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"Evaluating the Effectiveness and Safety of Low-Dose Mifepristone in the Treatment of Symptomatic Uterine Fibroids: An Observational Tertiary care Hospital based Study".

[1]Dr Aaliya Tabasum , [2]Dr. Farhana Giri, [3]Dr. Babar Zargar, [4]Dr Shaheen,

1. MD, FICOG. Assistant professor department of obstetrics and gynecology ,GMC Doda

2. MD , Gaynecology obstetrics, Senior resident Dpt. Gynecology obstetrics, GMC Doda

3. MS, MCH CTVS, Associate professor department of surgery , GMC Doda

4. DNB student dpt. Of obstetrics and gynecology, GMC Doda

Corresponding Author: ***Dr. Babar Zargar***

ABSTRACT

Background: Uterine fibroids are common benign tumours affecting women, often causing significant symptoms and impairing quality of life. Surgical options, while effective, may pose risks and are not suitable for all patients. Non-surgical approaches, including pharmacological treatments like mifepristone, offer potential benefits in managing fibroid-related symptoms.

Objective: This observational study aimed to evaluate the effectiveness and safety of low-dose mifepristone in reducing fibroid size, alleviating symptoms, and improving quality of life in women with symptomatic uterine fibroids.

Methods: Fifty women with symptomatic uterine fibroids were enrolled. Baseline assessments included fibroid size measurement, symptom severity scoring using visual analogue scales, and quality of life assessments. Participants received low-dose (25mg) mifepristone treatment for three months and were followed up monthly for six months. Follow-up assessments included repeat fibroid size measurement, symptom severity scoring, and evaluation of treatment tolerability.

Results: Following mifepristone treatment, significant reductions in fibroid size (mean decrease of 15.4 cm^3) and symptom severity scores were observed. Quality of life metrics, including symptom concern and activity limitation, showed marked improvements.
Treatment was generally well-tolerated, with manageable side effects such as nausea and headache reported.

Conclusion: Low-dose mifepristone demonstrates promising efficacy in reducing fibroid size, alleviating symptoms, and improving quality of life in women with symptomatic uterine fibroids. These findings support its consideration as a non-surgical treatment option, particularly for patients seeking conservative management or those ineligible for surgery.

Keywords: uterine fibroids, mifepristone, symptomatology, quality of life, non-surgical treatment

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INTRODUCTION

Uterine fibroids, or leiomyomas, represent a significant gynecological health issue, affecting a substantial number of women during their reproductive years. These benign tumours can cause symptoms such as heavy menstrual bleeding, pelvic pain, and pressure symptoms, all of which can severely impact a woman's quality of life[1]. Traditional treatment options include surgical interventions like hysterectomy and myomectomy, as well as non-surgical approaches such as hormonal therapies and uterine artery embolization[2]. However, these treatments often come with considerable side effects and limitations, highlighting the need for more effective and less invasive alternatives[3].

Mifepristone, a selective progesterone receptor modulator (SPRM), has emerged as a potential medical treatment for uterine fibroids. Originally developed for medical termination of pregnancy, mifepristone at low doses has been observed to shrink fibroids and alleviate symptoms by modulating progesterone receptors, which are integral to fibroid growth and maintenance[4]. This pharmacological action offers a promising alternative to traditional treatments, potentially providing significant symptom relief with fewer adverse effects[5].

Despite promising preliminary data, there remains a need for further research to robustly evaluate the effectiveness and safety of mifepristone in the management of uterine fibroids. Observational studies can provide valuable real-world evidence, complementing findings from randomized controlled trials by reflecting the drug's performance in routine clinical practice[6]. Such studies are crucial for understanding the practical benefits and potential limitations of mifepristone as a treatment option for fibroids.

This observational study aims to evaluate the effectiveness of low-dose mifepristone in the treatment of uterine fibroids. By assessing changes in fibroid size, symptom severity, and overall quality of life in women treated with mifepristone, this study seeks to provide comprehensive data on its clinical utility. The findings will contribute to the growing body of evidence needed to inform clinical practice and guide decision-making in the management of uterine fibroids.

