all subjects [5]. Elalfy et al. (2020) conducted a prospective study comparing the effectiveness of preservative-free steroid eye drops and preservative-free artificial tears in treating punctal edema in Egypt [12].
**Ethical Approval Statement:** All people included in the study were told about the study's protocols and their rights to refuse participation or withdraw from the study without giving reasons. Participants were assured of their privacy, and all information submitted would be kept strictly confidential. The administrative regulations were followed. Prior to the start of the work, the faculty of medicine, Fayoum University research ethical committee (REC), approved it.

**Funding:** This research is not funded.

**Conflicts of Interest:** All authors declare no conflict of interest.

**References**

12. Elalfy HY, Elsamkary MA, Eldidy AMS, Saad TM, Rashad SM, Fawzy SM. Medical