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Different dosages of mifepristone versus enantone to treat uterine fibroids

A multicenter randomized controlled trial

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Abstract

Background: To evaluate the efficacy and safety of 10 mg and 25 mg mifepristone per day compared with 3.75 mg enantone in treating uterine fibroids.

Methods: This is a Multicenter randomized controlled trial. A total of 501 subjects with symptomatic uterine fibroids were enrolled and randomized into the group of 10mg, 25mg mifepristone and 3.75 enantone (with 307, 102 and 92 subjects respectively), with 458 subjects completed the treatment. Three months of daily therapy with oral mifepristone (at a dose of either 10 mg or 25 mg) or once-monthly subcutaneous injections of enantone (at a dose of 3.75 mg) were used. Change in volume of the largest uterine fibroid was the primary efficacy variable, and secondary efficacy variables included changes in anemia and relevant symptom. Safety evaluation included the analyses of adverse events, laboratory values, and relevant endometrial changes.

Results: After three months of treatment, the mean volume of the largest leiomyoma was significantly reduced by mifepristone 10 mg or 25 mg or enantone 3.75 mg (40.27%, 42.59% and 44.49% respectively) ($P < 0.0001$). Percentage change from baseline in largest leiomyoma volume was not statistically significant among the three groups ($P = 0.1057$). Most of the patients in all groups experienced amenorrhea after the treatment. There were also significant elevations in red blood cell count, hemoglobin and hematocrit ($P < 0.0001$), and significant reductions in prevalence of dysmenorrhea, pelvic pressure, non-menstrual abdominal pain ($P < 0.0001$) in each group, while no significant difference among the three groups.

All study medications are well-tolerated, and no serious adverse event was reported. Treatment-related adverse event rate was significantly lower in mifepristone 10 mg group, compared to Enantone 3.75 mg group (13.59% vs. 32.58%, $P = 0.0002$). In both mifepristone groups, estradiol levels were maintained in the premenopausal range, whereas patients in the enantone group had a significant reduction to postmenopausal levels ($P < 0.0001$).

Conclusion: 10mg is as effective as 25mg mifepristone and 3.75 mg enantone with minimal drug-related side effects, and may provide an alternative for clinical application, especially for patient who are in perimenopause with uterine fibroids.

Abbreviations: FSH = follicle-stimulating hormone, GnRHa = gonadotropin-releasing hormone analog, ITT = intention-to-treat.

Keywords: amenorrhea, anemia, different doses, largest fibroid volume, mifepristone

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1. Introduction

Uterine fibroids are the most common disease in women of reproductive age. Approximately 20–50% of patients with leiomyoma have related symptoms such as excessive menstrual bleeding, which may lead to anemia, pelvic pressure, and increased uterine size.[1] No approved medical treatment to completely eliminate uterine fibroids is currently available. The application of medical treatments is limited to the reduction of related symptoms before surgery. Moreover, interest in nonsurgical treatments of uterine fibroids has grown.[2] Few medical options are currently available for preoperative and symptom management; 2 options are mifepristone and enantone.

Mifepristone can effectively inhibit the progesterone receptor,[3] which is contained in uterine fibroids.[4] This medication is beneficial in that it reduces bleeding, fibroid-related pain, and the size of the uterine fibroids.[5] The effectiveness of mifepristone in the treatment of uterine fibroids has been demonstrated with 5- and 10-mg doses over 3-, 6-, and 12-month treatment periods in several trials.[6–10] Other studies have shown that 10 mg of mifepristone is as effective as 25 and 50 mg with fewer side effects.[9,11–16]

Enantone is a gonadotropin-releasing hormone analog and is considered to be the most effective medical therapy for correction of anemia, reduction of fibroid size, and control of excessive menstrual bleeding.[17] Nevertheless, there are still concerns about the potential risks of drug-related side effects; especially with long-term use of enantone, patients may also experience bone mineral loss and menopausal symptoms. Most of these side effects can be prevented with a hormonal add-back; however, such treatment may reduce the ability of enantone to reduce the fibroid size.[18]

In this study, we compared the efficacy and safety of mifepristone (10 and 25 mg/day) with those of enantone (3.75 mg/month) over a 3-month period.

