ORIGINAL RESEARCH

To study effect of mifepristone intreatment of uterine leiomyoma in perimenopausal women

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ABSTRACT

Introduction: Depending on study populations and diagnostic methods, the prevalence of fibroids ranges from 4.5% to 68.6%. In the reproductive age group, fibroids may become clinically apparent and can cause significant symptoms in approximately 25% of women. In India, the prevalence of fibroids is reported to be 37.65% in rural populations and 24% in urban populations. Fibroids are the leading indication for hysterectomy, accounting for 39% of all hysterectomies performed annually in the United States. Although many are detected incidentally on imaging in asymptomatic women, 20% to 50% of women are symptomatic and may wish to pursue treatment. **Aim and Objective:** To study effect of mifepristone (25 mg) in treatment of uterine leiomyoma in perimenopausal woman. A) To Study the Effect of Mifepristone (25mg) On Uterine Leiomyoma. B) To Evaluate Any Symptomatic Improvement of Menorrhagia and Dysmenorrhea. **Material and methods**: This study was done at department of gynecology at NMCH Sasaram, Bihar over a period of 2 years from Dec 2019 to Dec 2021. Taking into consideration a hypothesis that 25 mg of Mifepristone daily for 3 months will offer at least 20% reduction in myoma volume from baseline. Non pregnant perimenopausal women of 45-50 years of age having symptomatic myomas (single or multiple) diagnosed by pelvic usg, who wish to conserve their uterus will be enrolled for the study. **Result:** Before the start of treatment 24 subjects had severe dysmenorrhea, 66 subjects had moderate dysmenorrhea, and 10 subjects had mild dysmenorrhea, after 3 month of treatment only 17 subjects had moderate dysmenorrhea and 83 subjects had mild dysmenorrhea, after 6 month of treatment all 100 study subjects had mild dysmenorrhea. Before the start of treatment, nine subjects had severe pressure symptoms, 13 subjects had moderate pressure symptoms,and after 3 months of treatment, only 11 subjects had moderate pressure symptoms. After 6 months of treatment, 7 subjects had moderate pressure symptoms, with no severe pressure symptoms. **Conclusions**: After treatment with 25 mg of mifepristone, fibroid volume, pressure symptoms, menorrhagia, and dysmenorrhea improve significantly, and the Haematocrit value improves significantly. In the present study, it was observed that there was a significant decrease in mass effect after treatment with mifepristone.

Key words: fibroid, mifepristone, menorrhagia, menopause

INTRODUCTION

Uterine fibroids are monoclonal tumours of the uterine smooth muscle cells and consist of large amounts of extracellular matrix that contain collagen, fibronectin, and proteoglycan.(1)

In India, the prevalence of fibroids is reported to be 37.65% in rural populations and 24% in urban populations (2). The initiating events of fibroid genesis remain speculative.The cells proliferate at a modest rate and their growth is dependent on the ovarian steroids oestrogen and progesterone, so most fibroids shrink after menopause. The biologically potent oestrogen estradiol induces the production of PR by means of ER-α. PR is essential for the response of fibroid tissue to progesterone secreted by the ovaries. Progesterone and PR are indispensable to tumour growth, increasing cell proliferation and survival and enhancing extracellular matrix formation. Oestrogen and ER- α are insufficient for fibroid growth in the absence of progesterone and PR.(3).

Perimenopause is the period prior to the cessation of menses. During this stage, the levels of important hormones are altered. For instance, follicle stimulating hormone (FSH) levels start to increase gradually, reflecting the end of the reproductive years, while oestrogen and progesterone gradually decrease. The prevalence of clinically symptomatic UFs peaks in the perimenopausal years and declines following

menopause.Consequently, the general approach when women are asymptomatic or have mild symptoms is to wait for menopause. If symptoms affect the quality of life at this stage, hysterectomy is the treatment of choice. (3)

Fibroids are the leading indication for hysterectomy, accounting for 39% of all hysterectomies performed annually in the United States. Other treatment for uterine myoma includes – myolysis, embolization of feeding arteries (invasive), medical management options are GNRH agonist and antagonists, selective estrogen modulators (SERM), Aromatase inhibitors ,Danazol,Gestrinone, anti-progestogens and progesterone receptor modulators

In the present study, we tried the 25 mg dose for speedy symptomatic improvement over a short period of 3 months. It is a relatively cheaper and newer alternative, in the area of study being conducted, though not a gold-standard treatment.Doses of 1 mg/kg or greater of mifepristone have been shown to antagonise the endometrial and myometrial effects of progesterone in women.

AIM

To study effect of mifepristone (25 mg) in treatment of uterine leiomyoma in perimenopausal woman.

