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Meta-analysis ofintravitreal conbercept as anadjuvant to vitrectomy forproliferative diabetic retinopathy

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

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 24 June 2025 and was last updated on 24 June 2025.

INTRODUCTION

Review question / Objective Intravitreal Conbercept (IVC) is an effective adjuvant to pars plana vitrectomy (PPV) for treating proliferative diabetic retinopathy (PDR), but the optimal timing remains uncertain. This meta-analysis aimed to evaluate the efficacy of preoperative IVC injection compared to control (no IVC or placebo) as an adjuvant to PPV forPDR.

Condition being studied Diabetic retinopathy (DR), the most common diabetic complication, is characterized by damage and abnormalities in retinal blood vessels, which can result in visual impairment and blindness. Depending on the severity, DR can be classified into three subtypes: non-proliferative DR, proliferative DR (PDR), and diabetic macular edema. PDR is one of the most common causes of blindness in DR patients and is linked to vitreous hemorrhage, traction detachment, and neovascular glaucoma. DR affected approximately 103 million adults worldwide in 2020, which is expected to reach 160 million by 2045. Therefore, it is critical to treat patients with PDR effectively.

Panretinal photocoagulation and vitrectomy are two traditional treatment options for PDR. Pars plana vitrectomy (PPV) remains the preferred treatment, as it removes long-standing hematoma in the vitreous cavity, blocks pathways to neovascularization, and restores stable intraocular structure to the retina. However, this procedure may increase risks of complications like retinal detachment and repeated vitreous hemorrhage, potentially delaying vision recovery and raising surgical costs. Vascular endothelial growth factor (VEGF) plays a central role in PDR development, and intravitreal anti-VEGF therapy has been shown to reduce the need for repeated vitrectomy and recurrent hemorrhage. As a novel anti-VEGF drug, Conbercept is a recombinant fusion protein with multiple targets, increased affinity, and the capacity to prevent new blood vessel growth. Studies indicate that intravitreal Conbercept (IVC) before PPV effectively accelerates visual recovery and reduces non-clearing vitreous hemorrhage.

METHODS

Participant or population A population of patients with proliferative diabetic retinopathy (PDR) treated with vitrectomy (PPV) with or without intravitreal compazine (IVC).

Intervention PPV + differently timed IVCs (injected at different times preoperatively).

Comparator PPV + IVCs (intraoperatively).

Study designs to be included RCT.

Eligibility criteria RCTs.

Information sources The data for this study were obtained from a comprehensive literature search by systematically searching three major electronic databases, PubMed, EMBASE, and the Cochrane Library (as of August 11, 2022), using the keyword combinations "diabetic retinopathy" and "Conbercept" for screening. In addition, reference lists of eligible studies and relevant review articles were manually searched to ensure completeness of literature coverage. The final literature included in the analysis was limited to the full text of randomized controlled trials (RCTs) and excluded studies that were repetitively published and did not specify the dosage of compazine (IVC) or combination of other medications. All search processes and screening results strictly followed the PRISMA-NMA guidelines.

Translated with DeepL.com (free version).

Main outcome(s) Primary outcomes included postoperative best-corrected visual acuity (BCVA, expressed as LogMAR value of the logarithm of the smallest viewing angle), duration of surgery, and change in central macular thickness. Secondary outcomes covered intraoperative hemorrhage, incidence of medical retinal tears, frequency of electrocoagulation use, need for silicone oil filling, and incidence of postoperative vitreous hemorrhage. These metrics were assessed by random-effects network Meta-analysis and the efficacy of different intervention regimens was ranked using the cumulative area under the ranking curve (SUCRA) with the aim of comprehensively evaluating the efficacy and safety of different intravitreal compazine (IVC) dosing schedules as an adjunct to vitrectomy (PPV) for proliferative diabetic retinopathy (PDR).

Quality assessment / Risk of bias analysis Risk of bias was assessed using the Cochrane Collaboration's revised RoB2 tool to critically evaluate all included randomized controlled trials (RCTs), focusing on the following core areas: (1) reasonableness of the randomization process (only 7 studies reported the randomization method in full); (2) risk of deviation from the intervention regimen; (3) completeness of the endpoints data (4 studies were rated as high-risk due to missing data) ; (4) objectivity of outcome measures; and (5) risk of selective reporting (all studies showed low risk in this category).

Strategy of data synthesis Mean difference (MD) and 95% confidence intervals were calculated using random-effects network Meta-analysis for continuous variables (e.g., LogMAR visual acuity, operative time), and risk ratios (RR) for dichotomous variables (e.g., complication rates).

Subgroup analysis None.

Sensitivity analysis

Data completeness validation

Studies with missing data on key outcomes (4 high-risk-of-bias studies) were re-analyzed after exclusion to ensure that results were not affected by missing data.

Sources of inconsistency were detected by node splitting for direct versus indirect comparisons (inconsistency modeling was used if there was significant inconsistency in BCVA).

Covariate Balance Tests

Balance across comparisons of baseline characteristics (duration of diabetes, age, etc.) between groups was assessed (Supplementary Table 2) to confirm that the network met the assumption of transmissibility.

Subgroup analyses of the potential impact of PPV surgical modality (23G/25G/27G) were performed (not achieved due to insufficient sample size, listed as a limitation).

Statistical model sensitivity

A random effects model was used to cover clinical heterogeneity, and 95% confidence intervals were reported for all outcomes.

Ranking probability assessment: comparison of SUCRA values revealed that even between groups with no statistically significant differences (e.g., MI vs Perioperative IVC postoperative hemorrhage), clinical ranking still showed MI to be superior (SUCRA:77.9% vs 59.4%).

Publication Bias Detection

The small sample effect was visually tested by comparing corrected funnel plots (Supplementary Figure 3), which were symmetrical for all outcomes and did not support significant publication bias.

Country(ies) involved China, Sichuan.

Keywords proliferative diabetic retinopathy, vitrectomy, conbercept, intravitreal, meta-analysis.

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