2. Methods

This randomized clinical trial included 3 treatment groups to evaluate the efficacy and safety of 10 mg/day of mifepristone, 25 mg/day of mifepristone, and 3.75 mg/month of enantone for 3 months to treat uterine fibroids. This study is based on the previously established evidence that low-dose mifepristone reduces fibroid size, relieves the associated symptomatology, and improves the patient's general condition.[15,19]

This study was approved by the Independent Ethics Committee of the Gynecology and Obstetrics Department, Peking University First Hospital, Beijing, China. Patients were recruited from 8 sites, and all patients provided written informed consent. The inclusion criteria were a uterine size equivalent to at least 10 weeks of gestation in a gravid uterus; if the uterine size did not reach that equivalent to 10 weeks of gestation, then the presence of 1 or more of the following symptoms: menorrhagia, dysmenorrhea, pelvic pressure, or anemia; and providing written informed consent. The exclusion criteria were postmenopause; submucosal fibroids; suspicion or diagnosis of uterine or endometrial malignancy; adnexal mass or endometriosis; coagulation dysfunction and bleeding tendencies; severe anemia, defined as a hemoglobin level of <6 g/dL; suspicion or diagnosis of pregnancy or breastfeeding; hepatic or renal malfunction; mifepristone therapy in the last 3 months; and allergy to the gonadotropin-releasing hormone analog drug class.

Qualified subjects were randomized into 3 treatment groups:

10-mg mifepristone group: starting from day 1 to 3 of the menstrual cycle, 1 10-mg tablet of mifepristone was taken orally every day for 84 days.

25-mg mifepristone group: starting from day 1 to 3 of the menstrual cycle, 1 25-mg tablet of mifepristone was taken orally every day for 84 days.

3.75-mg enantone group: starting from day 1 to 5 of the menstrual cycle, a subcutaneous injection of 3.75 mg of enantone was administered every 28 days for 84 days (3 injections).

Because mifepristone has been on the market in China for many years, according to the State Food and Drug Administration's regulations on supplementary application for additional indications, this study randomized 500 patients at a ratio of 3:1:1 to the 10-mg mifepristone group, 25-mg mifepristone group, and enantone group, respectively. The mifepristone tablets were supplied by Zizhu Pharmaceuticals Co. Ltd. (Beijing, China).

A complete gynecological examination and abdominal or vaginal ultrasound examination of the uterus were performed at the beginning and end of treatment. The fibroid volume was calculated using the following formula[20]:

fibroid volume = 0.5236ABC,

where A, B, and C are the diameters of the sphere in each of the 3 planes and are expressed in cubic centimeters. If the patient had more than 1 fibroid, the measurement of the largest fibroid was taken and its variations were used to evaluate efficacy. The volume of the uterus was also measured using the above equation.

Measurements taken at the end of each treatment visit were performed by sonographers who were blinded to the previous measurements, knowing only the localization of the fibroid to be measured. Blood samples were taken for hematological testing and determination of hepatic transaminase levels at the first and last visit.

The patients had 5 visits throughout the study: the screening visit (Visit 1), randomization visit (Visit 2), and 3 evaluation visits (Visits 3–5). There were no follow-up visits after the treatment. All patients were asked to report their bleeding situation and leiomyoma-related symptoms (Visits 1 and 3–5), which were graded on a 3-point scale (0 = no symptoms, 1 = light symptoms, 2 = severe symptoms). The symptoms were classified into 2 categories: pelvic pressure and pain. The scores were registered between the 2 groups at 4, 8, and 12 weeks of treatment.

The red blood cell count and concentrations of hemoglobin, liver transferase enzymes, cortisol, estradiol, and follicle-stimulating hormone were monitored before and after treatment. The primary efficacy variable was the change in fibroid volumes before and after treatment. The secondary efficacy variables were the changes in the red blood cell count, hemoglobin, and hematocrit and improvement in symptoms including menstrual blood loss, pelvic pressure, dysmenorrhea, and non-menstrual abdominal pain. The safety variables included adverse events and other laboratory parameters.

The drugs were coded using a statistics code table produced by SAS software (Cary, North Carolina) and dispensed according to the patient enrollment sequence and drug code in ascending order.