A. To Study the Effect of Mifepristone (25mg) on size and volume of Uterine Leiomyomas.
B. To Evaluate Any Symptomatic Improvement Of Menorrhagia And Dysmenorrhoea.

METHODOLOGY

This study was carried out in Narayan Medical College and Hospital, Jamuhar, Sasaram. This is a prospective study, period from December 2019 to December 2021. Patient included were Non pregnant perimenopausal women having symptomatic myomas visiting gynecology OPD at NMCH, SASARAM. A total of 100 patients were included in this study.

INCLUSION CRITERIA

1. Non pregnant female
2. Perimenopausal age groups 45-50 years
3. Symptomatic myomas
4. Pelvic ultrasonographycally diagnosed (single/multiple) myomas.
5. Patients who are not willing for surgical interference.

EXCLUSION CRITERIA

1. Excessive uterine bleeding with passage of clots for more than 8 days
2. Cycle length less than 21 days
3. Severe anaemia
4. Allergic to mifepristone'
5. Severe kidney and hepatic disorders.
6. On hormonal treatment for the past two months
7. History of breast cancer or other genital malignancy, suspicion of leiomyosarcoma or adnexal mass.

Non-pregnant perimenopausal women aged 45–50 years old with symptomatic myomas (single or multiple) that were diagnosed by pelvic usgwere enrolled in the study after a detailed history and the presenting complaints were recorded of all the patients.

These symptoms were classified based upon their severity.

1. Dysmenorrhea
- The dysmenorrhea was relieved by therapy.
- 1. mild dysmenorrhea, no analgesics needed
- 2-Moderate dysmenorrhea, analgesics required but can perform her daily physical activities
- 3-Severe dysmenorrhea requires painkillers and cannot be carried out daily physical activities.

2. Pelvic pain
- 0-pain relived in therapy
- 1-mild pain, does not require analgesics
- 2-Moderate pain-analgesics required but able to perform her daily physical activities.
- 3-Severe pain – analgesics are required and she is not able to perform her daily physical activities.

3. Menstrual blood loss classification and scoring
- 0-No bleeding, i.e., the patient became amenorrhoeic on therapy.
- 1-Scanty – less than normal menstrual bleeding occurs.
- 2-Average: A normal amount of blood loss occurs in menses.
- 3-heavy-patient has menorrhagia, i.e. Blood loss greater than normal loss occurs during menses.

4. A menstrual history was taken; a detailed menstrual history was not.
5. Obstetrical history including parity, age at the first child's birth, age at the last child's birth, and mode of delivery were taken.
6. Past history
7. Drug history
8. Family history
9. Personal history

Clinical examinations were done.

1. General physical examination
2. Systemic examination
3. Pelvic examination

Blood samples were collected to record the hemoglobin, blood counts, baseline liver and renal function tests, bleeding and clotting times, along with pelvic usg to know the exact volume of the uterus, number, size, volume and location of myomas and endometrial thickness at the start of treatment and then every four weeks.

Uterine volume was calculated by viscosmi formulae that is, $4/3\ \pi\ W/2 \times L/2 \times T/2$, where W is uterine width on transverse section at uterine fundus; L is uterine length on sagittal section from internal cervical os to fundus and T is uterine thickness measured on sagittal section between the anterior and posterior walls

Women were asked to keep monthly records of bleeding and other symptoms and side effects on a table calendar. After three months of follow up mifepristone

was withdrawn, but cases were followed up for the next three months in post treatment phase. Data were collected and analysed using appropriate statistical methods.

RESULTS

Statistical analysis was carried out with the help of Microsoft Excel and Epiinfo7.1 software. The description of the data was done in terms of the arithmetic mean +/- SD. (Or median) for quantitative data, while in the form of frequencies (%) for qualitative (categorical) data. P-values of < 0.05 were considered significant. For comparison of categorical variables (i.e., to examine the associations between qualitative and quantitative variables), the chi-square test were used if the number of elements in each cell is 5 or higher, and the Fishersexact test, otherwise.

In this study mean age of the study subjects was 46.76 yrs, with SD 1.37, The minimum age group was 45 yrs with maximum 49 yrs. the mean BMI was 29.32 with standard deviation 2.97. 55% subjects had parity II, 36% subjects had parity III and 9% subjects had parity I. Majority of 62% patients had uterus size 12-14 and the remaining 24% had 16-18, 12% had 8-10 and 2% had 20.68% patients had single fibroids and 32% had multiple fibroids.

Present study shows fibroid volume before and 3 and 6 month after treatment, before treatment mean volume was 201.4±62.48 which decreases to 142.38±47.88 and 122.53±47.64 after 3 and 6 month of treatment.