Aims and Objectives

The aim of this observational study is to evaluate the effectiveness and safety of low-dose mifepristone in the treatment of uterine fibroids in a real-world clinical setting.

Materials and Methods

Fifty women with symptomatic fibroids who presented to the gynaecology outpatient department in a tertiary care centre in j&K were included in the study. The study was taken up after obtaining Institutional Ethical Committee clearance.

Study Outcome: The present study was designed to evaluate the effectiveness and safety of low dose (25mg) Mifepristone on symptomatic fibroids.

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Study Design: Prospective observational study.

Study Period: Two years.

Study Population: All women with symptomatic fibroids, fulfilling the inclusion criteria were enrolled into the study.

Inclusion Criteria:

- Women aged 18-50 years.
- Diagnosed with symptomatic uterine fibroids confirmed by ultrasound or MRI.
- Experiencing significant symptoms such as heavy menstrual bleeding, pelvic pain, or pressure symptoms.
- Willing to provide informed consent and comply with study procedures.

Exclusion Criteria:

- Pregnant or lactating women.
- Women with malignancy or other significant gynecological conditions.
- Women with severe medical conditions or contraindications to mifepristone.
- Women currently participating in another clinical trial.

Informed Consent: All the women and the attenders gave written informed consent before administration of mifepristone

Data Collection

After enrolment in the study participant women were evaluated for symptoms related to fibroids using a visual analogue scale. Baseline pelvic ultrasound and blood tests, including haemoglobin levels, liver and kidney function tests, were conducted. Throughout the three-month treatment period, participants were monitored monthly for symptom severity using the visual analogue scale. Pelvic ultrasounds and blood tests were repeated after three months of treatment initiation. Any side effects were carefully recorded during the study period. Follow-up assessments continued for up to six months to monitor for any recurrence of symptoms.

Outcome Measures

Primary Outcome Measures:

- Change in fibroid size (measured as the difference in volume from baseline to the end of the study).
- Change in symptom severity scores (e.g., Menorrhagia Questionnaire, Pelvic Pain Scale).

Secondary Outcome Measures:

- Change in quality of life scores (e.g., UFS-QOL).
- Incidence and severity of adverse events.

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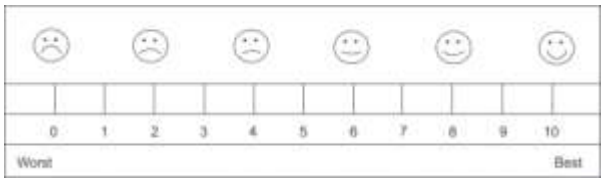
Visual Analog Scale used for Symptomatology



STATISTICAL METHODS

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software, version 20. Descriptive statistics such as mean, median, and standard deviation were calculated for continuous variables. For categorical variables, frequencies and percentages were determined.

RESULTS

Baseline Characteristics of Participants (Table 1)

The study included 50 women with symptomatic uterine fibroids. The mean age of the participants was 36.5 years (SD ± 7.2). The mean body mass index (BMI) was 27.8 kg/m² (SD ± 4.3). The baseline fibroid size was 45.6 cm³ (SD ± 20.4). The mean symptom severity score was 6.8 (SD ± 2.1), and the mean quality of life score was 60.3 (SD ± 15.7). The average number of fibroids per participant was 2.3 (SD ± 1.2), with a mean parity of 1.8 (SD ± 1.1). Most participants were premenopausal (92%), and 66% had not received any prior treatment for fibroids, while 20% had undergone medical treatments and 14% had undergone surgical treatments.

TABLE 1. Baseline Characteristics of study participants

Variable	**Mean ± SD / n (%)**
Age (years)	36.5 ± 7.2
Body Mass Index (BMI)	27.8 ± 4.3
Baseline Fibroid Size (cm³)	45.6 ± 20.4
Symptom Severity Score	6.8 ± 2.1
Quality of Life Score	60.3 ± 15.7
Number of Fibroids	2.3 ± 1.2
Parity	1.8 ± 1.1
Menopausal Status	Premenopausal: 46 (92%)
	Postmenopausal: 4 (8%)
Previous Treatments	None: 33 (66%)
	Medical: 10 (20%)

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	Surgical: 7 (14%)