3. Data analysis

The results are presented in absolute frequencies, percentages, mean values, standard deviations, and 95% confidence intervals for the mean values in fibroid and uterine volumes. A 2-sided *t*-test was adopted through the data analysis. Analysis of variance, a nonparametric test, or the chi-square test was used to evaluate homogeneity among the 3 treatment groups.

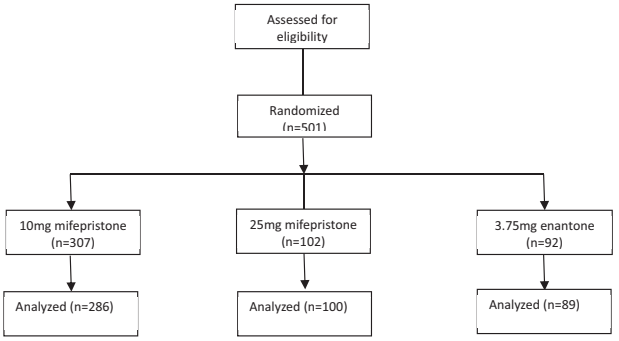

Figure 1. Study flowchart: details of patient randomization into 3 groups.

The main efficacy measure was calculated and compared among the 3 groups using the Cochran–Mantel–Haenszel/chi-square test stratified by sites, at $\alpha = 0.05$ and corrected by side effect. The 95% confidence intervals for intergroup differences were also calculated. The secondary efficacy measure was analyzed and compared among the 3 groups using analysis of variance at $\alpha = 0.05$ and corrected by side effect. The pre- versus post-treatment changes in hemoglobin, red blood cell count, hematocrit, pelvic pressure, and lower abdominal pain scores were analyzed using paired comparisons.

Statistical data processing, summaries, and analyses were performed using SAS software (Cary, North Carolina), version 8.2. The statistical analyses were performed by a biostatistics group at Peking University First Hospital.

4. Results

In total, 501 patients were randomized with 307 in the 10-mg mifepristone group, 102 in the 25-mg mifepristone group, and 92 in the 3.75-mg enantone group. The 3-month treatment was completed by 270 (87.95%), 96 (94.12%), and 85 (92.39%) patients with 17, 4, and 4 dropouts, respectively ($P = 0.2$). The intention-to-treat population comprised randomized patients who received at least 1 dose of the study medication with related information on the efficacy evaluation; it included 286 (93.16%), 100 (98.04%), and 89 (96.74%) patients, respectively. The safety population comprised randomized patients who received at least 1 dose of the study medication and had information on the safety analyses; it included 287 (93.49%), 100 (98.04%), and 89 (96.74%) patients, respectively (Fig. 1).

Table 1 shows the demographic and baseline characteristics of all patients included in the clinical trial. The 3 groups were comparable with no significant differences in any of the general characteristics, including the largest leiomyoma volume, hemoglobin, red blood cell count, hematocrit, dysmenorrhea, pelvic pressure, nonmenstrual abdominal pain, and others.

The menstrual duration (days) was statistically different between the 10-mg mifepristone and 3.75-mg enantone group, while the intergroup differences were not clinically significant.

All treatments significantly reduced the volume of the 3 largest fibroids ($P < 0.001$), with median reductions of 40.27% in the 10-mg mifepristone group, 42.59% in the 25-mg mifepristone group, and 44.49% in the 3.75-mg enantone group, all of which were comparable among the 3 treatment groups ($P = 0.11$) (Table 2). In addition, there was no significant difference in the distribution of changes in the largest fibroid volume among the 3 groups (Table 3).

At the end of month 1, the 10-mg (76.41%) and 25-mg (72.00%) mifepristone groups had a greater proportion of patients with amenorrhea than did the 3.75-mg enantone group (55.06%), and the difference between the 10-mg mifepristone and 3.75-mg enantone groups was statistically significant ($P = 0.01$). In addition, the menstrual blood loss in the mifepristone

Table 1

Baseline patient characteristics (intention-to-treat population).

