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Original Research Article

A study on the effect of mifepristone on uterine fibroids

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ABSTRACT

Background: Uterine fibroids are the most common pelvic tumors and most common benign tumors in women. Abnormal uterine bleeding and pain are common symptoms of fibroids. The objective of study was to study the effect of mifepristone on uterine fibroids on the basis of change in menstrual pattern, hemoglobin level, fibroid volume and alleviation of pain.
Methods: This prospective study had sample size of 40 subjects with uterine leiomyomas who were recruited from OPD after taking an informed written consent. Follow up of each subject was done after 3 months to see changes in various parameters after giving 3 months of mifepristone 25 mg once daily. Study tools included case reporting form, ultrasonography, blood investigations, pictorial blood loss assessment chart (PBAC) to compare change in menstrual pattern and visual analogue pain scale for comparing alleviation in pain.
Results: In this study, the majority of patients belonged to 41-45 years of age and were para 1 with dominant symptom of menorrhagia. At the end of 3 months the mean baseline fibroid volume decreased by 37.5%, mean hemoglobin improved from 9.37 to 11.05 gm/dl, mean PBAC score reduced from 90.6 to 8.9, 25% of patients had no pain and pain score in 32.5% patients was 1 and in 32.5% patients pain score was 2.
Conclusions: Three months treatment with 25 mg mifepristone daily, effectively controls bleeding, reduces fibroid volume ameliorates pain and abnormal bleeding, improves hemoglobin. It can be recommended as the optimum clinical treatment of fibroids in this dose.

Keywords: Dysmenorrhea, Fibroids, Leiomyoma, Menorrhagia, Mifepristone, PBAC, VAS

INTRODUCTION

Fibroid is the most common benign tumor of the uterus and most common benign tumor in women. The prevalence of fibroid increases with age up until menopause. A random sampling of women aged 35 to 49, found that among African American women by age of 35 the incidence of fibroid was 60%, and it was over 80% by age 50. White women have an incidence of 40% at age 35 and almost 70% by age 50.[1]

Majority of fibroids are asymptomatic. The symptomatic fibroids can cause abnormal uterine bleeding, dysmenorrhea, dyspareunia, subfertility, pressure symptoms, recurrent pregnancy loss, lower abdominal or pelvic pain and abdominal enlargement

The management of uterine fibroids depends upon symptoms, age, size and site of fibroid and fertility status. It can be expectant, medical or surgical.

Medical therapy includes nonsteroidal anti-inflammatory drugs, tranexamic acid, gonadotropin-releasing hormone agonists, gonadotropin-releasing hormone antagonists, progesterone mediated medical treatment like mifepristone, ulipristal acetate and progesterone releasing intrauterine device.[2]

Medical management in the form of drug therapy can be used for temporary palliation or as an alternative to surgery in many cases.

Mifepristone (RU486) is a synthetic estrange steroid with an anti-progestogen activity. As progesterone is needed for leiomyoma growth, mifepristone in low dose according to several studies has been found effective for decreasing the size of myoma and to reduce blood loss. It is on WHO's list of essential medicines.[3]

The aim of the study was to study the effect of 25 mg mifepristone on symptoms of fibroid uterus, it's effect on hemoglobin and volume of fibroid.

METHODS

Study design

This was a prospective observational study carried out at Manipal Hospitals Bangalore. Study population included women with fibroids, receiving 25 mg mifepristone orally for 3 months. The study took place from August 2021 to May 2022.

Sample size

Taking a hypothesis that 25 mg mifepristone daily for 3 months will offer at least 20% reduction in myoma volume from the baseline, with 80% power to detect the real difference and 5% significance, sample size calculated was 32. The sample size was calculated using the online site 'select statistical services' taking the study by Seth, et al: 'mifepristone in treatment of uterine myoma' as reference.[4] 40 women were included in the study.

Inclusion criteria

Women of reproductive age group (18-49 years) with symptomatic fibroids were included.

Exclusion criteria

Pregnant or lactating women. Women who wanted to become pregnant. Suspicious of ovarian or endometrial or uterine malignancies. History of hormonal treatment over last 3 months. Presence of renal, respiratory or heart disease, PID or other adnexal pathology. Uterine fibroids of size more than 20 weeks. Atypical endometrial hyperplasia. Patients allergic to mifepristone.

