e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(2); 197-201

Original Research Article

Role of Mifepristone in the Management of Uterine Fibroid: A Hospital Based Prospective Study

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Received: 05-01-2024 / Revised: 13-01-2024 / Accepted: 30-01-2024
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Conflict of interest: Nil

Abstract:

Background: Uterine fibroids are the most common benign tumors of uterus in the reproductive age group. Symptoms of fibroid may vary from women to women with most common symptom being heavy menstrual bleeding.

Methods: This is a hospital based prospective interventional study carried out in department of obstetrics and gynaecology department, Patna medical college and hospital Patna from July 2022 to June 2023.The aim of the study was to assess the effectiveness of tab. mifepristone on reducing several symptoms related to fibroid uterus. Mifepristone 50 mg was advised on alternate day for 3 months and the result was assessed.

Result: It was seen that mifepristone was very effective in reducing the mean PBAC score from baseline of 234.2 to 16.47 at the end of third month. Mean VAS score reduced from baseline of 5.61 to 2.26 at the end of third month. Mean fibroid volume reduced from 286.45 to 42.32 at the end of third month. Mean haemoglobin levels increased from 8.2gm/dl to 11.2 gm/dl.

Conclusion: Mifepristone has proved to be very effective in management of uterine fibroid .It has shown a significant decrease in uterine fibroid size, increase in haemoglobin levels, decrease in heavy menstrual bleeding.

Keywords: Mifepristone, Management, Uterine fibroid.

Introduction

Fibroids are benign, monoclonal tumor of the smooth muscle cells of the myometrium and contains large number of extracellular matrix composed of collagen, elastin, fibronectin ,and proteoglycan. [1]

These are the most common benign tumor which are found in women in reproductive age group. The prevalence of fibroid cases registered to gynaecological outdoor department are from 10-20%. Several studies have shown that approximately 76% females in their premenopausal phase will have uterine fibroid on histological examination [2]. The incidence of fibroid increases with age, 4.3 per 1000 woman-years for 25 to 29 years old and 22.5 for 40 to 44 years old. Exposure to endogenous hormones for prolonged period as found in early menarche, late menopause [3]. First degree relatives of women with fibroid have a 2.5 times higher chance of developing fibroid in future [4]. Other risk factors include increase in the average age of conception, ethnicity, body mass index, diet rich in beef and other red meat. Abnormal uterine bleeding is the most common symptom seen in these patients. The commonest symptom being heavy menstrual bleeding in around 50% cases. Other symptoms include other symptoms include other symptoms include other symptoms include Intramural fibroid are the commonest variety. Diagnosis is generally made on clinical examination of the patient and confirmed by ultrasonography. Fibroids are almost never fatal, but they may cause morbidity and significantly affect the quality of life [5]. Treatment varies from patient to patient depending upon the symptoms and future fertility expectations of a women. Medical management is given for symptomatic relief and to reduce the fibroid size. Definitive treatment is always surgery and accounts for overall 40% hysterectomies done in pre-menopausal females [6]. Progesterone plays a very important role in the pathogenesis of fibroids which have increased progesterone receptors A and B as compared to normal myometrial cells [7]. Mitotic activity is very high in fibroids at the peak of progesterone production [8]. Progesterone upregulates the expression of PCNA and EGF in fibroid cells [9]. It increases the expression of Bcl-

2 protein, and decreases the expression of TNF alpha leading to overall decrease in apoptosis.

Mifepristone is a progesterone receptor modulator with antagonistic properties along with glucocorticoid activities. A prospective, randomized controlled trial of mifepristone treatment found a 48% decrease in the mean uterine volume after 6 months [10]. It causes reduction in progesterone receptor number. It causes anovulation leading to amenorrhoea, inhibit steroid depended growth of fibroid. It decreases stromal VEGF leading to decreased blood flow thus relieving symptoms of menorrhagia [11].

Materials and Methods

This is a hospital based prospective interventional study was carried out in the department of obstetrics and gynaecology, Patna Medical College and hospital during the period of July 2022 to June 2023.Permission was obtained from the from the institutional ethical committee. Patients were selected from Gynaecology outpatient department. Written informed consent was obtained from all patients for clinical examination and for further advice. Detailed history taking was done. A complete general and gynaecological examination was done. Routine blood investigations including CBC, LFT, KFT and ultrasonography of lower abdomen for uterus and adnexa was advised.