Characteristic	10 mg mifepristone (N = 286)	25 mg mifepristone (N = 100)	Enantone (N = 89)	*P*
Age, y	43.41 ± 5.73	43.07 ± 6.38	42.75 ± 5.63	0.66
Weight, kg	62.01 ± 8.72	60.98 ± 6.72	63.17 ± 10.36	0.39
Height, cm	160.66 ± 4.29	160.30 ± 4.27	161.59 ± 4.35	0.13
SBP, mm Hg	116.88 ± 11.25	116.79 ± 12.19	119.36 ± 12.35	0.30
DBP, mm Hg	75.26 ± 7.83	75.54 ± 7.84	76.19 ± 8.02	0.60
Menstrual duration, d	6.27 ± 2.43	6.55 ± 2.07	6.64 ± 2.06	0.04[†]
Menstrual blood loss[*]				
Too little	3 (1.05)	2 (2.00)	1 (1.12)	0.71
Regular	112 (39.16)	41 (41.00)	30 (33.71)	
Too much	171 (59.79)	57 (57.00)	58 (65.17)	
Dysmenorrhea	145 (50.70)	51 (51.00)	47 (52.81)	0.93
Pelvic pressure	94 (32.87)	36 (36.00)	27 (30.34)	0.28
Nonmenstrual abdominal pain	81 (28.32)	25 (25.00)	28 (31.46)	0.83
Uterine volume, cm^3	241.34 ± 209.14	270.51 ± 255.13	242.17 ± 175.71	0.74
Largest leiomyoma volume, cm^3	61.66 ± 79.75	78.53 ± 117.56	67.20 ± 92.68	0.13
Hemoglobin, g/L	120.46 ± 21.11	123.15 ± 20.37	118.1 ± 21.15	0.26
RBC count, $\times 10^{12}$/L	4.21 ± 0.46	4.32 ± 0.49	4.19 ± 0.46	0.08
Hematocrit, V%	37.03 ± 6.28	37.26 ± 4.89	36.00 ± 4.85	0.32
Estradiol, pg/mL	125.378 ± 130.855	108.118 ± 88.075	112.771 ± 110.330	0.59
Follicle-stimulating hormone, mIU/mL	11.418 ± 13.347	13.143 ± 15.274	10.180 ± 8.718	0.62
Cortisol, μg/dL	114.381 ± 174.989	111.350 ± 138.328	124.207 ± 253.461	0.73

DBP = diastolic blood pressure, RBC = red blood cell, SBP = systolic blood pressure.

Values are presented as mean ± standard deviation or n (%). *P* values are from rank analysis of variance for continuous variables and the chi-square test for classification variables.

[*] *P* values are from Fisher's exact test.

[†] *P* value of 10 mg of mifepristone versus enantone is 0.03.

Table 2

Changes in largest leiomyoma volume among treatment groups (intention-to-treat population).

	10 mg mifepristone (N = 286)	25 mg mifepristone (N = 100)	Enantone (N = 89)	*P*
Before treatment	285 (61.66 ± 79.75)	100 (78.53 ± 117.56)	89 (67.20 ± 92.68)	0.13
After treatment	270 (41.68 ± 72.02)	96 (57.31 ± 79.75)	86 (36.23 ± 54.68)	0.02*
Change rate, n (%)	270 (−40.27)	96 (−42.59)	86 (−44.49)	0.11

Data are expressed as n (mean ± standard deviation) or n (%).

The n values in the table only indicate patients who had determinations both before and at the end of treatment. *P* values are from rank analysis of variance.

* *P* value of 25 mg mifepristone versus enantone is 0.01.

Table 3

Distribution of changes in the largest leiomyoma volume among treatment groups.

	10 mg mifepristone (N = 270)	25 mg mifepristone (N = 96)	Enantone (N = 86)	*P*
≤ −30%	158 (58.52)	59 (61.46)	55 (63.95)	
≥ −30% to ≤ −10%	44 (16.30)	13 (13.54)	16 (18.60)	
≥ −10% to ≤ 0%	16 (5.93)	4 (4.17)	7 (8.14)	
>0% to ≤ 20%	14 (5.19)	5 (5.21)	3 (3.49)	
>20%	38 (14.07)	15 (15.63)	5 (5.81)	
				0.50

Data are presented as n (%).

groups was substantially improved compared with that in the enantone group, with a significant difference ($P < 0.001$). After 2 months of treatment, the proportion of patients with amenorrhea was similar among the 3 treatment groups ($P = 0.92$).

