

INPLASY PROTOCOL

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None declared.

The role of Nepafenac in the prevention of macular swelling and its repercussions on visual outcome after cataract surgery - A systematic review and meta-analysis

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Review question / Objective: P – diabetic and non-diabetic patients undergoing phacoemulsification without macular edema; I – Nepafenac 0.1% or Nepafenac 0.3% in addition to topical steroids; C – topical steroids alone; O – Mean Differences of Foveal thickness (FT), total macular volume (TMV), best corrected visual acuity (BCVA), and intraocular pressure (IOP); S – Randomized controlled trials (RCTs).

Condition being studied: Macular swelling or macular edema after cataract surgery when uncontrolled may compromise the blood-ocular barrier and allow inflammatory cells and cytokines to enter the aqueous humor, resulting in discomfort for the patient, a slower rate of recovery, subpar visual results, and even more complications like the development of synechiae, increased IOP, macular edema (ME), corneal edema, and so forth.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 September 2022 and was last updated on 02 September 2022 (registration number INPLASY202290004).

INTRODUCTION

Review question / Objective: P – diabetic and non-diabetic patients undergoing phacoemulsification without macular edema; I – Nepafenac 0.1% or Nepafenac 0.3% in addition to topical steroids; C – topical steroids alone; O – Mean

Differences of Foveal thickness (FT), total macular volume (TMV), best corrected visual acuity (BCVA), and intraocular pressure (IOP); S – Randomized controlled trials (RCTs).

Rationale: The common perioperative regimen in cataract surgery in many

countries remains as topical steroids. Topical steroids therapy may successfully reduce postoperative ocular inflammation, but it also raises IOP, slows wound healing, and raises infection risks. A growing number of cataract surgeons are now interested in finding alternatives or complementary medications that are just as effective as steroids but have fewer adverse effects. Many recent RCTs, verifying the superiority of topical Nepafenac in addition to topical steroids over sole topical steroids, have emerged. Therefore, the objectives of this research were to carry out a systematic review and meta-analysis to investigate the impact of Nepafenac in the prevention of macular edema, its effects on visual outcome, and on intraocular pressure.

Condition being studied: Macular swelling or macular edema after cataract surgery when uncontrolled may compromise the blood-ocular barrier and allow inflammatory cells and cytokines to enter the aqueous humor, resulting in discomfort for the patient, a slower rate of recovery, subpar visual results, and even more complications like the development of synechiae, increased IOP, macular edema (ME), corneal edema, and so forth.

METHODS

Search strategy: For PubMed the following search strategy was used: (("prevention and control" [Subheading]) OR ("Primary Prevention"[Mesh]) OR ("Primary Prevention"[All Fields]) OR ("Pre-Exposure Prophylaxis"[Mesh]) OR ("Pre-Exposure Prophylaxis"[All Fields]) OR ("Prophylaxis") OR ("Prevention")) AND (("Macular Edema"[Mesh]) OR ("Macular Edema"[All Fields])) AND (("Phacoemulsification"[Mesh]) OR ("Phacoemulsification"[All Fields])) AND (("Nepafenac") OR ("nepafenac" [Supplementary Concept])) PubMed search was checked again on 20.07.2022 with the following search text: (("Phacoemulsification"[Mesh]) OR ("Phacoemulsification"[All Fields]) OR ("Cataract"[Mesh]) OR ("Cataract"[All Fields])) AND (("Nepafenac") OR

("nepafenac" [Supplementary Concept])). For EMBASE: ('prevention and control'/exp OR 'prevention and control' OR 'primary prevention'/exp OR 'primary prevention' OR 'pre-exposure prophylaxis'/exp OR 'pre-exposure prophylaxis' OR 'prophylaxis' OR 'prevention') AND ('macular edema'/exp OR 'macular edema') AND ('phacoemulsification'/exp OR 'phacoemulsification') AND ('nepafenac' OR 'nepafenac'/exp). For Scopus (All Fields): (("prevention and control" [Subheading]) OR ("Primary Prevention"[Mesh]) OR ("Primary Prevention"[All Fields]) OR ("Pre-Exposure Prophylaxis"[Mesh]) OR ("Pre-Exposure Prophylaxis"[All Fields]) OR ("Prophylaxis") OR ("Prevention")) AND (("Macular Edema"[Mesh]) OR ("Macular Edema"[All Fields])) AND (("Phacoemulsification"[Mesh]) OR ("Phacoemulsification"[All Fields])) AND (("Nepafenac") OR ("nepafenac" [Supplementary Concept])). For Cochrane Library: (Prophylaxis OR Prevention) AND (Macular Edema) AND (Phacoemulsification) AND (Nepafenac). For Clinicaltrials.gov: (Prophylaxis OR Prevention) AND (Macular Edema) AND (Phacoemulsification) AND (Nepafenac).