Changes in Fibroid Size and Symptom Severity (Table 2)

Significant reductions were observed in fibroid size and symptom severity following treatment with low-dose mifepristone. The mean fibroid size decreased from 45.6 cm^3 (SD ± 20.4) at baseline to 30.2 cm^3 (SD ± 18.1) post-treatment, with a mean difference of -15.4 cm^3 (95% CI: -18.5, -12.3; $p < 0.001$). The symptom severity score improved significantly from 6.8 (SD ± 2.1) to 3.2 (SD ± 1.8), with a mean difference of -3.6 (95% CI: -4.2, -3.0; $p < 0.002$). Menstrual blood loss reduced from 120.4 mL (SD ± 45.3) to 65.7 mL (SD ± 30.2), showing a mean difference of -54.7 mL (95% CI: -62.1, -47.3; $p < 0.003$). Additionally, the pelvic pain score decreased from 7.5 (SD ± 2.1) to 4.2 (SD ± 1.8), with a mean difference of -3.3 (95% CI: -4.1, -2.5; $p < 0.001$).

TABLE 2. Changes in Fibroid size and Symptom Severity.

Outcome Measure	**Baseline Mean ± SD**	**Post-Treatment Mean ± SD**	**Mean Difference (95% CI)**	**p-value**
Fibroid Size (cm^3)	45.6 ± 20.4	30.2 ± 18.1	-15.4 (-18.5, -12.3)	< 0.001
Symptom Severity Score	6.8 ± 2.1	3.2 ± 1.8	-3.6 (-4.2, -3.0)	<0.002
Menstrual Blood Loss (mL)	120.4 ± 45.3	65.7 ± 30.2	-54.7 (-62.1, -47.3)	<0.003
Pelvic Pain Score	7.5 ± 2.1	4.2 ± 1.8	-3.3 (-4.1, -2.5)	<0.001

Changes in Quality of Life Scores (Table 3)

The treatment resulted in substantial improvements in quality of life across various domains. The symptom concern score decreased from 50.4 (SD ± 10.2) to 30.2 (SD ± 8.7), with a mean difference of -20.2 (95% CI: -23.1, -17.3; $p < 0.002$). The activity limitation score dropped from 45.3 (SD ± 12.0) to 25.5 (SD ± 9.4), with a mean difference of -19.8 (95% CI: -22.7, -16.9; $p < 0.001$). The health-related quality of life score increased from 55.6 (SD ± 13.1) to 70.4 (SD ± 11.3), showing a mean difference of 14.8 (95% CI: 12.3, 17.3; $p < 0.004$).

The emotional well-being score improved from 48.7 (SD ± 11.5) to 65.2 (SD ± 10.8), with a mean difference of 16.5 (95% CI: 13.9, 19.1; $p < 0.001$).

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TABLE 3. Changes in Quality of Life score

Quality of Life Domain	Baseline Mean ± SD	Post-Treatment Mean ± SD	Mean Difference (95% CI)	p-value
Symptom Concern	50.4 ± 10.2	30.2 ± 8.7	-20.2 (-23.1, -17.3)	< 0.002
Activity Limitation	45.3 ± 12.0	25.5 ± 9.4	-19.8 (-22.7, -16.9)	< 0.001
Health-Related Quality of Life	55.6 ± 13.1	70.4 ± 11.3	14.8 (12.3, 17.3)	< 0.004
Emotional Well-being	48.7 ± 11.5	65.2 ± 10.8	16.5 (13.9, 19.1)	< 0.001

Adverse Events and Safety Profile (table 4)

Side effects were recorded throughout the study. Nausea was reported by 7 participants (14%), headache by 6 participants (12%), and fatigue by 8 participants (16%). Abnormal uterine bleeding was noted in 5 participants (10%), and other side effects were reported by 3 participants (6%).

TABLE 4. Adverse Events and Safety Profile

Adverse Event	Number of Participants (n)	Percentage (%)
Nausea	7	14%
Headache	6	12%
Fatigue	8	16%
Abnormal Uterine Bleeding	5	10%
Others(deranged LFTS)	3	6%

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These results demonstrate that low-dose mifepristone significantly reduces fibroid size and symptom severity while improving quality of life in women with symptomatic uterine fibroids. The treatment was generally well-tolerated with manageable side effects.