Patients included in this study were advised Tab Mifepristone 50 mg alternate days for 3 months. Follow up was done at 1 month and 3 months of starting medication. During follow up visit, patient were assessed to look for relief in symptom through PBAC (Pictorial Blood Assessment Chart) score and VAS (Visual analogue Scheme) score. Any adverse effects of medication if experienced by the patient was noted.

PBAC score is a semi quantitative method used for assessment of menstrual blood loss and usually done by counting the number of soaked pads, amount of soakage, presence of clots and episodes of flooding (12). Bleeding was considered menorrhagia when the score was more than 100.

VAS score is done to assess dysmenorrhoea, abdominal pain, backache and dyspareunia. Severity of pain was noted as told by the patient on the scale from 0 to 10 before and after the treatment.

Ultrasonography was done to assess the size, location, number and the type of fibroid and to rule out any other pelvic pathology.

Volume of fibroid was calculated by Ellipsoid method and the formula V = 0.5233(D1*D2*D3) was used. D1, D2 and D3 denotes longitudinal, transverse and cross sectional diameters of the fibroid. In case of multiple fibroids volume of each fibroid is added for total fibroid volume estimation.

A total of 70 patients were included in this study.

Inclusion Criteria

- Women between 25-50 years
- Symptomatic patients
- Fibroid size <15 cm on ultrasonography

Exclusion Criteria

- Any active genito-pelvic infection
- Derranged LFT AND KFT
- On per abdominal examination uterus >20 weeks.
- Fibroid size >15 cms on ultrasonography.
- Any history of intake of hormonal medications in past 3 months.
- Untreated abnormal pap smear
- Hb<6.0gm/dl
- Currently breastfeeding
- Menopausal
- Plan for pregnancy in near future.

Statistical Analysis

Data collection was done in Microsoft Excel and analysed using SPSS software. Statistical analysis was made using different statistical methods.

Results

Table 1 shows the age distribution of patients. Total 70 patients were included in the study among which 63 patients were followed for 3 months and 7 patients did not come for follow up. Majority of patients were from premenopausal age group .4 patients were in age group 25-35 years,16 patients were in age group of 36-40 years,34 patients were in age group of 41-45 years and 9 patients were in the age group of 46-50 years.

Table 1: Depicting age distribution of fibroid cases.

Age range	Number	Percentage
25-35	4	6.4
36-40	16	25.4
41-45	34	54.0
46-50	9	14.2
Total	63	100

Figure 2 shows the body mass index distribution of the study population. Mean body mass index was 24.6% kg/m2 and the range was between 18-35 kg/m2.Most of the patients were in normal range of BMI.49.6% patients were in range of 18-25 while others had high BMI of >25.

