



## Efficacy of low dose Mifepristone in the treatment of symptomatic uterine fibroids

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### Abstract

*Selective Progesterone Receptor Modulators (SPRMs) are one of the medical managements of the fibroids. Perimenopausal women with fibroids awaiting hysterectomy, younger women who want to conserve their fertility/uterus, women with big fibroids and severe anaemia are the ideal candidates for the usage of SPRMs. Mifepristone is the cheap, commonly used SPRMs. A study was conducted in a rural based medical college in South India to evaluate the efficacy of mifepristone in the management of fibroids.*

*Sixty women with menorrhagia, fibroids, uterine size less than 12 weeks pregnancy size were given 10 mg of mifepristone daily for three months. Pictorial Blood loss Assessment Chart (PBAC) scale, size of the uterus, size of the fibroids, haemoglobin level was monitored at the initiation of the treatment and at the end of the treatment. The mean PBAC score was 124.6 before and 17.87 after treatment. 78% of women were amenorrhagic during treatment. The mean volume of the uterus, the mean volume of the fibroids got reduced by 27.7% and 28.2% respectively. Hot flushes was the commonest side effect. Haemoglobin rose from 8.86 gms% to 10.88 gms%. Low dose mifepristone can be used as a temporary medication in the medical management of fibroids.*

**Keywords:** Fibroids; SPRMs; PBAC; Menorrhagia; Mifepristone.

### Introduction

Leiomyomas are the most common benign pelvic tumours in the reproductive age group. Fibroids including the smallest one are seen in 80% of women in this age group at routine ultrasonography examination. Seventy five percent of women with fibroids are asymptomatic. If symptomatic, the commonest symptom is menorrhagia with resultant anaemia. The other

symptoms of fibroids are pressure symptoms over bladder; discomfort in the pelvis, lower abdomen; infertility; sarcomatous change is extremely rare. Asymptomatic fibroids don't warrant treatment. Symptomatic fibroids are managed by conservative surgeries like polypectomy, myomectomy; definitive surgery is hysterectomy. Uterine artery embolization, ultrasound guided focussed energy delivery system and

radiofrequency myolysis are the novel radiological procedures done in the management of fibroids. The symptomatic medical management is by non steroidal anti inflammatory drugs, tranexamic acid. Oral contraceptives, progesterone, GnRh analogues, levonorgestrel releasing intrauterine systems are the hormonal interventions to treat leiomyomas temporarily. Selective Progesterone Receptor Modulators (SPRMs) are used to control bleeding and to reduce the size of the fibroids for three months pre operatively to prepare the patient for definitive surgery.

Fibroid growth is oestrogen dependent. Progesterone is also required for fibroid cell proliferation. It is observed that progesterone and progesterone receptor A, progesterone receptor B are elevated in the leiomyoma. SPRMs inhibit the release of LH from pituitary, resulting in anovulation and amenorrhoea. SPRMs acts on PRa, PRb causing pro apoptosis and inhibiting proliferation of leiomyoma cells, thereby reducing the size of the fibroids. Mifepristone, asoprisnil, ulipristol acetate are the SPRMs used clinically in the pre operative preparation of fibroids.

### **Aim of the Study**

To evaluate the efficacy of low dose mifepristone in reducing menorrhagia and decreasing the size of uterine leiomyoma.

### **Material and Methods**

The study was conducted in the outpatient department of Obstetrics and Gynaecology of Vinayaka Mission's Medical college and Hospital, Karaikal during the period April 2018 to December 2019. Most of the patients are from rural coastal districts. Approval of the ethical committee and informed consent of the patients was obtained.

Women in 26-45 years age group; having menorrhagia and fibroids are the subjects of the study. Women who completed their child bearing function, but not willing for hysterectomy or awaiting hysterectomy; women anxious to

conceive, having menorrhagia and fibroids, awaiting myomectomy; women who are willing for medical management of fibroids are enrolled for study. Women who had hormonal treatment in the past three months; women having uterine size more than 12 weeks pregnancy size; women with family history of uterine or breast malignancy; women with endometrial hyperplasia are excluded from the study.

General history, reproductive history, history of menorrhagia, dysmenorrhoea, earlier treatment history, planning for conception and for definitive surgery was obtained. General examination and a thorough gynaecological examination were done. In addition to the routine investigations, ultrasound examination was done for all cases. At ultrasonography- size of the uterus; number, location and size of all the fibroids measuring more than 1 cm was recorded. Quantification of blood loss was done using Pictorial Blood loss Assessment Chart (PBAC). Associated symptoms of fibroids like dysmenorrhoea and pressure symptoms were recorded.

Viscosmi formula was used for the calculation of the volume of the uterus that is  $\frac{4}{3} \pi W/2, L/2, T/2$  where W is uterine width on transverse section at uterine fundus; L is uterine length on sagittal section from internal os to fundus; T is uterine thickness measured on sagittal section between anterior and posterior uterine walls. Most of the myomas are spherical or elliptical, hence volume of fibroid was calculated by the formula  $0.523, A,B,C$  where ABC are the largest diameters of the fibroid in two planes measured perpendicularly. If there are multiple fibroids, the largest three fibroids are followed and taken up for assessment of the result.

