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Original Research Article

Therapeutic role of low-dose mifepristone in the management of uterine fibroids: clinical outcomes and contemporary perspective

Selvi Dhanagopal[1]*, Santhiya Swathy Muthu Selvam[2]

[1]Department of Obstetrics and Gynecology, Government Peripheral Hospital, Tondiarpet, Chennai, Tamil Nadu, India
[2]Department of Obstetrics and Gynecology, Dr. Aravind's IVF, Salem, Tamil Nadu, India

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***Correspondence:**
Dr. Selvi Dhanagopal,
E-mail: swathysanthiya@yahoo.com

ABSTRACT

Background: Uterine fibroids are the most common benign tumors of the female reproductive tract and are a major cause of menstrual disturbances and anemia. Conservative medical therapies are increasingly preferred over surgical options in women desiring uterine preservation. Mifepristone, a progesterone receptor antagonist, has shown promising results in reducing fibroid volume and associated symptoms. Objectives were to evaluate the clinical efficacy and safety of low-dose mifepristone (25 mg daily) in reducing fibroid size and improving clinical symptoms among perimenopausal women with symptomatic leiomyomas.
Methods: This prospective observational study was conducted from June 2024 to July 2025 at the Department of Gynecology, Government Peripheral Hospital, Tondiarpet, Chennai. Ninety-three perimenopausal women aged 35-50 years with ultrasonographically confirmed symptomatic fibroids were treated with 25 mg mifepristone daily for three months. Clinical parameters, uterine and fibroid volumes, hemoglobin, and endometrial thickness were evaluated before and after therapy.
Results: Amenorrhea was achieved in 92.7% of patients. Mean uterine and myoma volumes decreased to 63.7% and 53.6% of baseline, respectively. Mean hemoglobin levels increased by 2.8 g/dl (37%) post-treatment. Endometrial thickening was mild in most patients, with two cases of simple hyperplasia without atypia. Headache was the most frequent adverse effect (12%), with no major hepatic or renal complications reported. Hysterectomy was avoided in 87.8% of patients.
Conclusions: Low-dose mifepristone (25 mg daily) is a safe, effective, and affordable therapeutic option for managing symptomatic uterine fibroids in perimenopausal women. It significantly reduces fibroid and uterine volume, controls bleeding, and improves hemoglobin levels, minimizing the need for surgical intervention.

Keywords: Mifepristone, Uterine fibroids, Low-dose therapy, Amenorrhea, Conservative management

INTRODUCTION

Uterine leiomyoma are commonest benign gynaecological tumours occurring in up to 25% of women in reproductive age and about 40% have symptoms severe enough to warrant therapy.[1] Histologically, fibroids are benign neoplasms composed of disordered smooth-muscle cells buried in abundant quantities of extracellular matrix.[2,3] Risk factors includes age, genetics, parity, increased body mass index and use of depot injections.[4] The pathogenesis is complex, involving hormonal, genetic, and local tissue factors. Recent evidence highlights dysregulated progesterone receptor signaling, growth factor activation, and extracellular matrix remodeling as key pathways in fibroid development.[2] Early onset of menstruation has been associated with an increased risk of being diagnosed with leiomyomas, whereas late menarche appears to confer a protective effect. These associations are consistent with the role of gonadal steroids, at least in leiomyoma growth. Specifically, women with a menarche before age 10 have

a relative risk of 1.24 for developing leiomyomas, while those whose menarche occurred after age 16 have a significantly lower relative risk of 0.68.[5] Studies demonstrated that progesterone signaling promotes the growth and proliferation of fibroid cells through increasing proliferating cell nuclear antigen (PCNA) expression, which increases both the number of fibroid cells and the size of fibroid tumors.[6] In addition, progesterone induced expression of several WNT ligands, with the subsequent induction of β-catenin nuclear translocation and transcriptional activity of its heterodimeric partner T-cell factor and their target gene AXIN2, leads to the proliferation of fibroid side population (SP) cells.[7]

