Low dose mifepristone in medical management of uterine leiomyoma - An experience from a tertiary care hospital from north India

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Background & objectives: Uterine myoma is a common indication for hysterectomy in India. An effective medical treatment option may reduce hysterectomy associated morbidity. This study was undertaken to evaluate efficacy and safety of low dose mifepristone in medical management of myoma and to compare two doses - 10 vs. 25 mg/day.

Methods: In this randomized clinical trial, women with symptomatic myoma or myoma>5cm were included. Uterine size >20 wk, fibroids >15 cm were excluded. Pictorial blood loss assessment chart (PBAC) score was used to assess menstrual-blood-loss and visual analog scale (VAS) for other symptoms. Haemogram, liver function test, ultrasound with doppler and endometrial histology was performed. Patients were randomized and were given oral mifepristone as 25 mg/day in group 1 and 10 mg/day in group 2 for 3 months. Patients were followed at 1, 3 and 6 months.

Results: Seventy patients in group 1 and 73 in group 2 completed treatment. Mean PBAC score reduced from 253 to 19.8 and from 289.2 to 10.4 at 1 and 3 months in groups 1 and 2, respectively. At 3 months, 67 of 70 (95.7%) patients of group 1 and 66 of 73 (90.4%) of group 2 developed amenorrhoea which reverted after median 34 (range 4-85) days. Mean myoma volume decreased by 35.7 per cent (from 176.8 to 113.7 cm³) and 22.5 per cent (from 147.6 to 114.4 cm³) at 3 months in groups 1 and 2, respectively. Side effects seen were leg cramps in 7 of 70 (10%) and 5 of 73 (6.8%) and hot-flushes in 5 of 70 (7.1%) and 5 of 73 (6.8%) in groups 1 and 2, respectively. Repeat endometrial-histopathology did not reveal any complex hyperplasia or atypia in either group.

Interpretation & conclusions: Mifepristone (10 and 25 mg) caused symptomatic relief with more than 90 per cent reduction in menstrual blood. Greater myoma size reduction occurred with 25 mg dose. Amenorrhoea was developed in 90-95 per cent patients which was reversible. It can be a reasonable choice for management of uterine leiomyoma as it is administered orally, cost-effective and has mild side effects.

Key words: Amenorrhoea - fibroid - leiomyoma - mifepristone - medical management - uterine

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Uterine leiomyoma are commonest benign gynaecological tumours occurring in up to 25 per cent of women in reproductive age and about 40 per cent have symptoms severe enough to warrant therapy⁴. The definitive treatment for symptomatic myomas has always been surgical and myomas account for up to 40 per cent of all hysterectomies in premenopausal women⁵.

Non surgical treatment options for symptomatic myomas have limitations. Danazol reduces uterine volume by 18-23 per cent⁶, but is associated with marked androgenic side-effects and liver dysfunction. Gonadotrophin releasing hormone agonist (GnRH) reduces leiomyoma size to about 50 per cent in three months⁷ but is expensive, has to be given parenterally and is also associated with hypoestrogenism leading to hot flushes, vaginal dryness and bone loss⁸. Cessation of GnRH causes regrowth of myoma and recurrence of symptoms⁹. Uterine artery embolization has been shown to decrease leiomyoma size by 35-69 per cent, improve menorrhagia and reduce pain, but there are potential risks of premature ovarian failure and uterine synechia⁹.

Although the traditional concept supports a crucial role of oestrogen in promoting leiomyoma growth, recent evidence suggests that progesterone is essential for maintenance and growth of uterine leiomyoma and that oestrogen is required only for upregulation of progesterone receptors⁹. Hence, there was a surge of studies evaluating effect of antiprogestogens like ulipristal (PEARL Study), asoprisnil, and CDB-2914, a progesterone receptor modulator, in non surgical treatment of uterine myomas⁹,10.

Mifepristone (RU 486) is a progesterone receptor modulator with primarily antagonistic properties. It binds strongly to endometrial progesterone receptors, minimally to estrogen receptors and upregulates androgen receptors¹¹. In a placebo controlled trial low dose mifepristone (RU 486) has been shown to decrease myoma size as well as symptoms¹². Reduction in size with mifepristone might be due to the direct effect in reducing number of progesterone receptors. Besides, because of ovarian acyclicity seen with mifepristone, hormonal milieu similar to early follicular phase may also inhibit steroid dependent growth of myoma. Increase in androgen receptors also contributes to antiproliferative effects¹³. Mifepristone also delays or inhibits ovulation, which may produce amenorrhoea. Direct suppressive effects on endometrial vasculature as well as on reducing stromal vascular endothelial growth factor (VEGF) has also been suggested for reducing menstrual blood loss¹³,14.