Participant or population: Patients without ME undergoing cataract surgery.

Intervention: Topical Nepafenac in addition to topical steroid.

Comparator: Topical steroid.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: The inclusion criteria for this study comprised (1) Randomized controlled trials; (2) Including patients without ME and undergoing cataract surgery; (3) With two or more interventions in preventing Pseudophakic macular edema (PME), including at least Nepafenac and steroids; and (4) Reporting OCT values (FT and/or TMV) and/or BCVA and/or IOP outcomes.

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

Main outcome(s): Mean difference (MD) of FT and TMV.

Additional outcome(s): MD of Postoperative BCVA and IOP.

Data management: The search results' titles and abstracts were analyzed for eligibility, and then the full text was assessed to make sure the inclusion and exclusion criteria were satisfied. The author (M.A.) extracted the data from the included articles, and another verified it (A.I.). Author names, publication year, country, sample size, mean age, sex distribution, type of OCT device used, perioperative intervention for all patients, control group treatment, mean baseline post-operative, and change (baseline - postoperative) in FT, TMV, BCVA, and IOP were among the retrieved data.

Quality assessment / Risk of bias analysis: The risk of bias for randomized controlled trials was evaluated utilizing the Cochrane Collaboration's tool. The quality assessment evaluated treatment allocation concealment, randomized sequence generation, blinding in addition to selective outcome reporting, other types of bias, and integrity of the outcome data. We evaluated internal validity in individual research in a similar way using these evaluation methods. Two authors independently assessed the risk of bias in each study (M.A. and D.C.L.). When there was a dispute, a discussion was held to come to a decision.

Strategy of data synthesis: We performed the data analyses of the meta-analysis using R with Metafor package (OpenMeta [Analyst]). Between-study heterogeneity was checked using the χ^2 -based Q-test and I^2 . In accordance with the guidance of the Cochrane Handbook in order to recognize and quantify heterogeneity, we estimated I^2 values of 0% to 40% as not crucial; 30% to 60% as medium heterogeneity; 50–90% as

substantial heterogeneity; and 75% to 100% as considerable heterogeneity. We estimated the mean and standard deviation (SD) for RCTs that supplied medians and interquartile ranges in order to conduct statistical analyses of the collected data. The mean change and SD change were used in RCTs reporting outcomes at baseline and post-intervention data, if they were reported. However, if they were not reported, they were computed based on the before and after values in accordance with the Cochrane Handbook recommendations using the correlation coefficient from the same study or imputed from a related study in the event. Data from each trial were presented as the estimated MD with a 95% confidence interval (CI). A statistically significant p-value was considered when <0.05 . If two or more studies examined comparable groups and reported the same result using mean \pm SD or median (IQR), the analyses were carried out.

Subgroup analysis: Subgroup analysis according to the topical steroid administered, follow-up durations, and if FT was reported to be measured within the central 1 mm of the macula.

Sensitivity analysis: Leave-one-out meta-analysis was performed as a Sensitivity analysis on the primary outcome. This sensitivity analysis involves performing a meta-analysis on each subset of the studies obtained by leaving out exactly one study using restricted maximum likelihood method. This shows how each individual study affects the overall estimate of the rest of the studies.

Language restriction: Studies included had to be published in English.

Country(ies) involved: Romania, Syria.

Keywords: Nepafenac; Prednisolone; macular edema; prevention; phacoemulsification.

Dissemination plans: Publication in a peer-reviewed journal.

Contributions of each author:

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