There was no significant difference among the 3 groups in improvement of symptoms including dysmenorrhea ($P = 0.37$), nonmenstrual abdominal pain ($P = 0.69$), and menstrual blood loss ($P = 0.36$) after the treatment, except for pelvic pressure ($P = 0.04$) (Table 4). However, these symptoms were highly improved in all 3 groups after the treatment ($P < 0.001$).

There were significant elevations in the red blood cell count, hemoglobin, and hematocrit ($P < 0.001$) after treatment and significant reductions in dysmenorrhea, pelvic pressure, and nonmenstrual abdominal pain ($P < 0.001$) within each group. However, there were no significant differences among the 3 groups. The mean hemoglobin levels were increased by 8.51%, 6.16%, and 7.28% in the 10-mg mifepristone, 25-mg mifepristone, and 3.75-mg enantone groups, respectively.

The rate of adverse events was 20.21%, 25.00%, and 35.96% in the 10-mg mifepristone, 25-mg mifepristone, and 3.75-mg enantone groups, respectively (Table 5), and patients in the 3.75-mg enantone group reported significantly more adverse events than did patients in the other groups ($P = 0.01$). The rate of drug-related adverse events was 13.59%, 17.00%, and 32.58% in the 10-mg mifepristone, 25-mg mifepristone, and 3.75-mg enantone groups, respectively. The 10-mg mifepristone group had statistically significant fewer patients that reported adverse events than did the 3.75-mg enantone group ($P = 0.01$).

Although these treatments were well tolerated throughout the study, 5.21% and 7.84% of women in the 10- and 25-mg

Table 4

Number of patients with complete resolution of symptoms at the end of 3 months (intention-to-treat population).

	10 mg mifepristone (N = 286)	25 mg mifepristone (N = 100)	Enantone (N = 89)	*P*
Amenorrhea	271 (95.42)	98 (98.00)	81 (91.01)	0.09
Dysmenorrhea	278 (97.89)	100 (100.00)	87 (97.75)	0.37
Pelvic pressure	271 (95.42)	99 (99.00)	89 (100.00)	0.04*
Nonmenstrual abdominal pain	272 (95.77)	98 (98.00)	86 (96.63)	0.69
Menstrual blood loss decrease	280 (98.60)	100 (100.00)	87 (97.80)	0.71

Data are presented as n (%). *P* values are from Fisher's exact test.

* *P* value of mifepristone 10 mg versus enantone is 0.04.

Table 5

Rate of adverse events.

	10 mg mifepristone (N = 287)	25 mg mifepristone (N = 100)	Enantone (N = 89)	*P*
Drug related	39 (13.59)	17 (17.00)	29 (32.58)	0.01
All	58 (20.21)	25 (25.00)	32 (35.96)	0.01

Data are presented as n (%).

Table 6

Adverse events in all treatment groups.

	10 mg mifepristone (N = 307)	25 mg mifepristone (N = 102)	Enantone (N = 92)
Abdominal pain	12 (3.91)	5 (4.90)	5 (5.43)
Hot flashes and sweating	16 (5.21)	6 (5.88)	15 (16.30)
Nausea, vomiting, dry mouth, and inappetence	10 (3.26)	6 (5.88)	3 (3.26)
Headache, dizziness, fatigue, and somnolence	9 (2.93)	7 (6.86)	15 (16.30)
Irritability	6 (1.95)	2 (1.96)	9 (9.78)
Pain in low back and legs	7 (2.28)	2 (1.96)	3 (3.26)
Heart symptoms and palpation	6 (1.95)	0 (0.0)	2 (2.17)
Gastrointestinal discomfort and stomachache	16 (5.21)	8 (7.84)	0 (0.0)
Slight uterine bleeding	4 (1.30)	1 (0.98)	14 (15.21)
Increased vaginal secretion	5 (1.63)	1 (0.98)	0 (0.0)

Data are presented as n (%).

Table 7

Hormone concentrations before and at the end of treatment (safety population).

