INPLASY PROTOCOL

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None declared.

Combined 5-Fluorouracil and Low Molecular Weight Heparin for the Prevention of Postoperative Proliferative Vitreoretinopathy in Patients with Retinal Detachment

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Review question / Objective: **The aim of this meta-analysis is to evaluate the efficacy and safety of intraoperative infusion of combined 5-fluorouracil and low molecular weight heparin (LMWH) for the prevention of postoperative proliferative vitreoretinopathy in patients with retinal detachment.**
Condition being studied: **Postoperative proliferative vitreoretinopathy (PVR) is the primary cause of failure of retinal reattachment surgery. 5-fluorouracil (5-FU) inhibits the proliferation of fibroblasts, and suppresses collagen contraction. On the other hand, heparin reduces fibrin exudation, and inhibits the adhesion and migration of retinal pigment epithelial cells. We conduct this comprehensive literature search and meta-analysis to address whether intraoperative infusion of combined 5-FU and LWMH improves the primary success rate of pars plana vitrectomy, as well as reduces postoperative PVR. Our study aims to provide clinical evidence for retinal surgeons concerning their choice of intraoperative medication.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 August 2021 and was last updated on 31 August 2021 (registration number INPLASY202180117).

INTRODUCTION

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METHODS

Search strategy: On May 8th 2021, we searched PubMed, Embase, the Cochrane Library, CNKI, ClinicalTrials.gov, WHO ICTRP and ISRCTN website. The search strategy for PubMed was: (Proliferative Vitreoretinopathy OR Proliferative Vitreoretinopathies OR Vitreoretinopathies, Proliferative OR Vitreoretinopathy, Proliferative) AND (5FU OR 5-FU OR 5-Fluorouracil OR 5 Fluorouracil OR Fluoruracil) AND (Heparin, Low Molecular Weight OR LMWH OR Low Molecular Weight Heparin OR Low-Molecular-Weight Heparin OR Heparin, Low-Molecular-Weight OR Dalteparin OR Enoxaparin OR Nadroparin OR Tinzaparin).

Participant or population: Patients aged 16 years or older, diagnosed as retinal detachment and scheduled for pars plana vitrectomy were included. Patients with traumatic retinal detachment and proliferative diabetic retinopathy were excluded.

Intervention: Intraoperative infusion of combined 5-FU and LWMH.

Comparator: Normal infusion or normal saline.

Study designs to be included: Prospective comparative studies (both RCTs and non-randomized comparative studies).

Eligibility criteria: 1. The study must be prospective, and must have a control group; 2. Studies compare the effects of intraoperative infusion of 5-FU and LMWH with normal infusion; 3. The study must report at least one of our primary outcomes; 4. The study must have a follow-up time of at least 6 months.

Information sources: Electronic databases (PubMed, Embase, the Cochrane Library and CNKI) as well as official websites (ClinicalTrials.gov, WHO ICTRP and ISRCTN).

Main outcome(s): 1. Primary success at 6 months (defined as retinal reattachment after single vitreoretinal procedure). 2. Postoperative PVR occurrence.

Additional outcome(s): 1. Number of vitreoretinal reoperations. 2. Number of vitreoretinal reoperations due to postoperative PVR.

Quality assessment / Risk of bias analysis: RCTs will be evaluated by the Cochrane Risk of Bias Tool (ROB2), while non-randomized comparative studies will be evaluated by the ROBINS-I tool.

Strategy of data synthesis: Review Manager 5.4 (Cochrane library) will be used for data synthesis. Risk Ratio will be calculated along with 95% Confidence Interval. We will first perform tests for heterogeneity. When $I2 \leq 50\%$, fixed effect model will be used to synthesize data. When $I2 > 50\%$, subgroup analysis will be employed to find out the cause of heterogeneity. After this procedure, random effect model will be used if I2 still $> 50\%$.

Subgroup analysis: Subgroup analysis will be included in this study. Unselected rhegmatogenous retinal detachment patients, patients at high risk of postoperative PVR and patients with PVR grade C before operation constitute different subgroups.

Sensitivity analysis: No sensitivity analysis is planned in our meta-analysis.

Language: English, Chinese.

Country(ies) involved: China.

Keywords: proliferative vitreoretinopathy, 5-fluorouracil, low molecular weight heparin.

Contributions of each author:

Author 1 - Chen Chen - Conceived the study and performed database search, quality assessment, data extraction and meta-analysis.
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