

## Use of Long Term Low Dose Mifepristone in Treatment of Fibroid: Its Efficacy

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### Abstract

**Aim and Objective:** To study the effect of Mifepristone on the symptoms and size of fibroids, specially using a low- dose regimen for 6 months. **Material and Methods:** It was an observational prospective “Before-After” study. 50 women attending OPD of Dept of Obs and Gynae, NSMCH Bihta between June 2019-May 2021 with diagnosis of uterine fibroid were selected according to the inclusion criteria to study changes in various parameters after 6 Months treatment with Mifepristone 50mg once a week. Baseline investigations were done, 50mg Mifepristone weekly was used and patients re-assessed at 1 and 6 months. They were also further followed up till 3 months after stopping the drug to observe changes in menstrual pattern, fibroid volume, haemoglobin and liver function tests. Baseline endometrial biopsy and another at 6 months on cessation of drug therapy were done for all patients. **Results:** Majority of the study population comprised of perimenopausal women i.e 41-45 yrs. 50% were Para 2. The dominant presenting symptom was menorrhagia associated with dysmenorrhoea and pelvic pain. After 6 months of treatment with Mifepristone, the mean fibroid volume reduced 45%. Immediate reduction in bleeding per vaginum was observed in 100% and 90% attained amenorrhoea. The mean haemoglobin increased from 9.18 to 10.82 gm/dl. There was transient rise in SGPT/ SGOT levels at 6 months which reverted to normal at 9 months follow up. **Discussion and Conclusion:** To conclude, 6 months therapy with 50mg Mifepristone weekly is efficacious and acceptable for the treatment of symptomatic fibroid, specially in select group of patients.

**Keywords:** Fibroid (myoma), Mifepristone, Medical Treatment.

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### Introduction

Uterine fibroids are the most common benign tumors of the uterus and female pelvis, the incidence being 20-25% [1], Majority are asymptomatic. Symptomatic patients present with menstrual disturbances, infertility, lump abdomen or pressure effects [2]. Management can be surgical or medical.

Medical management may be given to minimize symptoms and signs and for

patients where surgery is contraindicated. Drugs available are- Anti-fibrinolytic Tranexamic acid, Danazole, GnRH analogues, Progestogens and the anti-progesterone Mifepristone.

Mifepristone, an anti-progesterone was approved by FDA on September 28<sup>th</sup>, 2000 with the trade name “Mifegyne” as an abortifacient. The immune reactivity of

progesterone receptors in the myoma and myometrial tissue was decreased significantly by this drug, suggesting that regression of these tumors may be obtained through a direct anti-progesterone effect. Varying dosage regimens are in use[3], this study using 50mg weekly for 6 months.

### Material and Methods:

This study was designed as an observational prospective “before-after” study. 50 patients attending OPD, Department of Obs & Gynae, NSMCH, Bihta between June 19 to May 21 were enrolled to study changes in various parameters after 6 months treatment with Mifepristone 50 mg once a week.

Inclusion criteria were fibroid size of 2.5 cm and above (as most fibroids below this cutoff are asymptomatic), perimenopausal patients and reproductive age group infertile patients and those accepting the use of barrier contraceptive during study period,

Patients who were keen to become pregnant, breast feeding patients, those on hormonal contraception or who had received any hormonal therapy in the last 3 months and had any contraindication to

receiving anti-progestins were excluded from study.

Permission from institutional ethical committee was obtained. Informed consent obtained from all the patients. Baseline investigations like CBC, LFT, RFT and Thyroid function test done. Endometrial biopsy was done pre-menstrually to rule out endometrial hyperplasia and transvaginal sonography was done to accurately document myoma volume. Menstrual blood loss also assessed.

The commercially available tablet of 200mg was carefully broken in 4 equal parts (each 50mg) and monthly dose packs given to the patient with instructions to take 1/4<sup>th</sup> tablet on a fixed day each week for total 6 months and called for review in OPD at 1, 6, 9 months. In case of any adverse effects, they were told to stop the drug immediately and report in emergency/OPD. They were also further followed up till 3 months after stopping the drug to observe the changes in menstrual pattern, fibroid volume, Hb and LFT. All the patients were advised to use barrier contraception to avoid an inadvertent pregnancy. An endometrial biopsy was repeated at 6 months of therapy to rule out drug induced hyperplasia.

### Results:

**Table 1: Characteristics symptoms of patients**

Serial No.	Symptoms	No.	%(before treatment)
1.	Menorrhagia	48	96
2.	Dysmenorrhoea	45	90
3.	Pelvic Pain	47	94
4.	Backache	12	24
5.	Infertility	10	20

**Table 2: Mean Haemoglobin changes**

1.	Baseline	9.18
2.	At 6 months	10.82
3.	At 9 months	10.9

1. Majority of patients fell in 41-45 yrs age group(perimenopausal)
2. 50% were Para 2
3. The dominant symptom was menorrhagia associated with dysmenorrhoea and pelvic pain
4. After 6 months of treatment with Mifepristone, the mean fibroid volume reduced by 45%
5. Immediate reduction in bleeding P-V was observed in 100%
6. 90% patients became amenorrhic
7. Mean Hb improved from 9.18 to 10.82 gm/dl which further improved at 9 month followup
8. Due to anti-progesterone effect, an oestrogen dominant milieu is created at the endometrium, thereby causing endometrial hyperplasia but without any atypia which is reversible.

#### Discussion and Conclusion:

Mifepristone as a treatment option for myoma was first reported by Murphy et al[3]. Current studies support that growth of myoma is dependent on progesterone and therefore anti-progestins (mifepristone) and selective progesterone receptor modulators (SPRM'S-ASOPRISNIL/ ULIPRISTAL) can be effective in treatment. Several clinical trials have been done since then with doses varying from 2.5 to 100 mg for 3-12 months[4].

In the present observational prospective "before-after" study, 50 mg mifepristone given once a week was used for 6 months. The rationale of this dose was for ease of administration considering the tablet size commercially available, as well as to improve patient compliance with the once a week, Sunday to Sunday schedule. The first dose was started within first 7 days of menstrual cycle once the endometrial biopsy report and pre-treatment investigations were available.

The mean myoma volume decreased by 45% which is similar with 25mg dose of Mukherjee et al[5] and 5 and 10 mg for 6 months by Fiscella et al[6].

Mifepristone caused significant improvement in fibroid related symptoms. Further followup at 3 months after cessation of therapy showed no further reduction which suggests no residual effect of drug. The rationale for use of this drug in infertile patients was to try and see if the size of fibroid would reduce to such a point where it would not be a significant factor causing her symptoms and eventually her infertility.

Endometrial hyperplasia without atypia[7] was reversible as menstruation resumed on cessation of the drug.

6 months therapy with 50mg of mifepristone given weekly is efficacious and acceptable for the treatment of symptomatic fibroid although its use as a primary medical therapy is limited due to recurrence after stopping treatment. It can be used specially for perimenopausal women whose myoma may regress after menopause and younger infertile patients with small size deep intra mural myoma not easily accessible to either hysteroscopic or laproscopic surgery.

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