	10 mg mifepristone (N = 287)	25 mg mifepristone (N = 100)	Enantone (N = 89)	*P*
Before treatment				
Estradiol, pg/mL	276 (125.406 ± 130.618)	96 (108.118 ± 88.075)	88 (112.771 ± 110.330)	0.431
Follicle-stimulating hormone, mIU/mL	276 (11.435 ± 13.326)	96 (13.143 ± 15.274)	88 (10.180 ± 8.718)	0.808
Cortisol, pg/mL	277 (114.008 ± 174.782)	95 (111.350 ± 138.328)	88 (124.207 ± 253.461)	0.522
At the end of treatment				
Estradiol, pg/mL	265 (101.418 ± 153.510)	95 (80.261 ± 89.371)	82 (54.423 ± 83.400)	<.001*
Follicle-stimulating hormone, mIU/mL	265 (9.306 ± 11.732)	95 (11.279 ± 11.848)	82 (7.571 ± 5.006)	0.619
Cortisol, pg/mL	265 (115.492 ± 161.402)	94 (114.889 ± 145.381)	82 (134.779 ± 313.514)	0.832

Data are presented as n (mean ± standard deviation). These n values only indicate patients who underwent hormone level measurements both before and at the end of treatment. *P* values are from rank analysis of variance.

* *P* values of the 10-mg mifepristone versus enantone and 25-mg mifepristone versus enantone are both <0.001.

mifepristone groups reported gastrointestinal discomforts and stomach ache, while no patients in the 3.75-mg enantone group experienced such effects during the treatment. In addition, a higher proportion of patients in the 3.75-mg enantone group than in both mifepristone groups experienced hot flashes, sweating, headache, dizziness, fatigue, somnolence, irritability, and slight uterine bleeding (Table 6).

Table 7 and Fig. 2 show the hormonal and estradiol value changes among the treatment groups before and at the end of treatment. The estrogen levels significantly decreased in each

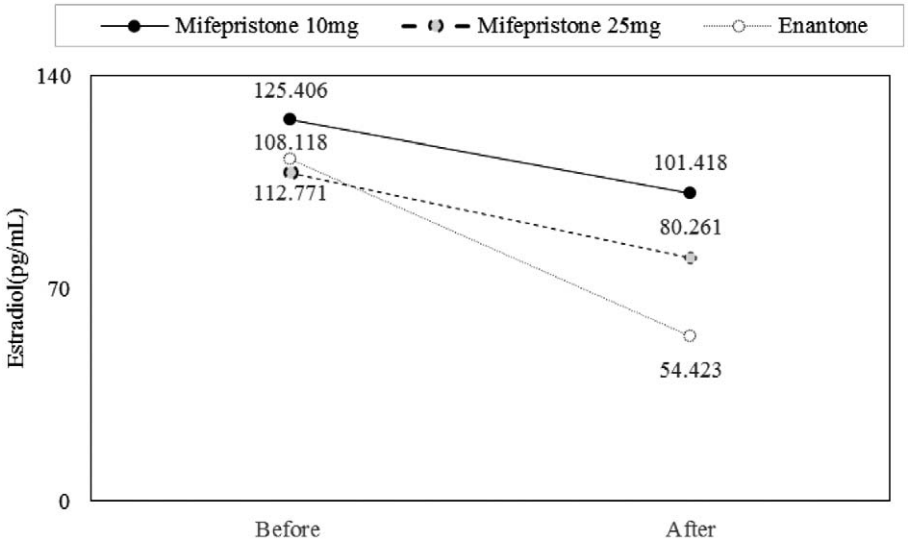

Figure 2. Changes in estradiol concentrations before and after treatment (safety population).

group ($P < 0.001$), and the reduction in the 3.75-mg enantone group was significantly greater than that in the 10- and 25-mg mifepristone groups. At the end of treatment, the estrogen level was similar to the menopausal level in the 3.75-mg enantone group and similar to the premenopausal level in the 10- and 25-mg mifepristone groups.

Mifepristone has antiglucocorticoid properties; however, 1 and 3 patients in the 10-mg mifepristone group had elevated cortisol levels. Although enantone has no antiglucocorticoid effects, 2 patients in the 3.75-mg enantone group also had elevated cortisol levels. Because there are wide swings in the cortisol levels throughout the day, the elevated cortisol levels of the 4 patients in the mifepristone groups were not considered to be significant.

