INPLASY

Comparison between topical NSAIDs in the prevention of pseudophakic cystoid macular edema: Systematic Review of RCTs with Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 August 2023 and was last updated on 17 August 2023.

INTRODUCTION

Review question / Objective P – Patients undergoing catarct surgery; I – NSAIDs in addition to topical steroids; C – another NSAIDs in addition to topical steroids; O – Mean Differences of Foveal thickness (FT), best corrected visual acuity (BCVA), and intraocular pressure (IOP); S – Randomized controlled trials (RCTs).

Rationale Macular edema is a common complication following cataract surgery, specifically phacoemulsification, which can lead to vision impairment and delayed visual recovery. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been used as a prophylactic treatment for macular edema after phacoemulsification surgery. However, there is still debate about their effectiveness and the optimal NSAID regimen to use. A systematic review of randomized controlled trials (RCTs) with network meta-analysis can provide a comprehensive and robust evaluation of the efficacy and safety of different NSAID regimens in preventing macular edema after phacoemulsification. This type of analysis allows for a comparison of multiple treatments simultaneously and can provide information on the relative effectiveness of each treatment compared to the others. The results of this research could potentially inform clinical decision-making and improve patient outcomes by identifying the most effective NSAID regimen for the prevention of macular edema after phacoemulsification. This research also has the potential to guide future clinical trials and contribute to the development of evidence-based guidelines for the prevention of macular edema after phacoemulsification surgery. Both topical nonsteroidal anti-inflammatory drugs (NSAIDs) and topical steroids have been used in the prevention and treatment of PCME. However, recent evidence suggests that topical NSAIDs are more efficient than topical steroids in the

prevention of PCME after phacoemulsification, especially in patients with Diabetes Mellitus.

Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are effective in preventing PCME by reducing inflammation and the production of prostaglandins. Nepafenac 0.1%, Nepafenac 0.3%, Bromfenac, Diclofenac, and Ketorolac are commonly used topical NSAIDs for PCME prevention.

There is limited evidence on the comparative efficacy of these topical NSAIDs, and head-to-head trials between all these drugs have not been conducted. Therefore, a network meta-analysis is needed to combine the evidence from existing RCTs.

Condition being studied Pseudophakic cystoid macular edema (PCME).

METHODS

Search strategy For PubMed: (("Phacoemulsification"[Mesh]) OR ("Phacoemulsification"[All Fields])) AND (("Nepafenac") AND ("Ketorolac")) OR (("ketorolac") AND ("diclophenac")) OR (("diclophenac") AND ("Bromfenac")) OR (("bromfenac") AND ("nepafenac")) OR (("Nepafenac") AND ("diclofenac")) OR (("ketorolac") AND ("bromfenac")). For Scopus: (("Phacoemulsification"[Mesh]) OR ("Phacoemulsification"[All Fields])) AND (("Nepafenac") AND ("Ketorolac")) OR (("ketorolac") AND ("diclophenac")) OR (("diclophenac") AND ("Bromfenac")) OR (("bromfenac") AND ("nepafenac")) OR (("Nepafenac") AND ("diclofenac")) OR (("ketorolac") AND ("bromfenac")). For Embase: ('Phacoemulsification'/exp OR 'Phacoemulsification') AND ('Nepafenac' AND 'Ketorolac') OR ('ketorolac' AND 'diclophenac') OR ('diclophenac' AND 'Bromfenac') OR ('bromfenac' AND 'nepafenac') OR ('Nepafenac' AND 'diclofenac') OR ('ketorolac' AND 'bromfenac')

Participant or population Patients undergoing cataract surgery.

Intervention Topical NSAID in addition to topical steroid.

Comparator Other topical NSAIDs in addition to topical steroid.

Study designs to be included Randomized controlled trials.

Eligibility criteria Our network meta-analysis and systematic review used the following inclusion criteria, structured in a PICOS format, for original papers: (1) patients who underwent cataract surgery; (2) the use of two or more topical nonsteroidal anti-inflammatory drugs to prevent pseudophakic macular edema (PME); (3) reported OCT values (FT and/or TMV) and/or BCVA and/or IOP outcomes; and (4) randomized controlled trials.

Information sources Five electronic databases including such as PubMed, Embase, Scopus, the Cochrane Library, and ClinicalTrials.gov.

Main outcome(s) Mean difference (MD) of BCVA, FT and IOP.

Data management One researcher extracted the data, which was verified by another researcher. In case of any discrepancies, the original article was reviewed to resolve them. The retrieved data included author names, publication year, country, sample size, mean age, sex distribution, perioperative intervention for all patients, change (baseline - postoperative) in mean and standard deviation in FT, and postoperative mean and standard deviation of BCVA, and IOP. The data for BCVA that had been recorded as ETDRS letters or Snellen score were converted to Logarithm of the Minimum Angle of Resolution (logMAR).

Quality assessment / Risk of bias analysis The bias risk for randomized controlled studies was assessed using the Cochrane Collaboration's tool. Two authors independently evaluated each study's risk of bias. In case of any disagreements, a discussion was conducted to reach a conclusion.

Strategy of data synthesis The network meta-analysis was carried out using the R environment for statistical computing and graphics, along with the netmeta R package. Clinical variation between the trials was presumed, so the restricted maximum likelihood was used to compute the estimates of the random effects model. The mean differences were estimated along with 95% confidence intervals. The network meta-analysis was performed using a frequentist approach. For all analyses, Nepafenac 0.1% was chosen as the reference group. First, the structure of comparisons was presented with the network graphs. Next, the proportion of direct and indirect evidence used to estimate each comparison was visualized. The mean path length and minimal parallelism statistics were computed to support these results. The pooled effect from direct comparisons, as well as the pooled effect from

direct and indirect comparisons, were computed for all comparisons and presented in a net league table. The forest plots, with Nepafenac 0.1% as the reference, were used to present the main comparisons. The treatment effect ranking was obtained using the P-scores frequentist method.

Subgroup analysis Not used.

Sensitivity analysis The inconsistency between direct and indirect evidence was explored with a net splitting analysis within forest plots and net heat plot. The chi-squared-based Q-test and I2 were used to examine between-study heterogeneity. A 0.05 level of significance was used for all analyses.

Language restriction English.

Country(ies) involved Romania.

Keywords NSAIDs; macular edema; visual outcome; prevention; phacoemulsification.

Dissemination plans Publication in a peer-reviewed journal.

Contributions of each author
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