Medical treatments used for UFs-related abnormal uterine bleeding include symptomatic agents, such as nonsteroidal anti-inflammatory drugs and tranexamic acid, and hormonal therapies, including combined oral contraceptives, gonadotropin-releasing hormone agonists/antagonists, levonorgestrel intrauterine systems, selective progesterone receptor modulators, and aromatase inhibitors. Nevertheless, few drugs are approved specifically for UF treatment, and most of them manage the symptoms. Surgical options include fertility-sparing treatments, such as myomectomy, or nonconservative options, such as hysterectomy, especially in perimenopausal women who are not responding to any treatment. Radiologic interventions are also available: uterine artery embolization (UAE), high-intensity focused ultrasound or magnetic resonance-guided focused ultrasound, and radiofrequency ablation.[8] Recent advances in interventional radiology-such as UAE, high-intensity focused ultrasound (HIFU), and magnetic resonance-guided focused ultrasound (MRgFUS)-offer minimally invasive alternatives but may still involve recurrence or limited access in low-resource settings. MRI-guided method of treatment of uterine fibroids and fibromas with the use of HIFU is relatively new and was introduced to clinical practice in the USA in 2004, after the U. S. Food and Drug Administration (FDA) accepted it.[9]

Medical therapy remains a desirable option, particularly in perimenopausal women or those seeking uterine conservation. The ideal agent should control bleeding, shrink fibroids, improve anemia, and minimize adverse effects. Tranexamic acid (TXA) is a suitable option for the management of abnormal uterine bleeding associated with uterine fibroids. TXA is a synthetic lysine-analog antifibrinolytic and therefore not a causal therapy for uterine fibroids.[10] COCs reduce abnormal uterine bleeding in women with uterine fibroids by 9.9 mL (13.4% reduction) as measured by the alkaline hematin method, and by 53.5% by the pictorial blood loss assessment Chart.[11] In women with ovulatory abnormal uterine bleeding, oral medroxyprogesterone acetate (MPA), norethindrone, megestrol acetate/micronized progesterone taken cyclically (starting on menstrual day 5 for 21 days) or continuously provides cycle control and reduction of menstrual blood loss.[12] Gonadotropin-releasing hormone (GnRH) agonists are peptides similar in structure to GnRH with amino acid substitutions that enhance their affinity for binding to receptor. This causes continuous stimulation, initially producing an increase in release of gonadotropins (flare effect) that can last 1-2 weeks, after which gonadal sex steroids decrease until reaching medical castration levels.[13] Pharmacologic options include gonadotropin-releasing hormone (GnRH) agonists and antagonists, selective progesterone receptor modulators (SPRMs), oral contraceptives, and aromatase inhibitors, but most have limitations such as hypoestrogenic side effects, high cost/symptom relapse after discontinuation.

Among the SPRMs, mifepristone has shown consistent efficacy and safety in reducing fibroid volume and improving bleeding patterns. Its mechanism involves competitive inhibition of progesterone receptors and modulation of growth factor signaling, leading to suppression of cell proliferation and induction of apoptosis. The SPRM (ulipristal and mifepristone), GnRH agonist, oral contraceptives, levonorgestrel intrauterine device, aromatase inhibitor, and GNRH antagonists are used in medical management of fibroids, however, out of these only GNRH analogs and SPRM are seen to have reduction in fibroid size.[14] Mifepristone (RU486) is a synthetic selective progesterone-receptor modulator that acts as a competitive antagonist at progesterone receptor in the presence of progesterone, but as a partial agonist in the absence of progesterone.[15] Systematic review and meta-analysis by Zhao et al demonstrated that low-dose mifepristone (5-25 mg/day) significantly reduces fibroid volume and menstrual blood loss while improving hemoglobin levels with minimal side effects. While higher doses (25 mg daily) showed a statistically significant reduction compared to lower doses (10 mg daily).[16] Similarly, a 2024 randomized controlled trial by Li et al confirmed dose-dependent improvements in symptom severity and quality of life among Asian women with uterine leiomyomas. Multicenter observational study further reported that 3 months treatment of 25 mg mifepristone effectively controls bleeding, reduces the uterine and myoma volume and thus can avoid blood transfusion and hysterectomy in a lot of symptomatic myoma cases.[17]

In parallel, newer oral GnRH antagonists such as relugolix and linzagolix have emerged as promising alternatives, offering reversible ovarian suppression with add-back therapy for improved tolerability. GnRH antagonists such as relugolix have been shown to suppress follicle-stimulating hormone (FSH) and luteinizing hormone (LH) production in a dose-dependent manner. They also inhibit the release of ovarian steroid hormones without inducing the flare-up phenomenon.[18] The oral GnRH antagonists (Elagolix, Relugolix, Linzagolix) represent a new alternative for the medical management of hormone-related gynaecological diseases such as UF and endometriosis. The efficacy is based on the fast and dose-related inhibition of circulating oestrogen levels, without the initial increase observed with GnRH agonists. GnRH antagonists rapidly bind to the GnRH receptor, block

endogenous GnRH activity and directly suppress LH and FSH production, avoiding unwanted flare-up side effects.[19] However, their cost and limited long-term data restrict widespread use in developing regions. Mifepristone, by contrast, is cost-effective, widely available, and well-tolerated, making it a practical option in resource-limited settings.