TABLE-1: HEMATOCRIT PAIRED SAMPLE STATISTICS

		N	MEAN	STD. DEV	STD. ERROR MEAN
PAIR 1	HEM-BEFORE	100	28.74	1.93	0.19
	HEM-3 MONTH	100	31.51	1.99	0.19
PAIR 2	HEM-BEFORE	100	28.74	1.93	0.19
	HEM-6 MONTH	100	33.09	1.92	0.19

PAIRED SAMPLE TEST

		PAIRED DIFFERENCE				
		MEAN	STD. DEV	T-VALUE	P-VALUE	95% CI
PAIR 1	HEM-BEFORE - HEM-3 MONTH	-2.77	1.31	-21.15	<0.001	(-3.03, -2.51)
PAIR 2	HEM-BEFORE - HEM-6 MONTH	-4.35	1.79	-24.24	<0.001	(-4.71, -3.99)

Table 1- The paired sample test between the Haematocrit values before and after treatment at 3 months and 6 months showed a statistically significant increase with p-value <0.001.

TABLE-2: EFFECT OF DRUG ON MENORRHAGIA BEFORE AND AFTER TREATMENT

Menorrhagia	Before	3 month	6 month
Mild	60	96	100
Moderate	24	4	0
Severe	16	0	0
Total	100	100	100

TABLE-2 shows effect of drug on menorrhagia. Before the start of treatment 16 subjects had severe menorrhagia, 24 subjects had moderate menorrhagia, and 60 subjects had mild menorrhagia, after 3 month of treatment only 4 subjects had moderate menorrhagia and 96 subjects had mild menorrhagia, after 6 month of treatment all 100 study subjects had mild menorrhagia. However two subjects had amenorrhea after treatment.

TABLE-3: DYSMENORRHEA OF STUDY SUBJECTS BEFORE AND AFTER TREATMENT

Dysmenorrhea	before	3 month	6 month
Mild	10	83	100
moderate	66	17	0
Severe	24	0	0
Total	100	100	100

TABLE-3 shows effect of drug on dysmenorrhea. Before the start of treatment 24 subjects had severe dysmenorrhea, 66 subjects had moderate dysmenorrhea, and 10 subjects had mild dysmenorrhea, after 3 month of treatment only 17 subjects had moderate dysmenorrhea and 83 subjects had mild dysmenorrhea, after 6 month of treatment all 100 study subjects had mild dysmenorrhea

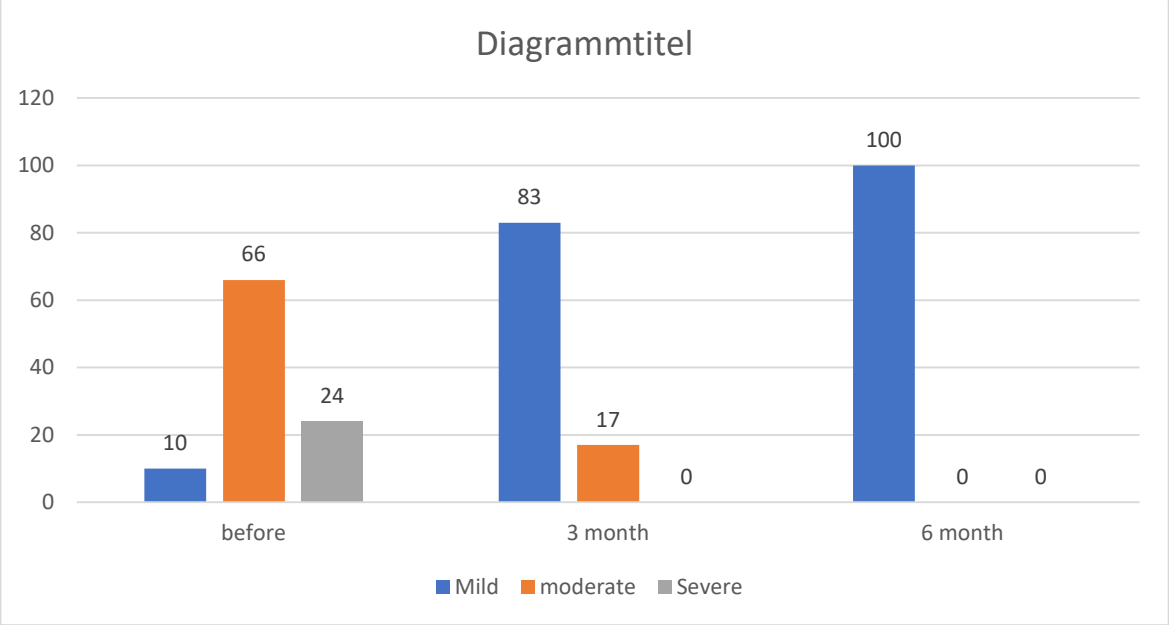


TABLE-4: COMPARISON OF PATIENTS BETWEEN BEFORE AND AFTER MASS EFFECT

MASS EFFECT	BEFORE	At 3 month	At 6 month
YES	58	15	7
NO	42	85	93
TOTAL	100	100	100