5. Discussion

The present study showed that the use of daily oral mifepristone at doses of both 10 and 25 mg had efficacy similar to that of once-monthly injections of enantone in terms of reducing fibroids in patients undergoing surgery. There was a significant reduction in the volume of the 2 largest fibroids in the 10- and 25-mg mifepristone groups and in the enantone group (40.27%, 42.59%, and 44.49%, respectively), with no significant differences among the groups ($P = 0.49$).

Compared with the enantone group (55.06%), the 10- and 25-mg mifepristone groups had more participants who developed amenorrhea after the first month of treatment (76.41% and 72.00%, respectively). The mean blood hemoglobin level, red blood cell count, and hematocrit were significantly improved with no significant differences among the 3 groups, as well as dysmenorrhea, partly due to the amenorrhea. In all groups, other fibroid-related symptoms, such as pelvic pressure and pain, were significantly relieved compared with the baseline in all 3 groups ($P < 0.001$). According to Fiscella et al,[15] mifepristone treatment was also beneficial for patients' health status and energy improvement.

A significant reduction in the uterine volume was observed in all 3 groups, and the enantone group (43.58%) exhibited a more significant reduction than both mifepristone groups. However, the incidence of treatment-related adverse events in the enantone group (32.58%) was higher than that in the 10- and 25-mg mifepristone groups (13.59% and 17.00%, respectively); these adverse events included hot flashes, mood changes, sweating, and vaginal dryness. In both mifepristone groups, the plasma estradiol levels were maintained in the mid-follicular range, whereas patients in the enantone group exhibited a significant reduction to postmenopausal levels ($P < 0.001$).

In this study, few patients had abnormal alanine transaminase or aspartate transaminase concentrations after treatment; the mechanism for this is unclear. However, none of these patients had elevated liver transaminase concentrations of >100 U/L with clinical significance. Only 1 patient in the 10-mg mifepristone group had an elevated cortisol level after the 3-month treatment. However, considering the anti-glucocorticoid properties of mifepristone and the short course of this study, the cortisol level should be noted in patients undergoing long-term use in the clinical setting.

There are some limitations of this study. It was not specifically designed to assess surgical outcomes, and we had no follow-up data about the patients' relapses and or resumption of their regular menstrual cycles after the treatment. All enrolled participants were Han Chinese, which may limit generalization of the results to other populations. Additionally, the duration of treatment was restricted to 13 weeks. Hence, more data on the benefits and risks of long-term treatment with mifepristone are needed. Furthermore, there are methodological limitations such as the lack of support for the sample size selection and blinding. Potential bias may have been introduced owing to the lack of blinding during the study. However, it was very difficult to apply blinding because mifepristone was orally administered and enantone was subcutaneously injected.

Based on the previous data and this study, 10 mg of mifepristone shows potential for greater clinical use. Additionally, compared with enantone and 25 mg of mifepristone, it offers a more suitable alternative for patients before surgery because it can be orally administered with a comparable reduction in fibroid size, fewer side effects, and improvement in the hemoglobin level, decreasing the potential risk of a blood transfusion during the surgery. However, further studies of the safety of long-term 10-mg mifepristone treatment are needed for clinical application, especially for perimenopausal patients who may be able to take it to decrease the size of uterine fibroids and relieve related symptoms until menopause. In this way, it may be particularly beneficial for perimenopausal patients in terms of lowering cost and improving quality of life.

6. Conclusion

Our observation of 501 patients divided into 10-mg mifepristone, 25-mg mifepristone, and 3.75-mg enantone groups for 3 months suggests that the largest fibroid significantly and comparably decreased in size among the 3 groups. Leiomyoma-related symptoms improved comparably as well; these symptoms included menstrual blood loss, hemoglobin levels, dysmenorrhea, and non-menstrual abdominal pain. Although these treatments were well tolerated during the study, patients in the 3.75-mg enantone group reported more adverse events than those in the mifepristone groups. Mifepristone at a dose as low as 10 mg/day may be effective in treating uterine fibroids before surgery, serving a similar purpose as enantone.

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