GnRH analogues are a well established option for medical management of myomas, but their use is not widespread. Mifepristone, on the other hand, is administered orally, has a few side effects and is less expensive than GnRH analogues. If proved to be an effective medical treatment option for uterine myoma, it may be a cost-effective substitute for GnRH analogues in low-resource settings. The initial studies with mifepristone suggested lesser efficacy with doses <10 mg and also concluded that an effective dose to cause a clinically significant (50%) decrease in leiomyoma volume was 25 mg daily¹⁵.

Therefore, this study was designed to evaluate efficacy and safety of mifepristone in medical management of uterine leiomyoma in Indian women and to compare two doses -10 vs. 25 mg per day.

**Material & Methods**

This prospective randomized clinical trial was conducted from February 2007 to February 2010, at the Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India, after obtaining ethical clearance from the Institute’s Ethics Committee. The study was registered in Clinical Trial Registry of India (CTRI/2012/03/002470). Women between 20-50 yr of age with single or multiple fibroids were included consecutively in the study if they were symptomatic (menorrhagia, dysmenorrhoea, abdominal lump, dull aching lower abdominal pain, dyspareunia) or if the largest fibroid was >5 cm on ultrasound. Ultrasound pelvis was done for all patients to exclude any other obvious causes like adenomyosis, endometriosis, adnexal mass for the above symptoms. Exclusion criteria remained more than 20 wk gravid size uterus, fibroids >15 cm by ultrasound, grade-0 submucosal fibroids, renal or hepatic dysfunction, suspected adenomyosis, current genital infection, endometrial hyperplasia with atypia and hormonal medication (Progestogens/ GnRH) within 3 months and women desiring pregnancy.

Demographic and baseline clinical profile including details of menstrual cycle, symptoms and their severity was noted. Menstrual blood loss was assessed by pictorial blood loss assessment chart (PBAC) scores¹⁶, which is a semiquantitative assessment that takes into account the number of pads soaked, their degree of soakage, passage of clots and episodes of flooding¹³. A score of 100 or more amounts to menorrhagia.

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Visual analog scale (VAS) score was noted for pain, dysmenorrhea, dyspareunia, pelvic pain and pressure symptoms, where patients were asked to describe their pain on a scale of 0 to 10, before and after the treatment, with “no pain” taken at zero and “worst possible pain” at 10.

A complete general and gynaecological examination was done. Blood testing was done for haemoglobin, liver and kidney function tests and serum oestradiol levels. Ultrasound was done to confirm the diagnosis of leiomyomas as well as to ascertain number, site, volume of myomas, to measure endometrial thickness and to rule out any other pelvic pathology. Volume of each myoma was calculated and added in cases with multiple myomas. Fibroid volume was calculated by the ellipsoid method and the formula $V=0.5233(D1 \times D2 \times D3)$ was used, where $D1$, $D2$ and $D3$ are the longitudinal, transverse and cross-sectional diameters of the fibroid, respectively. In multiple myomas, volumes of all myomas were added. Doppler ultrasound was done and blood flow noted in terms of uterine artery resistive-index (RI) and pulsatility-index (PI). Hysteroscopy was performed when endometrial polyp or submucosal myomas were suspected. Endometrial aspiration was performed to rule out any abnormal histopathology in married women and in unmarried women when required on the basis of increased endometrial thickness on ultrasound.

To detect a difference of 15 per cent between the two doses, taking P1 as 100 per cent for 25 mg/day dosage and P2 as 85 per cent for 10 mg/day dosage; thus taking Alpha=5 per cent and Beta=10 per cent, the sample size for each group was calculated to be 76 patients. Hence, 150 women meeting the inclusion criteria were recruited in the study after taking informed written consent. Patients were randomized into two groups according to computerized randomization. Mifepristone was given as 25 mg/day in group 1 and as 10 mg/day in group 2, starting initially from day 2-3 of periods. Duration of treatment was 3 months.

