INPLASY PROTOCOL

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Corresponding author:
Jian Zhang

jianzhang0218@outlook.com

Author Affiliation:
First Affiliated Hospital of Jiamusi University

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

Conflicts of interest: **No.**

Can neuroprotection effectively manage primary open-angle glaucoma? a protocol of systematic review and meta-analysis

Qi, YX[1]; Zhang, J[2]; Su, XJ[3].

Review question / Objective: **Can neuroprotection(NP) effectively manage primary open-angle glaucoma(POAG)?**
Condition being studied: **Primary open-angle glaucoma and neuroprotection.**
Information sources: **A comprehensive search procedure will be performed from the inception to the February 29, 2020 from the following electronic databases: Scopus, Web of Science, PubMed, EMBASE, Cochrane Library, CINAHL, WANGFANG, and CNKI. No language and publication date limitations will be applied to any electronic databases. An overview of search strategy for PubMed is created. Identical search strategies for other electronic databases will also be modified and applied. In addition to the electronic databases, we will also search clinical trials registries, conference proceedings, Google Scholar, and reference lists of relevant reviews.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 April 2020 and was last updated on 17 April 2020 (registration number INPLASY202040107).

INTRODUCTION

Review question / Objective: **Can neuroprotection(NP) effectively manage primary open-angle glaucoma(POAG)?**

Condition being studied: **Primary open-angle glaucoma and neuroprotection.**

METHODS

Participant or population: Any patients who were clinically diagnosed as POAG will be included in spite of their nationality, race, sex, age, and duration of POAG.

Intervention: All patients in the experimental group received NP intervention alone for their treatment.

Comparator: All patients in the control group could receive any treatments, such as surgery.

Study designs to be included: All potential randomized controlled trials (RCTs) that utilizing NP for the treatment of patients with POAG will be included in this study.

Eligibility criteria: All potential RCTs that utilizing NP for the treatment of patients with POAG will be included in this study. Any other studies, except the RCTs will be excluded.

Information sources: A comprehensive search procedure will be performed from the inception to the February 29, 2020 from the following electronic databases: Scopus, Web of Science, PubMed, EMBASE, Cochrane Library, CINAHL, WANGFANG, and CNKI. No language and publication date limitations will be applied to any electronic databases. An overview of search strategy for PubMed is created. Identical search strategies for other electronic databases will also be modified and applied. In addition to the electronic databases, we will also search clinical trials registries, conference proceedings, Google Scholar, and reference lists of relevant reviews.

Main outcome(s): Primary outcomes Visual acuity, Contrast sensitivity. Secondary outcomes Visual fields, Intraocular pressure, Blood pressure, Severity of oxidative stress, Antioxidant defense, Bioelectric activity of the retina, Total sensitivity of the retina for central field of view, Blood flow to the eye and optic nerve head, Rate of progression of glaucoma, and Incidence of adverse events.

Data management: All information will be extracted from each eligible trial by two independent authors using predefined standard data extraction sheet after an initial pilot with three included studies. If any divergences occur between two authors, another experienced author will be invited to help solve them by discussion. The extracted data form includes title, first author name, publication time, journal, country, inclusion and exclusion criteria, diagnostic criteria, sample size, patient characteristics (such as age, gender, disease duration and severity), research setting and design, details of interventions and controls, outcome indicators, safety, results, conclusions, follow-up data, and other related information.

Quality assessment / Risk of bias analysis: The methodological quality of each trial will be independently assessed by two authors utilizing Cochrane Risk of Bias Tool for RCTs specifically. This tool has 7 parts, and three different grades (high, unclear, and low risk of bias) will be employed to check each item. Any discrepancies will be settled by another experienced author through discussion.

Strategy of data synthesis: We will undertake statistical analysis using RevMan 5.3 software. Dichotomous data, such as rate of progression of glaucoma will be calculated as risk ratio and 95% confidence intervals (CIs). Continuous data, such as visual acuity and contrast sensitivity will be presented as mean difference or standardized mean difference and 95% CIs. We will examine statistical heterogeneity using I^2 statistic test. $I^2 \leq 50\%$ means low level of heterogeneity, and a fixed-effects model will be applied. When necessary, we will carry out meta-analysis if it is possible. $I^2 > 50\%$ suggests high level of heterogeneity, and a random-effects model will be exploited. In addition, we will run subgroup analysis to explore possible sources of obvious heterogeneity. We can not find out such sources, a meta-analysis will not be performed. Instead, we will carry out a narrative synthesis of outcome data.

Subgroup analysis: A subgroup analysis will be performed to identify the causes of significant heterogeneity based on the variations in study characteristics and population characteristics, and differences in interventions and comparators, and outcomes.

Sensibility analysis: A sensitivity analysis will be investigated to check the stability and robustness of the study findings by removing trials with high risk of bias.

Country(ies) involved: China.

Keywords: Primary open-angle glaucoma; neuroprotection; efficacy.