Methodology

Relevant medical, obstetric, menstrual, past, personal and family history were collected: case reporting form, ultrasonography, blood investigations- hemoglobin (Hb), liver function test, renal function test, serum TSH, pictorial blood loss assessment chart, visual analogue pain scale.[5,6]

Follow up of each subject was done after giving 3 months mifepristone 25 mg once daily. The changes in various parameters were noted once at 1st visit and then after taking mifepristone, like changes in uterine volume (in case of multiple fibroids, volume of the largest fibroid was taken into consideration), menstrual pattern, hemoglobin concentration etc.

RESULTS

In this study, out of 40 patients, 92.5% were more than 30 years of age. 7.5% patients were less than 30 years of age. Maximum number of patients were of age group 41-45 years and more than 46 years (11 patients in each group) with maximum age of 49 years. The mean age was 40.01.

In this study, 52.5% cases of fibroid uterus were seen in para-1, 25% were para-2, 15% were nullipara, 5% para-3 and 2.5% were para-4.

Table 1: Comparison of cases according to fibroid volume.

Fibroid volume in cc	Before treatment Range- 3.1-162			After treatment Range- 1.9-131	
	No. of patients		Percentage	No. of patients	Percentage
<10	05		12.5	09	22.5
10-20	09		22.5	09	22.5
20-30	04		10	11	27.5
30-40	06		15	03	7.5
40-50	04		10	04	10
50-60	01		2.5	00	00
60-70	04		10	00	00
>70	07		17.5	04	10
Total	40		100	40	100
Fibroid volume in cc	Before treatment N=40	After treatment N=40	Change in mean percentage	t-value	P value
Mean±SD	42.3±38.1	27.2±26.9	35.7% fall	5.54	0.000 sig. p<0.05

Table 2: Comparison of cases according to hemoglobin.

Hb in gm/dl	Before treatment Range- 4.4-12			After treatment Range- 8.1-13.2	
	No. of patients		Percentage	No. of patients	Percentage
<5	01		2.5	00	00
5-6.9	01		10	00	00
7-8.9	06		15	06	15
9-10.9	19		47.5	07	17.5
11-12.9	10		25	25	62.5
>13	00		00	02	05
Total	40		100	40	100
Hb in gm/dl	Before treatment N=40	After treatment N=40	Change in mean percentage	t-value	P value
Mean±SD	9.37±1.96	11.05±1.45	17.93% increase	8.61	0.0000 sig. p<0.05

The most dominant symptom of patients included in the study was menorrhagia. Out of 40, 28 (70%) presented with menorrhagia, 27 with dysmenorrhea and lower abdominal pain, 4 with polymenorrhea, 2 with constipation, 2 with dysuria and 1 with scanty flow.

Out of 40 people, 60% had multiple and 40% had single fibroid.

In this study, 32.5% (13/40) patients had subserous fibroids, 27.5% (11/40) had submucous fibroids, 20% (8/40) had transmural and 20% (8/40).

It was observed that after 3 months of treatment with mifepristone, the mean fibroid volume reduced from 42.3 cc to 27.2 cc and the percentage mean volume reduction of fibroid in the study population was 35.7%, which was statistically significant (Table 1).

Hemoglobin levels increased significantly from 9.37±1.96 gm/dl to 11.05±1.45 gm/dl. There was 17.93% increase in mean hemoglobin at the end of treatment (Table 2).

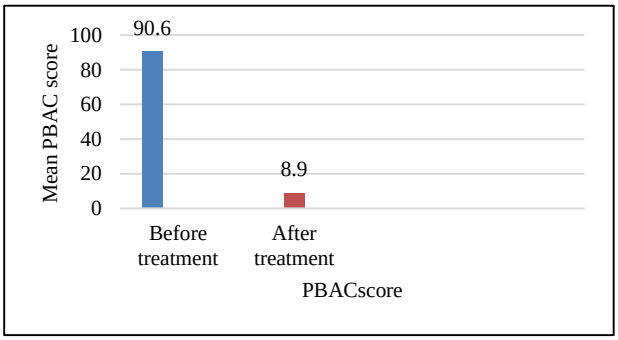

Figure 1: Comparison of mean PBAC score before and after treatment.