GRAPH-4: COMPARISON OF PATIENTS BETWEEN BEFORE AND AFTER MASS EFFECT

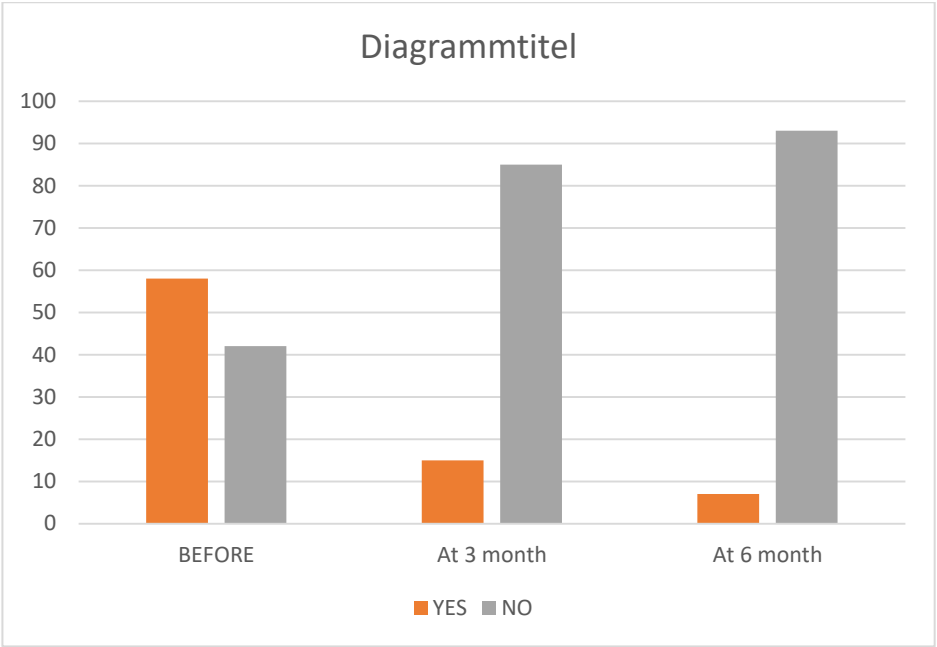


TABLE-5: DISTRIBUTION OF PATIENTS ACCORDING TO ANY ADDITIONAL TREATMENT

ANY ADDITIONAL TREATMENT	FREQUENCY	PERCENTAGE
YES(IRON SUPPLEMENT)	59	59
NO	41	41
TOTAL	100	100

In the above table, 59% patients had additional treatment of iron and 41% did not require any additional treatment.

