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Review

Levonorgestrel-releasing intrauterine system use in premenopausal women with symptomatic uterine leiomyoma: A systematic review

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ABSTRACT

A systematic review is done to determine the efficacy and safety of levonorgestrel-releasing intrauterine systems as a treatment using in premenopausal women with symptomatic uterine leiomyoma. We searched the Medline, Central and ICTRP databases for all articles published from inception through July 2013 that examined the following outcomes: uterine volume, uterine leiomyoma volume, endometrial thickness, then menstrual blood loss, blood haemoglobin, ferritin and hematocrit levels, treatment failure rate, device expulsion rate, hysterectomy rate and side effects. From 645 studies, a total of 11 studies met our inclusion criteria with sample sizes ranging from 10 to 104. Evidence suggested that levonorgestrel-releasing intrauterine systems could decrease uterine volume and endometrial thickness, significantly reduce menstrual blood loss, and increase blood haemoglobin, ferritin and hematocrit levels. There was no evidence for decreasing uterine leiomyoma volume. There were no adverse effects on the ovarian function except for ovarian cysts. Device expulsion rates were low, which associated with leiomyoma size (larger than 3 cm) but not with leiomyoma location. Irregular bleeding/spotting was observed at the beginning of the follow-up period and then decreased progressively. Results of this systematic review indicate that levonorgestrel-releasing intrauterine systems may be effective and safe treatment for symptomatic uterine leiomyoma in premenopausal women.

Contents

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1. Introduction

Uterine leiomyomas occur in 30–50% of reproductive-aged women [1,2], increasing to a 70–80% cumulative incidence by age 50 years [3]. They are commonly associated with menstrual abnormalities, pelvic pain or pressure, infertility and recurrent pregnancy loss, thus they can have a negative impact on multiple aspects of a women's life [4]. Although most leiomyomas are asymptomatic, some women have significant symptoms that need interventions [5].

Treatment options for symptomatic uterine leiomyomas have recently expanded beyond surgery. Medical therapies, including combined oral contraception, gonadotrophin releasing hormone analogues, progesterone receptor modulators, progestins and levonorgestrel-releasing intrauterine systems (LNG-IUSs) [6,7], have become more and more widely used. Currently, there is increased concern about safer and more effective methods for treatment of leiomyoma in women with uterine leiomyoma.

In recent years LNG-IUSs are increasingly being used for gynecological indications other than contraception. Current indications include but are not limited to: menorrhagia, uterine leiomyoma, endometriosis, adenomyosis, endometrial hyperplasia, early stage endometrial cancer [8–10]. LNG-IUSs were marketed as Mirena for general public use. Studies have reported high contraceptive efficacy and an improvement in menstrual blood loss with LNG-IUSs [11–12], including in women with uterine leiomyoma [13]. However, the effects of LNG-IUSs on uterine and leiomyoma volumes are still unclear and controversial. Some studies reported a reduction in uterine volume [13,14] and leiomyoma volume [13,15]; however, other studies concluded that no decreases in uterine volume [16] and leiomyoma volume [17] occurred. To date, there has been no review of the effect of LNG-IUSs on the endometrial thickness and ovarian function for treating symptomatic uterine leiomyoma.

In the assessments of the effects of LNG-IUSs for contraception in women with leiomyoma, Zapata et al. [18] has showed that LNG-IUSs could reduce menstrual blood loss, and increase blood haemoglobin, ferritin and hematocrit levels, and also studied IUD expulsion rate and spotting rate. However, they did not study other new outcomes of LNG-IUSs and leiomyoma size to expulsion rate. Hence, a new systematic review was also needed to evaluate the evidence concerning the effectiveness and safety of LNG-IUSs for treating symptomatic uterine leiomyomas in the comparison with other treatments, especially with regard to uterine and leiomyoma volumes, endometrial thickness, hysterectomy rate and adverse effects on ovarian function. The generated results will be fundamental to informing the integration of policies and interventions for the treatment of uterine leiomyoma.

2. Materials and methods

2.1. Search strategy

Electronic searches of databases and hand searches of other resources were conducted to search published and unpublished articles for review. We searched Medline (PubMed; up to July 2013), the Cochrane Central Register of Controlled Trials (CENTRAL; up to July 2013) and the WHO International Clinical Trials Registry Platform (ICTRP) for ongoing trials (July 2013) (Appendix). Only studies published in English were included and no limits were placed upon date of publications. We also examined the reference lists of all known primary and review articles to identify cited articles not captured by electronic searches. Finally, we made enquires about unpublished studies from researchers working in this field. The search strategy was performed independently by two authors and is shown in Fig. 1.

2.2. Criteria for considering studies

We included randomised controlled trials (RCTs), non-randomised trials, and observational studies that compared the efficacy