INPLASY PROTOCOL

To cite: Chen et al. The efficacy and safety of leuprolide acetate combined with Mirena in the treatment of adenomyosis: a systematic review and meta-analysis. Inplasy protocol 2021100059. doi: 10.37766/inplasy2021.10.0059

Received: 17 October 2021

Published: 17 October 2021

Corresponding author:
Chen Jinman

021323@gzucm.edu.cn

Author Affiliation:
Guangzhou University of Chinese medicine.

Support: **No Support.**

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

The efficacy and safety of leuprolide acetate combined with Mirena in the treatment of adenomyosis: a systematic review and meta-analysis

Chen, JM[1]; Wu, M[2]; Li, WJ[3]; Jian, ZP[4].

Review question / Objective: **The aim of this systematic review is to compare leuprolide acetate combined with Mirena and leuprolide acetate or Mirena or Placebo alone in terms of efficacy and acceptability in the adenomyosis to better inform clinical practice. To this end, the proposed systematic review will address the following question: Which is the best choice to reduce VRS dysmenorrhea score or PBAC menstrual volume score or Serum matrix metalloproteinase (MMP) 2 and 9 or vascular endothelial growth factor (VEGF) in adenomyosis, leuprolide acetate combined with Mirena or leuprolide acetate or Mirena or Placebo alone.**
Information sources: **A systematic search conducts in the Cochrane library, Embase, Pubmed and Web of Science. CNKI, CBM, et al.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 October 2021 and was last updated on 17 October 2021 (registration number INPLASY2021100059).

INTRODUCTION

Review question / Objective: **The aim of this systematic review is to compare leuprolide acetate combined with Mirena and leuprolide acetate or Mirena or Placebo alone in terms of efficacy and acceptability in the adenomyosis to better inform clinical practice. To this end, the proposed systematic review will address the following question: Which is the best choice to reduce VRS dysmenorrhea score or PBAC menstrual volume score or Serum matrix metalloproteinase (MMP) 2 and 9 or vascular endothelial growth factor (VEGF) in adenomyosis, leuprolide acetate combined with Mirena or leuprolide acetate or Mirena or Placebo alone.**

Condition being studied: Adenomyosis is a benign uterine disorder in which endometrial glands and stroma are pathologically demonstrated in the myometrium. Women affected by adenomyosis may present with abnormal uterine bleeding (AUB), dysmenorrhea, dyspareunia, or infertility but one third of them are asymptomatic. The treatment of adenomyosis includes drug treatment and surgical treatment. Patients who are young or have fertility requirements could choose drug treatment; those who do not have fertility requirements, have severe symptoms, and have failed conservative treatment can choose surgical treatment; those with prominent dysmenorrhea symptoms can be treated with conservative surgery. Surgical treatment includes total hysterectomy; conservative surgery includes endometrial ablation, hysteroscopic endometrial and adenomyoma resection, but conservative surgery is controversial, and exists risks for patients with fertility requirements. Therefore, more and more patients choose medication. Based on the pathogenic mechanism, several drug hormonal and non-hormonal treatments are used to treat pain and bleeding and improve fertility results. For example, GnRHa, progesterone, levonorgestrel intrauterine sustained release system (LNG-IUS, Mirena) and so on. In recent years, related studies have found that the combined treatment of leuprolide acetate and Mirena is effective in the treatment of muscular adenomyosis. The article conducts a systematic review and meta-analysis of the combined treatment of leuprolide acetate and Mirena in the treatment of muscular adenomyosis, in order to provide more clinical evidence for the treatment of muscular adenomyosis.

METHODS

Participant or population: Patients with adenomyosis.

Intervention: Leuprolide acetate combined with Mirena.

Comparator: Leuprolide acetate or Mirena or other interventions.

Study designs to be included: Randomized controlled trials (RCTs).

Eligibility criteria: Inclued：(1) randomized controlled studies; (2) Patients in the experimental group were treated with leuprolide acetate combined with Mirena while patients in the control group received other medications, such as leuprolide acetate or Mirena or Placebo alone; (3) The primary outcome is the improvement in pain associated with endometriosis, other outcomes include side effects and changes in the clinical laboratory parameters. Meta-analyses, reviews, case reports, conference abstracts, cohort studies, retrospective studies and trails without available data are excluded.

Information sources: A systematic search conducts in the Cochrane library, Embase, Pubmed and Web of Science. CNKI, CBM, et al.

Main outcome(s): The primary efficacy outcome is changes in VRS dysmenorrhea score, PBAC menstrual volume score; Serum matrix metalloproteinase (MMP) 2 and 9/vascular endothelial growth factor (VEGF) and so on.

Quality assessment / Risk of bias analysis: To assess study quality, the Cochrane risk of bias assessment tool will be used. Seven domains related to risk of bias are assessed in each study: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; (7) other bias.

Strategy of data synthesis: The Review Manager 5.3 software are used to conduct the meta-analysis. If there is no heterogeneity, choose fixed effects to merge data; if there is heterogeneity, first examine the source of the heterogeneity, and then choose an appropriate method to merge. For example, if the source of

heterogeneity is statistical heterogeneity, we would choose to merge data with random effects.

Subgroup analysis: Divide into subgroups based on control measures, Subgroup 1: Leuprolide acetate alone; Subgroup 2: Mirena; Subgroup 3: Placebo.

Sensitivity analysis: If a sufficient number of studies are identified for inclusion, we will conduct sensibility analysis by eliminating studies one by one to find the source of heterogeneity.

Country(ies) involved: China.

Keywords: Adenomyosis; leuprolide acetate; Mirena.

Contributions of each author:
Author 1 - Chen Jinman.
Author 2 - Wu Man.
Author 3 - Li Weijie.
Author 4 - Jian Zhengpu.