Since mifepristone is available in India for indication of medical abortion as 200 mg tablet, capsules of 10 and 25 mg were prepared from 200 mg tablet in the Pharmacology department by crushing the tablets in powder form, and then filling the capsules according to the weight. Capsules of 10 and 25 mg could be prepared from 200 mg tablet without adding inert substance.

Patients were followed up at 1 and 3 months while on therapy and then at 6 months i.e. 3 months after stopping therapy to look for recurrence of symptoms or regrowth of fibroid. On each visit clinical symptoms including bleeding and spotting, PBAC score, VAS score and any side effects were assessed. Amenorrhoea was defined as the absence of bleeding for two consecutive cycles. Ultrasound was done to determine the number of myoma and endometrial thickness.

At 3 months follow up; haemoglobin, liver function test (serum bilirubin, serum total proteins/albumin/ globulin, serum transaminases) and serum oestradiol were repeated. Ultrasound with uterine artery Doppler was also done to determine volume reduction and change in blood flow. Repeat endometrial aspiration was done after completing 3 months of treatment except in unmarried patients and in patients not giving consent for repeat test.

Statistical analysis: SPSS 15.0 (SPSS Inc., USA) was used for data analysis. Friedman test was used for assessing overall effect within the groups. Comparisons of various parameters within the group were done with Wilcoxon signed ranks test with Bonferroni correction. Wilcoxon rank sum test or t test was used for comparison between the groups at baseline and various follow ups, as applicable, as per the normality of data. $P<0.05$ was taken as significant. Repeated measure ANOVA test was done for assessing changes in haemoglobin.

Results

A total of 150 patients (75 in each group) were recruited and followed up at Gynae outpatient department after taking informed consent. Seventy patients in group 1 and 73 patients in group 2 completed three months treatment duration. Fig. 1 shows the details of patients excluded, recruited and treated.

Patients’ baseline characteristics were similar in both groups with mean age being 35.6±7.42 vs. 36.2±7.15 yr. Nineteen (25.3%) patients in group 1 and eight (10.7%) in group 2 were unmarried. Mean PBAC score was 289 (20-1000) and 253 (22-1086), median endometrial thickness was 7.0 (3-21) and 6.7 (3-16.8) mm. Mean myoma volume was 176.8 (5.4-923) and 147.6 (1.22-1358) cm$^3$ in groups 1 and 2, respectively. Before the start of treatment, all women had spontaneous menstrual cycles.

PBAC reduced significantly from baseline to 3 months therapy in both groups ($P<0.001$) and the effect started at the very first cycle. PBAC score at
various follow up is shown in Fig. 2. Reduction in mean PBAC score was significant in both the groups - 92.4 and 96.4 per cent, respectively in groups 1 and 2 after completion of treatment. With mifepristone, 67 of 70 (95.7%) in group 1 and 66 of 73 (90.4%) in group 2 developed amenorrhoea, which reverted after median 34 (5-85) days of stopping therapy and was scanty in 12.5 per cent, moderate in 43.8 per cent, heavy in 18.7 per cent and very heavy in 25 per cent. Two patients, one each in the two groups presented with continuous and heavy bleeding for more than one month with no response to progesterone therapy. All the three patients (including 2 nulliparous) had uncontrollable bleeding with severe anaemia (haemoglobin <5 g%), necessitating blood transfusion. On starting treatment they responded within one week. At 6 months, i.e. 3 months after stopping therapy, PBAC score increased but not to the initial level in both groups (Fig. 2).

Twenty five (33.3%) patients in group 1 and 28 (37.3%) in group 2 presented with abdominal pain. There was marked relief with significant decrease in VAS score in both groups with therapy \((P<0.01)\). Relief of abdominal pain persisted even 3 months after stopping treatment. Thirty five (46.7%) patients in group 1 and 50 (66.7%) in group 2 presented with dysmenorrhoea (Table I). Treatment decreased VAS score significantly \((P<0.01)\) in both groups. Twelve (16%) patients in group 1 and 13 (17.3%) in group 2 presented with dyspareunia which also decreased significantly \((P<0.01)\) in both the groups. Pain, backache and pelvic pressure improved with treatment in both groups. One patient complained of rectal pain which disappeared with treatment. Six patients complained of urinary symptoms which also were cured with therapy.
Volume of fibroids decreased with treatment in both groups \((P<0.05)\) and effect of treatment was comparable (Table II). The percentage decrease in overall myoma volume was 35.7 per cent in group 1 and 22.5 per cent in group 2 \((P<0.05)\). In group 1, volume reduced by 24.8 per cent in cases with single myoma versus 32.4 per cent reduction in added volume in multiple myomas. Similar reduction of 24.8 per cent occurred in single myomas in group 2, but lesser reduction was observed in multiple myomas (27.5%). At three months post-treatment follow up, uterine volume further reduced, then it increased again but was still lesser than the baseline.

