

Response to reviewer's comment

Reviewer #1:

1. The authors need to mention the formulation of anti-VEGF - sub-conjunctival/topical. Which formulations were more effective? Which anti-VEGF was more cost-effective?

Response: Thanks for your comments. We apologized for the unclear statement. In the last paragraph of the "Results" section of original submission, we described about the effect from different type of anti-VEGF application, not limited to subconjunctival versus topical, but also the combination with other therapy, such as photodynamic therapy (PDT). The second last paragraph of the "Discussion" section of original submission also addressed this point. However, since there was one study with direct comparison between different formulation of anti-VEGF treatment, it is not possible for the present systematic review/meta-analysis to identify the superiority. We acknowledged that it is a limitation of the present study and described this into the "Discussion" section of the manuscript as following "Our study could not reveal a solid conclusion for this aspect due to the limited data available. Further trials are still needed to seek the ideal administration of anti-VEGF agents in CoNV." Regarding the cost-effectiveness, because bevacizumab is a relatively cheap anti-VEGF agent, and the evidence of the present study was from mainly bevacizumab, it is difficult to compare with other anti-VEGF agents in this point. We acknowledged that it is a limitation of the present study and added this into the "Discussion" section of the revised manuscript as following "Lastly, one of the limitation of the present study was the failure of providing evidence about the cost-effectiveness of different formulation of anti-VEGF agents, since no study included conducting this analysis."

2. The authors shall add one paragraph on What were the complications of these anti-VEGF? Any sight-threatening complication?

Response: Thanks for your comments. We apologized for the unclear statement. In the second last paragraph of the "Results" section of original submission, titled as "Adverse Events", addressed the point you mentioned. Only one study, Dohlman et al., reported the systemic complication of anti-VEGF therapy that one patient developed atrial fibrillation in the bevacizumab group. Regarding the sight-threatening complication, Kim et al. reported persistent epithelial defects with corneal melting after the bevacizumab injection in two patients with limbal stem cell deficiency. The other three trials also reported corneal epithelial defects. However, most patients healed after treatments using local antibiotics, artificial tears, and bandage contact lens. We had also done Figure 5, which demonstrates the pooled effect of bevacizumab on the risk of developing epithelial defects. The results revealed a non-significant reduction of the risk of developing epithelial defect in the bevacizumab group compared with placebo (RR = 0.56, 95% CI: 0.30 to 1.06) and without heterogeneity across trials ($p = 0.50$, $I^2 = 0\%$).

3. The authors must mention - what new information this meta-analysis adds to the existing literature.

Response: Thanks for your comments. The aim of the present study is to address the debating issue of anti-VEGF treatment for CoNV. In this study, we found evidence demonstrating that anti-VEGF agents, mainly bevacizumab, are an effective and safe treatment for CoNV, and reduce CoNV of all causes and prevent the corneal graft from rejection and failure in corneal transplantation patients. These points are the new information we would like to express and described in the "Discussion" section of the original manuscript.

4. The authors must take the help of any English - editor. Thanks

Response: Thanks for your comments. The manuscript had been English editing by Science & English Editing Department, Herbonica International Company Limited.