Despite these encouraging findings, evidence from large, prospective Indian studies remains sparse. Existing data are often limited by small sample sizes, short duration, and lack of standardized volumetric assessment. Therefore, this study evaluates the clinical outcomes of low-dose mifepristone (25 mg daily for three months) in perimenopausal women with symptomatic uterine leiomyomas, emphasizing its efficacy, safety, and potential to reduce surgical intervention.

METHODS

Study design and setting

This prospective observational study was conducted over1 year (2024-25) in the Department of Gynecology at the Govt Peripheral Hospital, Tondiarpet. Ethical approval was obtained from the Institutional Ethics Committee, and informed consent was secured from all participants.

Participants

Ninety-three perimenopausal women aged 35-50 years with symptomatic uterine fibroids were enrolled. Inclusion criteria included ultrasonographically confirmed leiomyomas associated with menorrhagia, pelvic pain, or anemia. Women desiring uterine preservation were considered eligible.

Exclusion criteria included fibroids >10 cm in diameter, current pregnancy, malignancy or suspicion of leiomyosarcoma, history of breast or genital tract cancer, severe hepatic or renal impairment and hormonal therapy within the previous two months.

Intervention

Participants received 25 mg of mifepristone daily for three months, starting between the 3rd and 5th day of their menstrual cycle. The medication was prepared by subdividing commercially available 200 mg tablets into precise 25 mg doses.

Assessments

Baseline evaluations included complete blood count, liver and renal function tests, pelvic ultrasonography to measure uterine and myoma volumes, endometrial thickness measurements.

Uterine and fibroid volumes were calculated using the prolate ellipsoid formula: Volume=0.523×A×B×C

Where A, B, and C represent the three largest perpendicular diameters.

Clinical follow-up occurred monthly during treatment and for three months post-treatment.

Key parameters in follow up included: Menstrual bleeding (recorded by participants and categorized as menorrhagia, polymenorrhagia, or menometrorrhagia).

Pain scores using a 5-point Likert scale. Hemoglobin levels and endometrial thickness.

Statistical analysis

Data were analyzed using descriptive statistics. Mean, standard deviation (SD), and percentage change were calculated for clinical and ultrasonographic parameters.

RESULTS

Baseline characteristics

Of the 93 women enrolled, the mean age was 38.5±4.9 years. Menorrhagia was the most common symptom, reported by 91.5% of participants, followed by pelvic heaviness (26.8%) and pelvic pain (21.9%). The mean baseline uterine volume was 302,124 mm³, and the mean baseline dominant myoma volume was 143,958 mm³. Baseline mean hemoglobin was 8.9 g/dl.

Table 1: Age group.

Age group (in years)	N (%)
20-40	32 (34.4)
41-60	62 (65)
>60	5 (5)

More than half of the patients (65%) belonged to the age group 41-60 years. 34.4% were aged 20-40 years, and only 5% were over 60.

Table 2: Parity.

Parity	N (%)
Nullipara	5 (5)
Primi para	17 (18)
Multi para	71 (81.9)

The majority of the patients (81.9%) were multiparous, followed by 18% primiparous and 5% nulliparous.

Table 3: Clinical features.

Clinical features	N (%)
AUB	67 (72)
Infertility	17 (18.2)
Pressure symptoms	19 (20)

AUB was the most common symptom (72%), with 20% experiencing pressure symptoms and 18.2% reporting infertility.

Table 4: Type of fibroid.

Type of fibroid	N (%)
Intramural	71 (76.3)
Submucous	9 (9)
Subserous	7 (7)
Pedunculated	6 (6)

Intramural fibroids were the most prevalent (76.3%), followed by submucous (9%), subserous (7%), and pedunculated (6%).

Table 5: Degeneration.

Degeneration	N
Yes	26
No	67

Treatment outcomes

Bleeding control

Menstrual bleeding ceased within 4-5 days in most women, and 92.7% achieved amenorrhea during treatment. Seven women (8.5%) showed no response and required hysterectomy.

