

Manuscript ID: 69087-- Revision Notes

Dear experts and editorial board.

I have carefully read the review comments of the review experts and the editor of your journal, and I would like to explain the following aspects of the revision of the paper as follows:

Comment 1: Please expand the discussion.

Answer: First of all, we thank the reviewers for their valuable and professional suggestions. We have added to the discussion section of the article as suggested by the reviewers. The additions are mainly in paragraph 1 and paragraph 4, as follows:

Paragraph 1: Given the chronic nature of the disease, the awareness of lifelong management needs to be focused in the clinical decision making. Meanwhile, patients are urgently in need of safe, effective and reliable drugs for endometriosis. To clarify the advantage of dienogest in the treatment of endometriosis, our meta-analysis included seven RCTs with a total of 1493 patients to comprehensively evaluate its efficacy and safety. In term of efficacy, our results showed that dienogest was superior to placebos and GnRH-a in pain relief. Regarding safety, dienogest exhibits significant advantages over GnRH-a with low incidence of side effects. Taken together, dienogest may be the preferred first-line option for endometriosis.

Paragraph 4: Nowadays, research on the mechanism of dienogest to relieve pelvic pain caused by endometriosis is still in the exploratory stage. Some scholars have found that dienogest can inhibit the production of tumor necrosis factor alpha (TNF- α) and interleukin 1 beta (IL- β) by agonizing progesterone receptors, and ultimately achieve the effect of inhibiting nerve growth factor (NGF), which has been shown to be an important factor in pelvic pain caused by endometriosis. It has also been suggested that the good efficacy of dienogest in endometriosis might be related to the expression of NF- κ B, Bcl-2, because dienogest can increase the activity of NF- κ B and thus increase the apoptosis of endometrial mesenchymal cells. Only by fully understanding the mechanism of dienogest can we better implement its application in the treatment.

Comment 2: Also please add funnel plots to the study.

Answer: Funnel plots are a powerful tool for evaluating publication bias in the included literature. We have added a description of the funnel plot in the section on methods and results in this paper, as follows:

Methods section: The funnel plot was used to assess publication bias.

Results section: At the same time, visual inspection of the funnel plot of the changes in VAS scores showed an asymmetrical plot, suggesting some degree of publication bias and more studies are needed to validated the results (Supplementary Figure 1).