In this study maximum patients (42.5%) had a PBAC score between 101-150 before treatment, while at the end of the treatment maximum patients (72.5%) were amenorrhic with a PBAC score of 0. In 22.5% patients PBAC score was between 1-50 at the end of treatment. Assessment of mean blood loss by PBAC score showed reduction from 90.6 to 8.9. As a consequence, the dysmenorrhea and pelvic pain were relieved, and subsequently, there was a rise in hemoglobin (Figure 1).

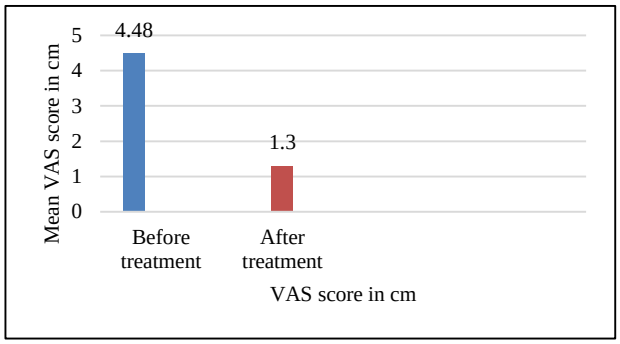

Figure 2: Comparison of VAS score before and after treatment.

In this study, there was a significant reduction in VAS score with treatment. 25% patients had no pain, in 32.5% patients the pain score was 1 and it was 2 in 32.5% patients. There were no patients in the pain score level from 6 to 8 at the end of treatment (Figure 2).

DISCUSSION

Fibroids are estrogen and progesterone dependent tumor. Mifepristone can be effective in treatment of fibroids by its anti progesterone properties.

Some clinical trials using doses of 5-50 mg mifepristone were conducted for duration between 3-12 months. Seth et al reported 53.62% reduction in fibroid volume and hemoglobin rise to 137% after treatment with 25 mg mifepristone for 3 months.[4] Kettle et al, reported amenorrhea in 100% over one year at 100 mg dose, while 5-10 mg led to amenorrhea in 40-70%.[7] A fall 48% in mean uterine volume and amenorrhea in 61% after 6 months of 10 mg mifepristone was seen in a study by Eisinger et al.[8] In a comparative study of 5 mg, 25 mg and

50 mg dosage by Murphy et al showed 25 mg dose causes clinically significant decrease in fibroid volume.[9]

The reduction in size of fibroid and bleeding is likely to be because of functional, structural and micro vascular effects of mifepristone on endometrium and uterine musculature. In this study 25 mg mifepristone reduced fibroid volume by 35.7%, while Bagaria et al showed 26-32% decline with 10 mg mifepristone over 3 months, and Mukherjee et al observed a decrease by 47% with 25 mg dose daily for 6 months.[10,11]

In this study increase in mean hemoglobin percentage by 17.93% while Alakananda et al showed 8.5% increase in hemoglobin and Hari et al observed an increase by 13.9%.[12,13] Similar study by Rani et al showed increase in hemoglobin by 1.5±SD.[14]

In this study, PBAC score decreased by 90.18% (from mean 90.6 to 8.9) while Kapur et al observed a decrease in PBAC score from 111.7 to 7.12 at the end of 6 months with 50 mg mifepristone once a week and Kulshrestha et al showed a decline in score from 253 to 19.[15,16]

In present study, 72.5% (29/40) developed amenorrhea with a PBAC score of 0. In a study by Shaikh et al, 97.9% (46/47) developed amenorrhea among the patients receiving mifepristone 50 mg biweekly for 3 months while 97.8% (44/45) developed amenorrhea in patients receiving 25 mg daily for 3 months.[17] One more study by Arora et al found all patients amenorrhic at the end of treatment of 50 mg mifepristone biweekly for 6 months.[18]

In present study, results show a significant reduction in VAS score by 70.98% while Shaikh et al showed that at the end of 3 months VAS score of all participants was less than or equal to 3.[17] Seher et al showed decrease in pain measured by numeric pain control scale. 55% had no pain and in 22% score was 2.[19]

CONCLUSION

Three months treatment of 25 mg mifepristone effectively controls bleeding and reduces fibroid volume. It significantly helps in ameliorating symptoms of pain and abnormal bleeding. The improvement in hemoglobin is also remarkable at the end of treatment. It can be recommended as the optimum clinical treatment of fibroids in a dose of 25 mg once a day for 3 months.

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