# Effects of mifepristone on uterine leiomyoma in premenopausal women: a meta-analysis

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**Objective:** To conduct a meta-analysis of the studies assessing the effects of mifepristone on the uterus, uterine leiomyoma, and leiomyoma-related symptoms in premenopausal women.
**Design:** Meta-analysis.
**Setting:** Centers for reproductive care.
**Patient(s):** Premenopausal women who suffered from leiomyoma.
**Intervention(s):** We identified all of the studies published before December 2012 that compared the status of patients with leiomyoma before and after treatment with mifepristone.
**Main Outcome Measure(s):** Leiomyoma-related symptoms, uterine or leiomyoma volume, changes in endometrial thickness.
**Result(s):** A meta-analytic technique was used to study 11 randomized controlled trials involving 780 women with symptomatic uterine leiomyomas. The subjects received 2.5–25 mg/d of mifepristone for 3–6 months. Mifepristone could effectively reduce uterine and leiomyoma volume and alleviate leiomyoma symptoms, including hypermenorrhea, the mean menstrual blood loss, pelvic pain, pelvic pressure, anemia, and dysmenorrhea. There was no significant difference in the rate of atypical endometrial hyperplasia between the mifepristone treatment group and the placebo group.
**Conclusion(s):** Mifepristone significantly reduced uterine and leiomyoma volume and alleviated leiomyoma-related symptoms. We recommend 2.5 mg of mifepristone administered daily for 3 or 6 months as the optimum clinical treatment for leiomyoma. There is insufficient evidence that mifepristone treatment led to atypical endometrial hyperplasia. (Fertil Steril® 2013;100:1722–6. ©2013 by American Society for Reproductive Medicine.)
**Key Words:** Mifepristone, leiomyoma, meta-analysis

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Uterine leiomyomas are the most common benign tumors in the female reproductive system. Recent studies have determined that the lifetime risk of leiomyomas in women aged 45 years and more is greater than 60% (1). Menorrhagia, abnormal uterine bleeding, pelvic pain or pressure, infertility, and recurrent pregnancy loss are generally associated with leiomyoma. Although surgical and radiological therapies are frequently used for the management of these tumors, medical therapies, including GnRH agonists and progesterone modulators, are the first-line treatment of leiomyomas (2). Recent investigations have demonstrated that progesterone is essential for the maintenance and growth of uterine leiomyomas (3).

Mifepristone (known as RU-486), an anti-progesterone drug, has been shown to be effective in the treatment of uterine leiomyoma, resulting in decreased leiomyoma size and symptoms (4, 5). Mifepristone's effects vary with different durations of treatment or dosages (2.5 mg/d for 6 months [4], 25 mg/d for 6 months [5], 5 or 10 mg/d for 1 year [6], and 50 mg every other day for 3 months [7]).

In this study, meta-analysis techniques were used to assess the effects of mifepristone treatment

Received April 30, 2013; revised and accepted August 22, 2013; published online October 2, 2013.
Q.S. has nothing to disclose. Y.H. has nothing to disclose. W.J. has nothing to disclose. W.Z. has nothing to disclose. M.C. has nothing to disclose. X.Z. has nothing to disclose.
Supported by a grant from the Family Planning Commission of Zhejiang (no. 2011-28) and sponsored by Zhejiang Provincial Program for the Cultivation of High-level Innovative Health Talents.
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Fertility and Sterility® Vol. 100, No. 6, December 2013 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2013.08.039

on leiomyomas, as described in randomized controlled trials, and to recommend the optimum duration and dose of mifepristone for the management of uterine leiomyomas in premenopausal women.

## MATERIALS AND METHODS

### Search Strategy

A computerized search of the MEDLINE, EMBASE, and Cochrane databases was undertaken with the MeSH terms "mifepristone" and "leiomyoma" and the date range of 1985 to 2012. All of the publications appearing before December 2012 in these databases were included. We reviewed the reference lists in the retrieved articles. This study contains unpublished trial abstracts. These abstracts were found by searching the relevant journals and conference proceedings. The approval of the study was obtained from the local research ethics committee.