GRAPH-5: DISTRIBUTION OF PATIENTS ACCORDING TO ANY ADDITIONAL TREATMENT

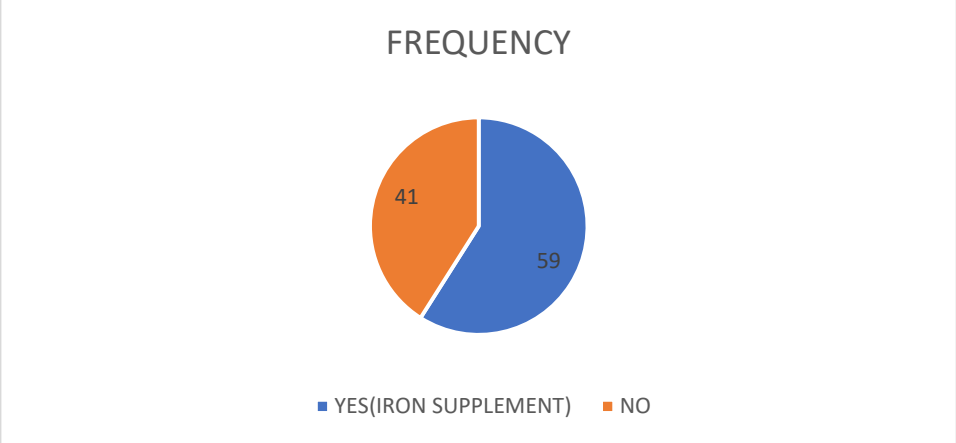
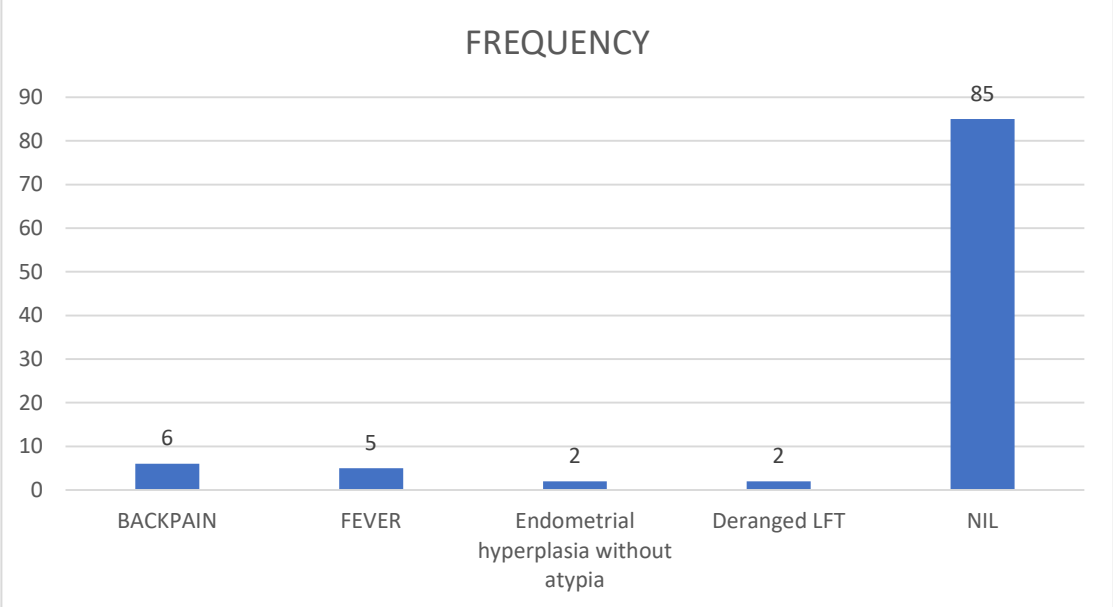


TABLE-6: DISTRIBUTION OF PATIENTS ACCORDING TO ANY COMPLICATIONS

Any complications	Frequency	Percentage
Backpain	6	6
Fever	5	5
Endometrial hyperplasia without atypia	2	2
Deranged lft	2	2
Nil	85	85
Total	100	100

In the above table, 6% patients had back pain and 5% had fever, 2 study subjects had endometrial hyperplasia without atypia and 2 subjects had deranged LFT and rest 85 subjects had no complications.

GRAPH-6: DISTRIBUTION OF PATIENTS ACCORDING TO ANY COMPLICATIONS



DISCUSSION

UFs are common benign tumors that occur in women throughout their reproductive years with a peak incidence in perimenopausal years, and subsequently the incidence of UFs decreases in post menopause. During the past century, hysterectomy and myomectomy have been the main treatment for the women with symptomatic leiomyomas. Uterine fibroids affect a large segment of the perimenopausal population and can negatively impact daily living and QOL of those affected. Because of the high estimated prevalence in perimenopausal age groups and costs associated with surgical treatments, the direct and indirect costs of uterine fibroids are substantial for both the health care system and the individual patient. Medical management of UFs may provide symptomatic relief and could be used as a bridge into menopause in which, UFs are thought to regress. It is still not clear why some UFs regress and others do not

during this stage of life, however, hormonal regulations are thought to be involved.

Fibroid being a tumour of hyper oestrogenic 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 (SERMs Raloxifene) are effective in reducing the size of fibroid and improve symptoms in most of cases.[4] 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 haemoglobin by controlling bleeding and renders surgery unnecessary as patient reaches menopause, because fibroid being a hormone depended tumours stops to grow after menopause. Mifepristone has both antiprogesterone and antiglucocorticoid properties in dose dependent manner. (5)

Mifepristone, as a treatment option for myoma, was first reported by Murphy *et al* in 1993. Further studies evaluated mifepristone in doses varying from 2.5 to 50 mg/day given for 3 to 6 months and doses as high as 50 mg and as low as 5 mg were found effective in ameliorating myoma related symptoms like dysmenorrhea, menorrhagia and pelvic pressure, and reducing myoma volume by 26-57 per cent and inducing amenorrhoea in 41-100 per cent.

With higher doses speedy and better control of bleeding is achieved, this improves the general condition of women and hemoglobin levels, relieves anxiety and provides women a sense of well being and affectivity of treatment but produce hot ushes and a comparative study of 5 mg, 25 mg and 50 mg dosage and suggested 25 mg to be the most effective dose to cause clinically signi∟cant decrease in leiomyoma volume.

We chose 25 mg daily to achieve rapid symptomatic improvement (improved compliance with low drop out rate) in short period of time (3 months) with minimal side effects.