Tab. Mifepristone 10 mg was started on second day of menses and continued once a day for three months irrespective of bleeding status. 100 mg of iron supplementation given. Clinical examination was done every month. At the end of three months, all the investigations done at the initiation of the treatment were repeated. Special emphasis was laid on Hb level and size of the fibroids.

PBAC was maintained by the woman, the quantitative assessment of bleeding was done before and during treatment. Subjective assessment of dysmenorrhoea and pressure symptoms was done at clinical interviews. Size of the uterus and the size if the fibroids were recorded. PBAC<2 was taken as amenorrhoea and PBAC<75 was taken as non menorrhagia. The results of initial examination and at completion of treatment were compared.

The data was analysed using SPSS 16 software. The pretest, post test, mean values and standard deviation distribution was done using paired t test. Pre test and post test proportions were done using chi square test.

### Results

76 women were recruited for assessment. 65 women qualified for the study by using exclusion criteria and were started on treatment. Five women didn't use the drug properly or were lost for follow up. Sixty women completed the study as per protocol and are presented here.

**Table 1** Age of the women

Age group years	Number of women	Percentage
<30	3	5
31-35	13	21.7
36-40	27	45
41-45	13	21.7
>46	4	6.7
Total	60	100

Two thirds of the women are in the age group of 36-45 years. The mean age is 37.68 years.

**Table 2** Location of the fibroids

Location of fibroid	number	Percentage
Intramural	54	56.8
Submucosal	32	33.7
Subserosal	9	9.5
Total	95*	100

\*multiple fibroids in some women

Single fibroid was seen in 31 women.

Two fibroids were seen in 23 women

Three or more fibroids were seen in 6 women. (The largest three fibroids were taken into assessment)

At initiation of treatment 41 women complained of dysmenorrhoea. Only four women had painful menses at the completion (only thirteen out of

sixty women had menses, other 47 are amenorrhoeic)

**Table 3.**

Parameter	Pre Rx	Post Rx	% decrease	P value
Mean PBAC score	124.6	17.87	85.7	< 0.0001
SD	51.85	34.72		
Mean uterine volume	331.69	239.68	27.7	< 0.0001
SD	216.05	157.23		
Mean fibroid volume	38.94	27.96	28.2	< 0.0001
SD	68.62	46.71		

Of the 60 women treated, 47 women (78.3%) became amenorrhoeic and 14 women were having menses, but low volume.

Haemoglobin rose from 8.86 gms% to 10.88gms% after three months of treatment and iron supplementation

Hot flushes was observed in five women, weakness and leg pains in six women.

### Discussion

In the perimenopausal women with fibroids and menorrhagia, various researchers did study on the efficacy of mifepristone in reducing blood loss and decreasing the uterine and myoma volumes. Murphy et al were the earliest to identify the utility of RU 486 (Mifepristone) in menorrhagia twenty five years ago. Using 10 mg of mifepristone, they reported a reduction of PBAC score from 111.5 to 2.36 with 22 of 25 women reporting amenorrhoea after three months of treatment.

In the past decade several researchers did study on the usage of mifepristone in perimenopausal menorrhagia with fibroids and achieved consistent results. Kulashresta et al with 10 mg of the drug daily reported reduction of PBAC score by 92.4% and reduction of fibroid volume by 22.5%. Seema Sararan et al., Vikram Gupta et al., Smitha Nanda et al reported reduction in the blood loss by 90-98%; reduction in the volume of uterus by 22-36%; reduction in the volume of fibroids by 22-46%. In the present study, after 3 months of treatment with 10 mg of mifepristone daily, the mean PBAC score was less by 85,7% , the mean volume of the uterus was less by 27,7 % and the mean myoma volume was less by 28.2 %. The success rates of present study of ours compares

with the success rates of the researchers quoted earlier in all parameters.

To compare the efficacy of 10 mg daily dose of mifepristone and 25 mg daily dose, Kulshrestha et al did a study on similar people. The results of 10 mg vs 25 mg were—the reduction in mean PBAC score were 92.4% vs 96.4% and the reduction in mean fibroid volume were 22.5% vs 35.7%. A similar study done by Ruchi Saxena et al also established that the efficacy of 10 mg mifepristone was almost same as that of 25 mg after three months of daily usage. Anupama Hari et al extended the study—women were assessed initially, and after three months of usage of 25 mg mifepristone daily; no drug for the next three months and the results at six months. The reduction in blood loss, reduction in uterine volume, reduction in myoma volume were 95.6%, 34.3%, 51.2% respectively at three months of usage and 71.8%, 29.4%, 47.4% respectively at reevaluation after three months of drug free period at six months.

In perimenopausal women with fibroids and menorrhagia, Anupam Kapur et al administered 50 mg of mifepristone once a week for nine months and they were followed for a further three months. In these women, 88.89% attained amenorrhoea and there was 44.5% reduction in fibroid volume.

### Conclusions

The utility of mifepristone in the control of bleeding in women with fibroids and menorrhagia with a dose of 10 mg daily is established and the reduction in PBAC score is to the tune of 85%. The reduction in the volume of the uterus and the volume of the fibroid is moderate-28%. Further research is needed to establish the lowest dose of the drug, the frequency of the drug usage daily or weekly, without compromising the result, and the continuation of the result after discontinuation of the drug.

**Conflict of Interest:** Nil

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