At completion of three months therapy, 30 of 70 (42.8%) patients in group 1 and 33 (45.2%) in group 2 had endometrial thickness of >8 mm which decreased again at 3 months after stopping therapy. Baseline and

<table>
<thead>
<tr>
<th>Table I. Effect of treatment on VAS score of various symptoms</th>
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<tr>
<td>VAS score</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Dysmenorrhoea</td>
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<tr>
<td>Mean median (range)</td>
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<tr>
<td>Pain</td>
</tr>
<tr>
<td>Mean median (range)</td>
</tr>
<tr>
<td>Backache</td>
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<tr>
<td>Mean median (range)</td>
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<tr>
<td>Dyspareunia</td>
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<td>Mean median (range)</td>
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*Significant reduction from baseline among each group \((P<0.01)\)

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<tr>
<th>Table II. Effect of treatment on endometrial thickness, haemoglobin, oestriadiol, myoma volume and Doppler indices</th>
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<tr>
<td>Group I (N=75)</td>
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<td></td>
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<tr>
<td>Endometrial thickness (mm) Median</td>
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<tr>
<td>Haemoglobin (g%) Mean±SD</td>
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<tr>
<td>Serum oestriadiol (pg/ml) Mean±SD</td>
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<td>Myoma volume (cm³) Mean median (range)</td>
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<tr>
<td>Doppler indices Mean±SD RI</td>
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<td>Mean±SD PI</td>
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*\(P<0.05\) when compared to baseline; RI, resistivity index; PI, pulsatility index
repeat endometrial histopathology at three months is shown in Table III. Repeat endometrial aspiration was done in 43 patients in each group and did not show any complex hyperplasia or atypia in either group. There was a significant rise in haemoglobin levels in both the groups with treatment, \((P<0.05)\) (Table II). Mean baseline oestradiol in both the groups was comparable and with treatment, it increased in group 1 and decreased in group 2, but the changes were insignificant. Among Doppler parameters, baseline resistive index and pulsatility index were comparable in both groups. Doppler indices increased with treatment in both the groups, indirectly suggesting decrease in the blood flow. Though significant increase was seen only in pulsatility index in group 1, the difference was not significant between the groups.

The common side effects were leg cramps seen in seven (10%) and five (6.8%), hot flushes in five (7.1%) and five (6.8%), weakness in five (7.1%) and seven (2.7%) and palpitations in one (1.4%) and three (4.1%) patients in groups 1 and 2, respectively. Transient rise in serum transaminases was seen in two patients each (2.8 and 2.7%). Two patients (2.8%) in group 1 had pigmentation over face which disappeared after stopping treatment. Three patients (4.1%) had headache and two (2.7%) had sleepiness in group 2. Mood swings, diarrhoea, joint pain, breast tenderness and mild gastritis were also noted by one patient each. In group 1, one patient discontinued mifepristone after one week due to allergic reaction (itching and rashes all over the body).

**Long term follow up:** Sixty patients in group 1 and 64 in group 2 reported at 12 months \((i.e. 9 \text{ months post-treatment})\). Approximately, one third of patients (35 and 28.1%, respectively) were asymptomatic in groups 1 and 2, with median PBAC score being 85 (26-1117) and 74(32-210) and myoma volume being 20.1 (0.54-179.9) and 25.6 (2.1-600) cm\(^3\), respectively.

The remaining patients in both groups complained of menorrhagia, which required interventions in form of restarting the same treatment (3.3 and 4.7%), alternate oral medical therapy (5 and 3.1%), levonorgestrel–intrauterine-system insertion (8.3 and 11.6%) including patients with persisting endometrial hyperplasia, uterine artery embolization (1.7 and 4.6%), myomectomy (10 and 9.1%) or hysterectomy (36.7 and 39.1%), respectively in groups 1 and 2. One patient in group 1 conceived within 2 months after stopping treatment and had spontaneous abortion at 8 wk period.