With higher doses speedy and better control of bleeding is achieved, this improves the general condition of women and haemoglobin levels, relieves anxiety and provides women a sense of well being and affectivity of treatment but produce hot flushes and other anti-glucocorticoid sideeffects. 25 mg to be the most effective dose to cause clinically significant decrease in leiomyoma volume. In the present study we chose 25 mg of Mifepristone daily to achieve rapid symptomatic improvement (improved compliance with low dropout rate) in short period of time (3 months) with minimal side effects

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.*,(6) reported fall of 48% in mean uterine volume while amenorrhoea in 61% only after 6 months of 10 mg mifepristone. Another study by Kettle *et al*., reported amenorrhoea in 40-70% over one year at 5-10 mg dose, while 100 mg led to 100% amenorrhoea. AUB is the main reason of worry in women as it affects their daily routines, work efficiency and health status, therefore mostly opts for hysterectomy as one time management in developing countries. With higher doses speedy and better control of bleeding is achieved, this improves the general condition of women and haemoglobin levels, relieves anxiety and provides women a sense of well being and affectivity of treatment but produce hot flushes and other anti-glucocorticoid side-effects. Murphy *et al*.[7] had a comparative study of 5 mg, 25 mg and 50 mg dosage and suggested 25 mg to be the most effective dose to cause clinically significant decrease in leiomyoma volume. We chose 25 mg daily to achieve rapid symptomatic improvement (improved compliance with low dropout rate) in short period of time (3 months) with minimal side effects

Mechanism of reduced bleeding and myoma size is likely to be due to structural, functional and micro vascular effects of Mifepristone on the endometrium and uterine musculature in dose and duration dependent manner.

AGE

In this study mean age of the study subjects was 46.76 yrs, with SD 1.37, The minimum age group was 45 yrs with maximum 49 yrs.In a study by **AnupamKapur** et al (2016) (8)majority of patients fell in 41–45 years age-group. Mean age was 26.9+7.1 in a study by **Cui-Lan Li** et al (2015)(9). In a study by **Chongdong Liu** et al (2017)(10) mean age of patients receiving 10mg mifepristone was 43.41±5.73 and of those receiving 25mg mifepristone was 43.07±6.38.In a study by **AnupamaHari** et al (2017) majority was in between 40 and 45 years of age which was 72%. The mean age was 42.1 ±4.52. In a study by **M. Engman** et al (2009)(11) the mean age (+SD) was 40.9+7.6 and 40. 8+4.7, respectively, in the control group and mifepristone group.

PARITY

In our study region out of 100 patients attending the gynaecology OPD with fibroid uterus the distribution of the parity amongst the study groups were, 55 patients were second para and 9 patients were primiparous while the rest were parity three and above. Multiparous patients were found to have fibroids more frequency than nulliparous in their perimenopausal years.

BMI

In the current study the mean BMI was 29.32 with standard deviation 2.97. In a study by **AnupamaHari** et al (2017)(12) he means BMI was 27±3.66. In a study by **JosepLluisCarbonell** et al (2013)(13) mean BMI in 2.5 mg mifepristone treatment group was 24.9 ± 3.7 and in 5 mg group it was 25.2 ± 4.0. In a study

by **Shikha Seth** et al (2013) (14)mean BMI were 24.12 Kg/M2±3.81. In a study **S.V. Nachiketha** et al (2019)(15) mean body mass index was 25.5 Kg/m2 and range was from 18 to 36 Kg/m2. Most of patients (55%) in this study were in normal range of BMI (18-25) and 45 % of patients had high BMI (>25). Obesity is associated with hyper estrogenic state contributing to myoma growth.

SIZE OF UTERUS

In the above table, majority of 62% patients had uterus size 12-14 and the remaining 24% had 16-18, 12% had 8-10 and 2% had 20.In a study by **AnupamaHari** et al (2017)(12)mean uterine volume before treatment was 156.87 ± 63.65 and Mean Value at 3 months of treatment was 103.038 ±36.33. In a study by **JosepLluisCarbonell** et al (2013)(13) mean uterine volume in 2.5 mg mifepristone treatment group was 455 ± 314 and in 5 mg group it was 426 ± 305. In a study by **Mei Wang** et al (2019)(16) before treatment uterine volume was 59.78 ± 9.31. In a study by **Shikha Seth** et al (2013) (14)Mean uterine volume decreased to 63.69% (SD ± 22.2), while mean volume of dominant leiomyoma decreased to 53.62% (SD ± 48.5) after three months of complete treatment. Intra-mural and sub serous responded well, while in out of five sub mucous myomas, two pedunculated ones prolapsed out of cervix and required polypectomy and one was non - responder and one had hysterectomy for recurrence.