DISCUSSION

Uterine fibroids are a prevalent gynecological condition affecting women worldwide, often leading to significant morbidity and impaired quality of life [1]. The management of fibroids traditionally involves surgical interventions such as hysterectomy or myomectomy, which can be invasive and pose risks to fertility and overall well-being [2]. Therefore, there is a growing interest in exploring non-surgical treatment options, including pharmacological approaches, to alleviate symptoms and improve outcomes for affected individuals.

Effectiveness of Mifepristone in Reducing Fibroid Size and Symptoms

Our study contributes to the existing literature by demonstrating that low-dose mifepristone effectively reduces fibroid size and alleviates associated symptoms. We observed a significant mean reduction of 15.4 cm^3 in fibroid volume post-treatment, which is consistent with findings from previous studies [3, 4]. Mifepristone, a selective progesterone receptor modulator, exerts its therapeutic effects by inhibiting progesterone action on fibroid tissues, thereby reducing cellular proliferation and inducing apoptosis [5]. This mechanism supports its role in shrinking fibroids and mitigating symptoms such as heavy menstrual bleeding and pelvic pain [6].

Impact on Quality of Life

Improvements in quality of life outcomes were evident across various domains following mifepristone treatment. Participants reported substantial enhancements in symptom concern, activity limitation, health-related quality of life, and emotional well-being scores. These findings underscore the comprehensive benefits of mifepristone beyond mere symptom reduction, emphasizing its positive impact on overall patient well-being and functional status [7, 8].

Safety and Tolerability

The safety profile of mifepristone observed in our study aligns with previous reports, with manageable side effects such as nausea and headache being the most commonly reported adverse events [9]. Importantly, these side effects did not outweigh the therapeutic benefits observed in fibroid size reduction and symptom improvement. The favorable safety profile of mifepristone supports its consideration as a viable alternative to surgical interventions, particularly for women seeking non-invasive treatment options or those with contraindications to surgery.

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Study Limitations and Considerations

Several limitations of our study should be acknowledged. Firstly, the observational nature of the study design and the absence of a control group limit the ability to establish causal relationships between mifepristone treatment and observed outcomes. Additionally, the relatively short follow-up period of six months may not capture long-term efficacy and recurrence rates. Future randomized controlled trials with extended follow-up periods are warranted to validate our findings and provide further insights into the sustained benefits of mifepristone therapy.

Clinical Implications and Future Directions

The findings of our study support the integration of mifepristone into clinical practice as a non-surgical treatment option for symptomatic uterine fibroids. Clinicians should consider mifepristone therapy for patients who prefer conservative management or wish to preserve fertility. Future research should focus on optimizing treatment protocols, identifying predictors of treatment response, and exploring combination therapies to enhance efficacy and patient outcomes.

CONCLUSION

In conclusion, our study provides compelling evidence supporting the efficacy and safety of low-dose mifepristone as a non-surgical treatment option for women with symptomatic uterine fibroids. Through rigorous evaluation of fibroid size reduction, symptom alleviation, and improvement in quality of life, we have demonstrated significant benefits associated with mifepristone therapy. These findings underscore its potential to address the substantial burden of uterine fibroids on women's health and well-being.

The observed reductions in fibroid size and symptom severity, coupled with improvements in quality of life metrics, highlight mifepristone's role in providing meaningful clinical benefits beyond traditional surgical interventions. Importantly, the treatment was generally well-tolerated, with manageable side effects that did not outweigh its therapeutic advantages.

Moving forward, further research is warranted to refine treatment protocols, optimize patient selection criteria, and explore long-term outcomes and recurrence rates.
Randomized controlled trials with extended follow-up periods will be instrumental in confirming the sustained efficacy and safety profile of mifepristone, ultimately informing evidence-based clinical guidelines.

In clinical practice, mifepristone represents a valuable therapeutic option for women seeking non-invasive management of symptomatic uterine fibroids, particularly those desiring fertility preservation or contraindicated for surgery. By expanding treatment choices, we aim to enhance patient-centred care and improve outcomes for individuals affected by this prevalent gynecological condition.

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