### Selection of Studies and Validity Assessment

Because of the language limitations, only studies published in English or Chinese were included for further analysis. We excluded case report studies, studies that were not published as full reports, and studies with an inappropriate comparison group or without control subjects. The inclusion criteria were randomized clinical trials of daily mifepristone administration for uterine leiomyoma that measured leiomyoma-related symptoms and uterine or leiomyoma volume before and after treatment. To determine the validity, the quality of each study was assessed according to the modified Jadad scale (8) (Supplemental Table 1, available online), and a score $\geq 4$ was considered a high quality article.

### Data Abstraction

Any studies on the effects of mifepristone on uterine leiomyoma in premenopausal women were examined in detail. The data from potentially relevant articles were abstracted independently by two reviewers, and the differences were resolved by consensus.

### Data Synthesis

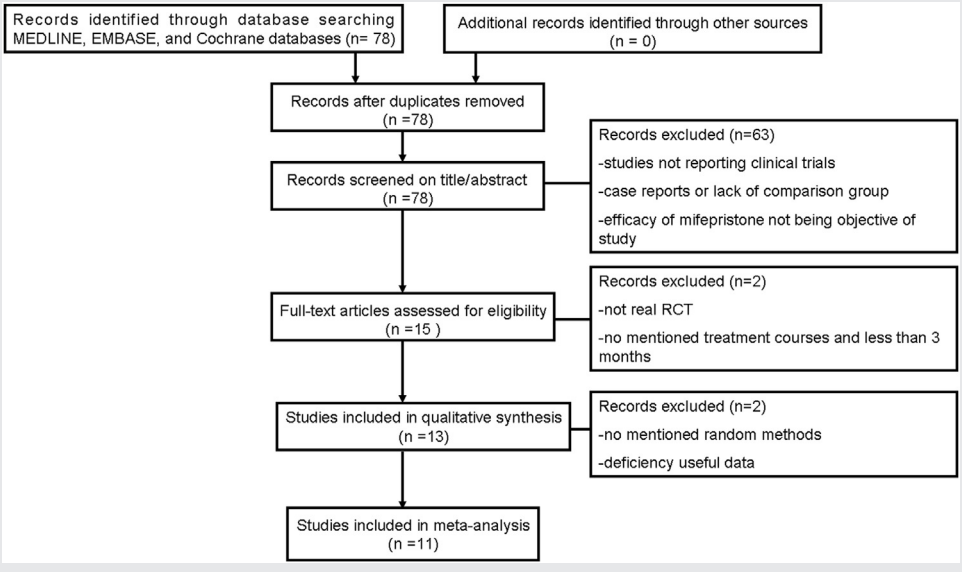
A qualitative meta-analysis was conducted by summarizing, comparing, and contrasting the abstracted data. The quantitative meta-analysis was conducted on the risk factors from two or more studies. RevMan 5.0 software (Cochrane Collaboration) was used, and heterogeneity was evaluated using the $\chi^2$ test, $P$ values, and $I^2$ statistics (9). If heterogeneity might be accepted ($P>.10$), a fixed-effects model was used for the meta-analysis. Otherwise, a random effects model was used to conduct the meta-analysis. A subgroup analysis was performed to explore the possible reasons for the heterogeneity.

## RESULTS

A total of 780 women with symptomatic uterine leiomyoma from 11 randomized controlled trials were included in this meta-analysis (4–6, 7, 10–17). A flow diagram for the literature search is presented in Figure 1.

As shown in Figure 2 (Supplemental Figs. 1–3, available online), compared with a placebo, mifepristone could effectively reduce uterine and leiomyoma volumes and alleviate leiomyoma symptoms, including hypermenorrhea, pelvic pain, pelvic pressure, and dysmenorrhea. Mifepristone could significantly decrease the mean menstrual blood loss and increase hemoglobin levels. Because the results indicated that taking mifepristone significantly increased

**FIGURE 1**




Flow diagram for the literature search. RCT = randomized controlled trial.

*Shen. Mifepristone and uterine leiomyoma. Fertil Steril 2013.*