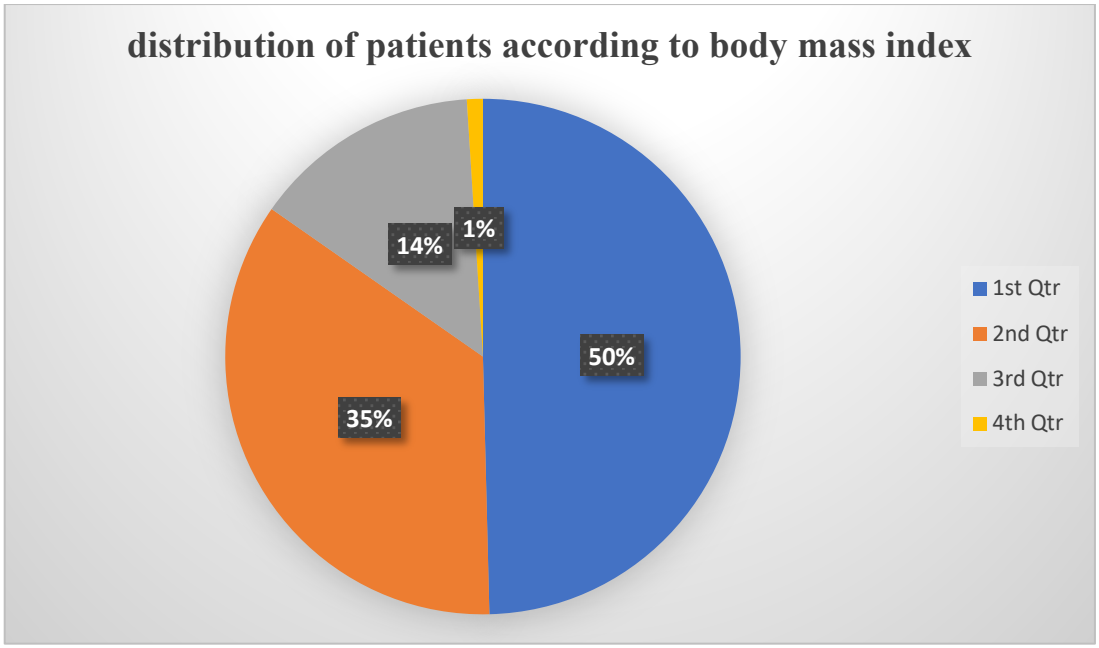

Figure 1: Distribution of patients according to body mass index

Table 3 shows presenting symptoms distribution among the study population with most common symptom being heavy menstrual bleeding. 86% patient complaint of heavy menstrual bleeding. 59% patients suffered from pain related symptoms like dysmenorrhoea, lower abdominal pain, backpain. 2% patient complaint of abdominal lump.

Complaint of patients	Percentage
Heavy menstrual bleeding	86
Pain related symptoms	59
Abdominal lump	2

Figure 4: Shows the distribution based on fibroid type among the study population. Most common was submucosal fibroid that is 7.8%.68.1% were intramural fibroids, 24.1% were sub-serosal fibroids.78% patients had single fibroid and 22% had multiple fibroids.

Type of fibroid	Percentage distribution
Submucosal	7.8
Intramural	68.1
Subserosal	24.1
Total	100

Figure 5: Shows the effect of mifepristone on PBAC score

Period	Mean	SD	Median	Minimum	Maximum	P value
Baseline	234.2	45.66	218	71	274	
One month	38.92	28.28	33	23	209	<0.0001
3 months	16.47	22.34	16	11	156	<0.0001

Figure 5 shows the effect of mifepristone on PBAC score which indicates the blood loss. Baseline PBAC score was 234.2. At the end of first month it reduced to 38.92 and at 3 month it was 16.47 which is shows significant reduction in blood loss.

Figure 6: Shows the effect of mifepristone on VAS score.

Period	Mean	SD	Median	Minimum	Maximum	P value
Baseline	5.61	2.84	8	0	10	
3 months	2.26	1.86	3	0	6	<0.0001

Figure 6 shows the effect of mifepristone on visual analogue scale .Baseline score was 5.61 which reduced to 2.26 at the end of third month.

The reduction in PBAC score and VAS score shows the overall improvement in the quality of life of the patient after treatment.

Figure 7: Shows the effect of mifepristone on fibroid volume

Period	Mean	SD	Median	Minimum	Maximum	P value
Baseline	286.45	1747.3	40.34	4.72	16724	
3 months	42.32	58.66	18.66	2	680.31	<0.0001

Figure 8: Shows the effect of mifepristone on haemoglobin levels

Period	Mean haemoglobin value
Baseline	8.2gms%
3 months	11.2gms%

Figure 8 shows the effect of mifepristone on haemoglobin levels .Baseline mean haemoglobin level was 8.2 gms% which raised to 11.2 gms% and thus decreasing the anemia related symptoms like fatigue,s hortness of breath, palpitations, loss of appetite etc

Discussion

SPRMs have shown a promising results in several studies. Several drugs are included in this class such as mifepristone, ulipristal acetate and asoprisnil[13,14]. Murphy et al in 1993 used mifespristone for the first time in the treatment of fibroid uterus. Later on, several studies were done all across the world comparing the results of different doses of mifepristone use and for varying time duration. Mifepristone doses vary from 2.5 mg to 50 mg per day. Eisinger et al.in a 17 case pilot study used 2.5mg mifepristone and observed a lesser reduction in the size of fibroid but a similar quality of life in comparison with 5mg(15).Murphy et al compared different doses of mifepristone and concluded that 25mg to be the most effective dose in reducing the fibroid size. Heavy menstrual bleeding is the chief complain of most of the women coming to seek treatment because it hampers the overall quality of life. In our study heavy menstrual bleeding constituted 86%. S. V. Nachiketha et al (2019) found out that patients with heavy menstrual bleeding was 84.7% and pain related symptoms were 67.3%.Similarly study conducted by Vinod Raghav et al states that patient with heavy menstrual bleeding constituted 86%, abdominal pain 28%, dysmenorrhoea 18%, dysparunia 8%.(16). S. V. Nachiketha et al mentioned baseline,1 month and 3 month PBAC score be 212.61, 35.28, and 20.39 respectively. Results were comparable with the study of kulshrestha et al that is baseline, 1 month, and 3 month PBAC score be 289.2,44.9, and 19.8 respectively in patients who were given 25mg daily for 3 months. In our study most of the patients had amenorrhoea while on medication. In present study the total reduction in fibroid volume was 39% percent which was comparable with other studies. S. V. Nachiketha et al mentioned 36% reduction in volume with 25 mg mifepristone. Raise in hemoglobin level was 2.8gms% at the end of treatment.