Uterine and fibroid volume reduction

After three months, mean uterine volume decreased to 63.7% of baseline, while mean myoma volume decreased to 53.6%.

Hematological improvement

Hemoglobin levels increased by 2.8 g/dl (37%) after treatment.

Endometrial changes

Endometrial thickness increased progressively but remained below 20 mm in most women. Two cases showed simple hyperplasia without atypia.

Adverse effects

Headache was the most frequent side effect (12%). No significant hepatic or renal adverse events were reported.

Post-treatment outcomes

At three months follow-up, menstruation returned in most participants. Four women required hysterectomy for recurrent heavy bleeding. Overall, hysterectomy was avoided in 87.8% of women.

DISCUSSION

Uterine fibroids (leiomyoma or myoma), benign monoclonal tumors, commonest benign tumors in women. AUB and the, resultant anemia, pelvic pain, infertility, and/or recurrent pregnancy loss are generally associated with uterine fibroids. Although curative treatment of this tumor relies on surgical therapies, medical treatments are considered the first-line treatment to preserve fertility and avoid or delay surgery. Fibroids cause HMB because of various reasons, increased endometrial surface, uterine volume, interference with contractility, aberrant angiogenesis and associated endometrial hyperplasia and endometrial polyp. Fibroid being a tumor of hyper-estrogenic environment, therefore medical treatment that lowers estrogen levels as GnRH agonists (Lupride) and antagonists (Cetrorelix), Danazol, Gestrinone, Cabergoline, reduces aromatase activity (Letrozole) or modifies estrogen response (SERM-Raloxifene) are effective in reducing the size of fibroid and improve symptoms in most of cases. Current studies support that growth of myoma in humans is progesterone dependent also and therefore antiprogestins (Mifepristone) and selective progesterone receptor modulators (SPRMs-Asoprisnil) can be effective in treatment. Hormonal treatment reduces size, improves hemoglobin by controlling bleeding and renders surgery unnecessary as patient reaches menopause, because fibroid being a hormone depended tumor stops to grow after menopause. Mifepristone has both antiprogesterone and anti-glucocorticoid properties in dose dependent manner.

Clinical trials using 5-50 mg doses of Mifepristone were conducted for varying periods between 3 to 12 months but exact dose and the duration are yet to be determined. Eisinger et al reported fall of 48% in mean uterine volume while amenorrhoea in 61% only after 6 months of 10 mg mifepristone.[20] The effects of mifepristone, as a progesterone receptor modulator with anti-progesterone activity, were investigated by Chung et al who established that PCNA expression was significantly reduced in a mifepristone-treated group compared with those in a control group.[21] Short-term use of SPRMs resulted in improved quality of life, reduced menstrual bleeding and higher rates of amenorrhoea than were seen with placebo. Thus, SPRMs may provide effective treatment for women with symptomatic fibroids.[22]

CONCLUSION

The outcome of Mifepristone therapy is multifactorial and depends on SPRM influence on receptors, proliferation, apoptosis and fibrosis in myoma tissue. The results of the study indicate that a good response toMifepristone, manifested by a volume reduction of myoma, may be associated with a decrease in fibrosis, ER/PR and PCNA and Ki67 immuno-expression as well as an increase in cell apoptosis in uterine myoma. The strengths of our study were adequate sample size for statistically valid results.

Limitations of the study were not using PAEC to classify endometrial histopathology.

In future, studies can be planned to ensure effect of preoperative mifepristone on surgical planes and surgical ease, degeneration of myomas and to reduce blood loss.