### Table III. Endometrial aspiration at baseline and after 3 months of treatment

<table>
<thead>
<tr>
<th>Histopathology (HPE)</th>
<th>Group 1</th>
<th>Group 2</th>
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<tbody>
<tr>
<td></td>
<td>Baseline (n=75)</td>
<td>At 3 months (n=43)</td>
</tr>
<tr>
<td>Proliferative (including disordered proliferative) endometrium</td>
<td>18 (24)</td>
<td>23 (53.5)</td>
</tr>
<tr>
<td>Secretary endometrium</td>
<td>27 (36)</td>
<td>5 (11.6)</td>
</tr>
<tr>
<td>Hyperplasia without atypia</td>
<td>7* (9.4)</td>
<td>4 (9.4)</td>
</tr>
<tr>
<td>Asynchronous endometrium</td>
<td>4 (5.3)</td>
<td>2 (4.7)</td>
</tr>
<tr>
<td>Interval endometrium</td>
<td>1 (1.3)</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Inadequate</td>
<td>-</td>
<td>3 (6.9)</td>
</tr>
<tr>
<td>Cystic dilated glands with stroma</td>
<td>-</td>
<td>2 (4.7)</td>
</tr>
<tr>
<td>Decidualized stroma</td>
<td>-</td>
<td>3 (6.9)</td>
</tr>
<tr>
<td>Not done</td>
<td>19 (24)</td>
<td>27</td>
</tr>
<tr>
<td>Discontinued/Lost to follow up</td>
<td>-</td>
<td>5</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages

*Post-treatment HPE: Group 1
1- Hyperplasia without atypia persisted
2- Cystic glandular hyperplasia
3- Proliferative endometrium

**Post treatment HPE: Group 2
1- Hyperplasia without atypia persisted
2- Cystic glandular hyperplasia
3- Interval endometrium
of gestation. Another patient in group 2 conceived and delivered at 28 wk period of gestation.

**Discussion**

Because of antiproliferative endometrial effect, amenorrhoea and anovulation caused by mifepristone and ulipristal, these progesterone receptor modulators (PRMs) have been advocated for the treatment of myoma, endometriosis and dysfunctional uterine bleeding.\(^{10,14}\)

Mifepristone, as a treatment option for myoma, was first reported by Murphy et al in 1993.\(^{17}\) 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 dysmenorrhoea, menorrhagia and pelvic pressure, and reducing myoma volume by 26-57 per cent and inducing amenorrhoea in 41-100 per cent.\(^{15,18-25}\) Ultra low dose of 2.5 mg also resulted in appreciable symptomatic relief, modest 11 per cent reduction in uterine volume suggesting a possible dose effect with improvement in quality of life.\(^{26}\) Similar results with ulipristal (5-10 mg) have been reported with 91-92 per cent reduction in menstrual blood loss, amenorrhoea rates of 73-82 per cent, 12-21 per cent reduction in myoma volume.\(^{10}\)

In the present study, 10 mg mifepristone was found to be as effective as 25 mg in relieving menorrhagia, pain and other myoma related symptoms, although size reduction was more with 25 mg dose, these effects being comparable to other studies of 3 months duration,\(^{15,18-19,24}\) though more reductions have been reported in studies of longer duration.\(^{20-22,25}\) Effect on single myoma was similar with both doses (about 24% reduction), but added volume reduction in multiple myomas was greater with higher dose. Similar results have been documented earlier.\(^{12}\) Improvement in symptoms was noted as early as in the first month of therapy as also reported in another study.\(^{24}\) After stopping treatment, symptomatic relief persisted till three months. At three months post-treatment follow up, PBAC increased but not to the initial levels, though uterine volume further reduced. Similar residual improvement has been reported in an earlier study, where authors have also reported notable clinical improvement persisting in most patients one year after stopping treatment even though fibroids reached their pre-treatment size. This residual effect might be due to some time taken for the normalization of the progesterone receptors.\(^{25}\) Two patients conceived after stopping treatment, indicating that fertility resumes soon after stopping mifepristone.