NUMBER OF FIBROIDS

In the above table, 68% patients had single fibroids and 32% had multiple fibroids. Study by **Shikha Seth et al**(14)shows Median number of leiomyomas at baseline sonography was two (range: 1-5) and it was two (range: 1-4) at the end of 3 months, study by **AllaSatyanarayan Reddy et al**(17)shows Single fibroid was seen in 31 women, Two fibroids were seen in 23 women, Three or more fibroids were seen in 6 women.

SIGNAL INTENSITY OF FIBROID

In our study 73 of the study subjects had low intensity fibroids and 27 with high intensity fibroids on ultrasonography.Uncomplicated leiomyomas are usually hypoechoic, but can be isoechoic, or even hyperechoic compared to normal myometrium.

Calcification is usually seen as echogenic foci with shadowing on ultrasonography.

HEMATOCRIT

In the present study Haematocrit values before and after treatment at 3 months and 6 months showed a statistically significant increase with p-value< 0.001.In a study by **Chongdong Liu** et al (2017) (10)mean haemoglobin of patients receiving 10mg mifepristone was 120.46±21.11 and of those receiving 25mg mifepristone was 123.15±20.37. In a study by **Deepti Jain** et al (2018)(18)haemoglobin at the start of therapy ranged between 7.8 gm% and 12.5 gm% and all women showed a rise in haemoglobin and at 3 months the mean haemoglobin was 11.2 ± 0.67 gm%. In a study by **M. Engman** et al (2009) (11)Haemoglobin counts improved significantly (P 1⁄40.003) from 121+5 g/l to 133+3 ml (mean+SE) within the mifepristone group. In a study by **Meeta Gupta** et al (2020)(19) mean haemoglobin was 8.6 (gm%) that increased to 9.7 (gm%) at 12 months after the medical treatment. Study by **Vidushikulshreshtra et al** (20)shows there was a significant rise in haemoglobin levels in both the groups with treatment, (P<0.05). Study by **Shikha Seth et al** (14)shows Haemoglobin counts improved significantly 2.8 gram + SD 1.49, from mean 8.9 gram% at start. Base line endometrial thickness (ET) at start of treatment was 7.6 + 2.8 which progressively increased in all '82' cases during the treatment phase with mean 51.9% rise over three months.

MASS EFFECT

In the current study 58% subjects had mass effect before start of treatment, at 3 month 15 subjects had mass effect whereas 7 subjects had mass effect at 6 month after treatment.

Study by **AllaSatyanarayana Reddy et al** (17)shows 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 revaluation after three months of drug free period at six months. In perimenopausal women with fibroids and menorrhagia, **AnupamKapur et al**(8)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.

IMMEDIATE NONPERFUSED VOLUME

In the present study out of 100 patients treated, 43% of them attained between 40 and 60 % NPV Ratio, with a mean value of 48.37%. In a study by **AnupamKapur** et al (2016)(8) baseline fibroid volume was 204.08 which decreased to 113.16 after 6 month treatment. In a study by **Chongdong Liu** et al (2017) (10)< 30% shrinkage occurred in 58.52%, ≥ 30% to 10% in 16.30%, ≥ 10% to 0% in 5.93%, >0% to 20% in 5.19%. In a study by **Meeta Gupta** et al (2020)(19) at 3 months, there was no change in size in 11.11% patients. At 12 months, one patient (1.85%) had no change in tumour size. At 3 months, 0.5–0.9 mm change was noted in 29.63% patients; total 24.07% patients had 0.5–0.9 mm change at 12 months. A change of 1–1.4 mm in size was noted in 38.89% patients at 3 months, which increased to 42.59% patients at 12 months. Change in size of 1.5–1.9 mm was in 14.81% patients at 3 months and in 16.67% patients at 12 months.

FIBROID SHRINKAGE

In the present study the mean fibroid volume at the time of registration was 201.4cc which had reduced to 142.38cc after 3 months of treatment and 122.53 cc in 6 months follow-up phase.In a study by **Deepti Jain** et al (2018)(18) the mean decrease in size was 49.65% ± 23.65% from 0 to 3 months, 11.95% ± 28.84% from 3 to 6 months, and 33.59% ± 18.86% from 6 to 9 months. In a study by **S. V. Nachiketha** et al (2019) (15)after completing 3 months of treatment mean fibroidvolume was reduced to 30.45cm3 which is statisticallysignificant. Overall 38.7% reduction in fibroid volume is observed in this study.

PRESSURE SYMPTOMS

In our study the 9 subjects had pressure symptoms urinary and rectal symptoms due to the pressure effects of the leiomyoma and after 3 months of the therapy with 25 mg of mifepristone only 5 had pressure symptoms which further persisted in only 3 patients in 6 monthly follow-ups.