In conclusion, our results showed that mifepristone 25 mg led to symptomatic relief in patients with myoma with more than 90 per cent reduction in menstrual blood loss. However, significantly greater reduction in overall myoma sizeand endometrial changes specific to progesterone receptor modulator occurred with no evidence of atypia. Reversible amenorrhoea developed in 90-95% patients. Mifepristone can be a valid choice especially in perimenopausal age women in whom myomas would reduce after menopause and unmarried female who want to avoid surgery. As a primary medical therapy is limited due to recurrence after stopping treatment, it can be used as an adjunct in preoperative cases, especially in patients with severe anaemia, big fibroids, where surgery is difficult or unresectable leiomyoma are encountered.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Adamson GD. Treatment of uterine fibroids current findings with gonadotrophin releasing hormone agonists. Am J Obstet Gynecol. 1992;166:746-51.
2. Sankaran S, Manyonda IT. Medical management of fibroids. Best Pract Res Clin Obstet Gynaecol. 2008;22(4):655-76.
3. Parker WH. Etiology, symptomatology, and diagnosis of uterine myomas. Fertil Steril. 2007;87(4):725-36.
4. Wise L, Laughlin-Tommaso S. Epidemiology of Uterine Fibroids: From Menarche to Menopause. Clin Obstet Gynecol. 2016;59(1):2-24.
5. Marshall LM, Spiegelman D, Goldman MB. A prospective study of reproductive factors and oral contraceptive use in relation to the risk of uterine leiomyomata. Fertil Steril. 1998;70(3):432-9.
6. Ishikawa H, Ishi K, Serna VA, Kakazu R, Bulun SE, Kurita T. Progesterone Is Essential for Maintenance and Growth of Uterine Leiomyoma. Endocrinology. 2010;151:2433-42.
7. Ono M, Yin P, Navarro A, Moravek MB, Coon JS, Druschitz SA, et al. Paracrine activation of WNT/beta-catenin pathway in uterine leiomyoma stem cells promotes tumor growth. Proc Natl Acad Sci USA. 2013;110:17053-8.
8. Vannuccini S, Petraglia F, Carmona F, Calaf J. The modern management of uterine fibroids-related abnormal uterine bleeding. Fertil Steril. 2024;122(1):20-30.
9. Al Hilli MM, Stewart EA. Magnetic resonance-guided focused ultrasound surgery. Semi Reproduct Med. 2010;28(3):242-9.
10. Ng W, Jerath A, Wąsowicz M. Tranexamic acid: a clinical review. Anaesthesiol Intensive Ther. 2015;47(4):339-50.
11. Sangkomkamhang US, Lumbiganon P, Pattanittum P. Progestogens or progestogen-releasing intrauterine systems for uterine fibroids (other than preoperative medical therapy). Cochrane Database Syst Rev. 2020;11(11):CD008994.
12. Bradley LD, Gueye NA. The medical management of abnormal uterine bleeding in reproductive-aged women. Am J Obstet Gynecol. 2016;214(1):31-44.
13. Ascoli M, Puett D. The gonadotropin hormones and their receptors. In: Strauss JF, Barbieri RL, eds. Yen and Jaffe's Reproductive Endocrinology: Expert Consult-Online and Print. 9th ed. Elsevier Inc. 2023;35-55.
14. Sohn GS, Cho S, Kim YM. Working Group of Society of Uterine Leiomyoma. Current medical treatment of uterine fibroids. Obstet Gynecol Sci. 2018;61(2):192-201.
15. Kakade AS, Kulkarni YS. Mifepristone: current knowledge and emerging prospects. J Indian Med Assoc. 2014;112:36-40.
16. Chen L, Jia L, Li H, Yuan Y, Wang S, Tian L, et al. Effect of mifepristone on uterine fibroids: A systematic review and meta-analysis. J Gynecol Obstet Hum Reprod. 2025;54(5):102929.
17. Seth S, Goel N, Singh E, Mathur AS, Gupta G, Effect of mifepristone (25 mg) in treatment of uterine myoma in perimenopausal woman J Midlife Health. 2013;4(1):22-6.
18. Donnez J, Taylor HS, Taylor RN, Akin MD, Tatarchuk TF, Wilk K, et al. Treatment of endometriosis-associated pain with linzagolix, an oral gonadotropin-releasing hormone-antagonist: A randomized clinical trial. Fertil. Steril. 2020;114:44-55.
19. Van Poppel H, Klotz L. Gonadotropin-releasing hormone: an update review of the antagonists versus agonists. Int J Urol. 2012;19:594-601.
20. Eisinger SH, Bonfiglio T, Fiscella K, Meldrum S, Guzick DS. Twelve month safety and efficacy of low dose mifepristone for uterine myomas. J Minim Invasive Gynecol. 2005;12:227-33.
21. Chung YJ, Chae B, Kwak SH. Comparison of the inhibitory effect of gonadotropin releasing hormone (GnRH) agonist, selective estrogen receptor modulator (SERM), antiprogesterone on myoma cell proliferation in vitro. Int J Med Sci. 2014;11:276-81.
22. Murji A, Whitaker L, Chow TL, Sobel ML. Selective progesterone receptor modulators (SPRMs) for uterine fibroids Cochrane Database Syst Rev. 2017;4(4):CD010770.

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