Despite several studies done on mifepristone in myomas, only one study has reported effects on uterine blood flow which reduced up to 40 per cent, as determined by increase in resistive index with 25 mg dose, however, the number of patients was limited.\(^{18}\) In the present study, there was increase in all Doppler indices implying increased resistance to blood flow with treatment.

In the present study, the increase in endometrial thickness seen might be due to unopposed oestrogenic effect on the endometrium by mifepristone.\(^{24}\) But once the treatment was stopped, the endometrial thickness normalized. This is also highlighted in other studies.\(^{14,27}\)

Mifepristone is well tolerated drug with no serious adverse effects.\(^{14}\) Biochemical hypothyroidism has been reported with chronic administration.\(^{28}\) Common side effects reported are mild hot flushes seen in 10-38 per cent patients with no correlation to dose,\(^{25,29}\) fatigue in 8-12 per cent, and increase in liver transaminases in 4-7 per cent. In our study, only one patient discontinued treatment within one week due to allergic reaction, other side effects seen were mild.

In all previous studies with low dose mifepristone, there was a concern of endometrial hyperplasia which was documented in 28 per cent cases treated with 5-10 mg mifepristone for six months,\(^{20}\) which decreased to 14 per cent when reviewed, as many of the hyperplasias were actually cystic glandular dilatation.\(^{21,30}\) The endometrial changes specific to progesterone receptor modulators have been now designated as progesterone receptor modulator- associated endometrial changes (PAEC) which include cystic dilatation of glands with mixed oestrogenic (mitotic) and progestogenic (secretory) features, non-synchronous endometrium, pseudostratification of epithelium, pseudo-decidualized stroma, abnormal, dilated thin blood vessels with no evidence of atypical hyperplasia.\(^{31}\) Despite paucity of mitoses, PAEC may be mistaken for endometrial hyperplasia. In our study, endometrial histology at the end of therapy did not show any complex hyperplasia or atypia.

None of the patients in the present study had heavy bleeding during therapy. In a one-year study, no severe
bleeding was reported during treatment\textsuperscript{21}. Bagaria \textit{et al}\textsuperscript{24} suggested starting mifepristone from day 1-3 in early follicular phase so that it starts acting before the development of dominant follicle otherwise, it leads to collapse of dominant follicle and withdraw bleeding.

In a six months study with 2.5 mg daily mifepristone, there was no further reduction in uterine volume or relief in menorrhagia after 3 months. Amenorrhea rates reduced from 65 per cent at three months to 32 per cent at six months\textsuperscript{24}. In another study of 12 months duration, no further volume reduction was seen after six months and increased rates of breakthrough bleeding or spotting was reported\textsuperscript{15}. Besides, intermittent administration has been suggested for long term mifepristone use, with treatment duration of 3-4 months followed by an off-drug interval till menstruation occurred\textsuperscript{21}. Though it is now known that endometrial thickening with more than three months treatment is due to cystic dilatation and not due to hyperplasia, yet intermittent therapy would be more reassuring to the treating clinicians.

The strengths of our study were adequate sample size for statistically valid results and inclusion of Doppler parameters. Limitations of the study were not using PAEC to classify endometrial histopathology.

In future, studies may be planned to assess effect of preoperative mifepristone on surgical planes and ease of surgery, degeneration of myomas and blood loss.

In conclusion, our results showed that mifepristone (10 and 25 mg) led to symptomatic relief in patients with myoma with more than 90 per cent reduction in menstrual blood loss. However, 25 mg dose had significantly greater reduction in overall myoma size as well as in multiple myomas. Endometrial changes specific to progesterone receptor modulator occurred but there was no evidence of atypia. Amenorrhea developed in 90-95 per cent patients which was reversible. Mifepristone can be a reasonable choice especially in perimenopausal women in whom myomas would regress after menopause and unmarried patients who want to avoid surgery. Although its use as a primary medical therapy is limited due to recurrence after stopping treatment, it can be used as a preoperative adjunct, especially in patients with pre-operative severe anaemia, large fibroids, where surgery is technically difficult or where leiomyoma are unreatsectable. In addition, some women undergoing hysterectomy will benefit from a less invasive vaginal rather than an abdominal procedure.

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Conflict of interests: Last author (JT) is presently working as Assistant Editor of IJMR. Other authors declare that they have no conflict of interest.

References


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