EsteveCarbonell JL et al (2013)(21), in his study on 2.5 mg versus 5 mg mifepristone in treatment of leiomyoma found 93.3% and 84.4% patients got rid of the urinary disturbances at the end of 3 months and 6 months respectively with 2.5mg of mifepristone and 91.4% and 77.14% got relieved at the end of 3 months and 6 months respectively with 5 mg of mifepristone.

BLOOD LOSS

In our present study Before the start of treatment 16 subjects had severe menorrhagia, 24 subjects had moderate menorrhagia, and 60 subjects had mild menorrhagia, after 3 month of treatment only 4 subjects had moderate menorrhagia and 96 subjects had mild menorrhagia, after 6 month of treatment all 100 study subjects had mild menorrhagia. However two subjects had amenorrhea after treatment. Study by **Anupamkapur et al**(8)shows Mifepristone also caused significant improvement in leiomyoma-related symptoms. Mean blood loss (MBL) declined in 100 % of our patients. Of these, 88.89 % became amenorrhoeic and the rest showed a decreased MBL.

DYSMENORRHOEA

In our study, 10,66,24 subjects were suffering from mild, moderate and severe dysmenorrhea receptively a the time of registration which reduced 83 patients with mild dysmenorrhea and 17 with moderate which none of the patients had severe dysmenorrhea after 3 months of initiation of the treatment with 25 mg of mifepristone. On follow up after 6 months all the patients had only mild symptoms of dysmenorrhea. Thus mifepristone 25 mg can significantly reduce dysmenorrhea in patients with symptomatic fibroids.

ADDITIONAL TREATMENT

In our present study 59 patients required additional treatment in form of ferrous ascorbate tablets containing elemental iron of 100 mg once daily dosing depending upon the severity of anaemia, for improving the QOL and attaining the optimal state of well being.

COMPLICATIONS

In this study 6% patients had back pain and 5% had fever, 2 study subjects had endometrial hyperplasia without atypia and 2 subjects had deranged LFT and rest 85 subjects had no complications. Other study done on this topic in a study by **Chongdongliu** et al (2017) (10)2.28% had pain in low back and leg, 3.91% had abdominal pain, 5.21% had hot flashes and sweating, 1.95% had irritability, 1.63% had increased vaginal secretion, 2.93% had headache, dizziness, fatigue, and somnolence. In a study by **Anupama Hari** et al (2017) (12)among 50 patients, none of them had any major side effects. In 14 patients, there were minor side effects out of which nausea and abdominal pain are common, seen in 4 patients each. 3 patients had hot flushes, in 2 LFT's were raised but not more than two times the upper limit of normal and 1 patient had backache. In a study by **Deepti Jain** et al (2018) (18)some women complained of weakness, however, side effects such as nausea, vomiting, rash, and fever were not reported by any of the 10 women enrolled in the study. Endometrial hyperplasia has been reported in few studies at the end of 3 months with mifepristone administration. However, in these studies with endometrial hyperplasia, no cellular atypia has been found. In **Deepti Jain**(18) study, endometrial hyperplasia was seen in 1 woman where endometrial thickness increased to 15 mm, but no atypia was found on histopathology which is in accordance with our study in which 2 patients had endometrial hyperplasia without atypia. In a study by **Mei Wang** et al (2019)(16) the number of patients with adverse reactions of lower abdominal pain, nausea and vomiting, limb weakness and irregular

CONCLUSION

The incidence of uterine leiomyomas rises with age and peaks at perimenopausal age groups. Uterine fibroids can cause painful and heavy uterine bleeding, as well as interfere with daily living and self-image in the perimenopausal age .The treatment of uterine leiomyomas in the perimenopausal period should not be disregarded just because the pathology and symptoms are unlikely to persist after menopause; nonetheless, opting for a speedy cure with entire surgical removal of the uterus should be avoided because the direct and indirect expenses of uterine fibroids are significant for both the health care system and the individual patient, due to the high estimated prevalence and treatment costs. In the location of our study, UFs are the most common cause of hysterectomy, accounting for 30 to 50 percent of all hysterectomies.

In our study, the majority of patients had single fibroids. We can conclude that after treatment with 25 mg of mifepristone, fibroid volume, pressure

symptoms, menorrhagia, and dysmenorrhea, and the Haematocrit value improves significantly. we can conclude that Mifepristone is well tolerated drug with no serious adverse effects.

The use of mifepristone in the medical management of UFs has attracted interest in recent years, with numerous studies covering a wide variety of dosages and treatment durations. The optimum dose and length of treatment have yet to be established.

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