Conclusion

Mifepristone has proved to be a very effective in the management of uterine fibroid. It has shown a significant decrease in the volume of fibroid along with increase in haemoglobin levels and ,decrease in PBAC score and VAS score. The study have shown no significant adverse effects due to medication.

References

1. Whiteman MK, Hillis SD, Jamieson DJ, et al. Inpatient hysterectomy surveillance in the United States, 2000-2004. Am J Obstet Gyecol 2008;(1):34.e1-e7.
2. Cramer SF, Patel A. The frequency of uterine leiomyomas. Am J Clinic Pathol. 1990; 94(4): 435-8.
3. Marshall LM, Spiegelman D, Goldman MB, et al .A prospective study of reproductive factors and oral contraceptives use in relation to the risk of uterine leiomyomata. FertilSteril 1998;70(3):432-439.
4. Vikhlyaeva EM, Khodzhaeva ZS, Fantschenko ND, Familial predisposition to uterine leiomyomas. Int J Gynaecol Obstet 1995;51(2):127-131.
5. Rowe MK, Kanouse DE, Mittman BS, et al. Quality of life among women undergoing hysterectomies. obstetgyecol 1999;93(6):915-921.
6. Carlson KJ, Nichols DH, Schiff I. Indications for hysterectomy. New Eng Med. 1993; 328(12): 856-60.
7. Englund K, Blanck A, Gustavsson I, et al. Sex steroid receptors in human myometrium and fibroids: changes during the menstrual cycle and gonadotropin-releasing hormone treatment. J Clin Endocrinol Metab. 1998;8 3(11): 4092-4096.
8. Kawaguchi K, FujiiS, Konishi I, et al. Mitotic activity in uterine leiomyomas during the menstrual cycle. Am J Obstet Gynecol 1989; 160(3): 637-641.
9. Maruo T, Matsuo H, Samoto T, Shimomura Y, Kurachi O, Gao Z, Wang Y, Spitz IM, Johansson E. Effects of progesterone on uterine leiomyoma growth and apoptosis. Ster. 2000; 65(10-11): 585-92.
10. Fiscella K, Eisinger SH, Meldrum S, et al. Effect of mifepristone for symptomatic leiomyomata on quality of life and uterine size: a ran-

domized controlled trial. Obstet Gynecol 2006;108(6):1381-1387.
11. Kulshrestha V, Kriplani A, Agarwal N, Sareen N, Garg P, Hari S, Thulkar J. Low dose mifetristone in medical management of uterine leiomyoma -an experience from a tertiary care hospital from north India. Indian J Med Res. 2013;137(6):1154.;137(6):1154.
12. Narvekar N, Critchley HO, Cheng L, Baird DT. Mifepristone-induced amenorrhoea is associated with an increase in microvessel density and glucocorticoid receptor and a decrease in stromal vascular endothelial growth factor. Human Reproduct. 2006; 21(9): 2312-8.
13. N. Chabbert-Buffet, G. Meduri, P. Bouchard, and I. M. Spitz, selective progesterone receptor modulators and progesterone antagonists: mechanisms of action and clinical applications, Human Reproduction Update, 2005;11(3): 293-307.
14. I. M. Spitz, Mifepristone: where do we come from and where are we going? Clinical development over a quarter of a century, Contraception, 2010; 82(5): 442-452.
15. S. H. Eisinger, J Fiscella, T. Bonfiglio, S. Meldrum, and K. Fiscella, Open-label study of ultra-low-dose mifepristone for the treatment of uterine leiomyomata, European Journal of Obstetrics Gynecolgy and Reproductive Biology, 2009; 146(2): 215-218.
16. Angomchanu R, Kapur AN. Role of mifepristone in conservative management of fibroids:fc4. 05.Bjog: An International Journal of Obstetrics and Gynaecol. 2014; 121:43.