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ORIGINAL RESEARCH

Role of Ullipristal in fibroid uterus - A Comparative study between Ullipristal, Mifepristone and Fibronorm

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ABSTRACT

Introduction- The frequency of uterine fibroids varies because the majority of patients have no symptoms; however, menorrhagia and iron deficiency anaemia, which can cause persistent fatigue, are the most common clinical features that prompt women to seek therapy. The present study was conducted to compare the effect of ullipristal, mifepristone and fibronorm in uterine fibroids.

Material and methods- The prospective cohort study was conducted at department of obstetrics and gynecology among 150 patients diagnosed with uterine fibroids who visited the outpatient clinic during the study period of one year.Group A were those who received ullipristal, group B received mifepristone and group C received fibronorm having 50 patients in each group. The outcome analyzed were mean age, loss of menstrual blood by Pictorial blood loss assessment chart (PBAC) and fibroid size and symptoms pre and post study.

Results – The mean age of patients in our study was between 35 to 45 years among three groups.The value of mean PBAC post study was 154.22±40.7 for group A, 134.23±38.5 for group B and 140.21±41.2 for group C and results were significant with p value 0.006. There was significant decrease in fibroid size and fibroid volume after the study among all the three group with p value <0.001.

Conclusion – Treatment of uterine fibroids by three drugs was associated with reduction in fibroid size, reduced blood loss and fibroid volume but ullipristal acetate was more beneficial in case of large size of fibroids.

Keywords – Fibroid Volume,Fibronorm, Mifepristone,Ullipristal,Uterine Fibroids, Uterus

INTRODUCTION

One of the most frequent benign uterine fibroids that affect women in the reproductive age range is uterine fibroids.[1] One possible presentation of these conditions is either fully asymptomatic (discovered by accident during an ultrasound for another purpose) or manifest as menorrhagia, pelvic mass, obstructive uropathy, anaemia due to blood loss, or infertility.[2] For certain patients, these symptoms could significantly lower their quality of life. Because most uterine fibroids are asymptomatic and go undiagnosed for years, their incidence varies. According to certain research, over 75% of women over 50 mayhave symptomatic or asymptomatic fibroids.It is estimated that between 25 and 30 percent of people have uterine fibroids that cause symptoms.[3]

Although the specific cause of fibroids is unknown, a number of factors, including genetic, hormonal, and biological ones, have been implicated in the disease's pathophysiology. nulliparity, obesity, and a younger menarche age are risk factors for fibroids.[4]

The most common method for diagnosing uterine fibroids is ultrasound examination, which typically reveals a well-defined hypoechoic lesion inside the myometrium with distinctive peripheral vascularity on Doppler testing. [5]

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There are currently anti-progesterones available for treating fibroids, mifepristone (a progesterone receptor antagonist) and ulipristal acetate (a selective progesterone receptor modulator) and fibronorm. Both have equal efficacy, but mifepristone is becoming more and more popular due to its lower cost.

With minimal impact on estradiol levels or anti-glucocorticoid activity, ulipristal acetate, a selective progesterone receptor modulator (SPRM), inhibits ovulation by acting on progesterone receptors in the myometrium and endometrium.[6] A three-month course of ulipristal acetate at doses ranging from 5 mg to 20 mg daily effectively lowers the amount of fibroid tumours and controls excessive bleeding.Mifepristone acts in multiple ways. It downregulates progesterone receptors, which is crucial, and binds strongly to the endometrial progesterone receptor. It also suppresses or postpones ovulation, which can result in amenorrhoea. It has also been proposed that lowering stromal VEGF and having a direct suppressive effect on the endometrial vasculature can help to minimize menstrual blood loss.Mifepristone is superior to GnRH analogue because it may be taken orally, has less side effects, and costs less.[7,8] A dietary supplement called Fibronorm is used to treat issues related to uterine fibroids. Its active constituents, tripterygiumwilfordii root extract, green tea extract, and vitamin D3, work together to lower the size of fibroid growth and relieve uterine fibroid symptoms.[9]

Hence the present study was conducted to compare the effect of ullipristal, mifepristone and fibronorm in uterine fibroids.

MATERIAL & METHODS

The prospective cohort study was conducted at department of obstetrics and gynecology among patients visited to outpatient clinic during the study period of one year. Ethical permission was taken from institutional ethical committee before the commencement of study. Informed consent was taken from each patient after explaining them the complete procedure of study.

Total 150 patients diagnosed with uterine fibroids and divided into three groups were included on the basis of eligibility criteria. Group A were those who received ullipristal, group B received mifepristone and group C received fibronorm.

Inclusion criteria- Women who had uterine volumes greater than 200 cm^3 and who presented with one or more symptomatic fibroids were chosen for this research.

Exclusion criteria- Patients with simultaneous adenomyosis or pregnancy, suspected adnexal masses, suspected cancer cases, severe anaemia (Hb <7g%), hepatic, renal, respiratory, or blood clotting diseases were excluded from the study.

In every case, a thorough history and demographic profile were recorded. Menstrual blood loss was measured by counting the number of soaked pads, the level of soakage, and the amount of clots that passed. Any prior instances of menorrhagia, dysmenorrhea, or dyspareunia were noted. A thorough systemic and general examination was conducted, then a gynecological examination. All patients underwent routine investigations such as complete blood counts and assessments of their liver, kidney, and heart functions. To determine the precise quantity and location of fibroids, a transvaginal ultrasound examination was performed. The outcome analyzed were mean age, loss of menstrual blood byPictorial blood loss assessment chart (PBAC)and fibroid size and symptoms pre and post study.

PBAC is an easy and quicker method for evaluating menstrual blood loss objectively. The overall score is determined by summing together all of the scores for the sanitary napkins used during the menstrual cycle using the scales that are outlined below. The patients were instructed to keep a menstruation journal in which they would note the total number of days they had bled, the quantity of sanitary pads they had used, the level of soaking of each pad, and the quantity and size of clots they had passed. They were also asked to use certain sanitary napkins with comparable absorbent capabilities. The number of sanitary pads used during the course of a 24-hour period was counted. At the conclusion of the month, the total score was determined by adding the scores for each day. Sanitary napkins that had been soaked were scored as follows: 1 for faintly stained, 5 for substantially dirty, and 20 for thoroughly saturated pads. Small clots received a score of 1, and big clots received a score of 5. The entire range of possible scores depended entirely on the quantitative and qualitative level of menstrual bleeding. >80 mL of menstrual blood loss is considered abnormal PBAC score ≥100, which is correlated with menorrhagia.

Software from SPSS 25.0 was used to tabulate and analyse the results. Charts and graphs were created using Microsoft Word and Excel.

RESULTS

The mean age of patients in group A was 38.5±5.6 years, group B was 39.46± 4.7 years and in group C was 37.42±6.3 years as shown in table 1. Menstrual blood loss assessment was done by using Pictorial blood loss assessment chart. The value of mean PBAC pre study was 263.79±48.3 for group A, 238.34±49.5 for group B and 247.56±45.9 for group C and results were significant with p value 0.003. The value of mean PBAC post study was 154.22±40.7 for group A, 134.23±38.5 for group B and 140.21±41.2 for group C and results were significant with p value 0.006 as shown in table 2.

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There was significant decrease in fibroid size and fibroid volume after the study among all the three group with p value <0.001 as shown in table 3 and graph 1.

Table 1:Comparison of mean age among three groups

Variable	Group A	Group B	Group C
Mean age (years)	38.5±5.6	39.46± 4.7	37.42±6.3

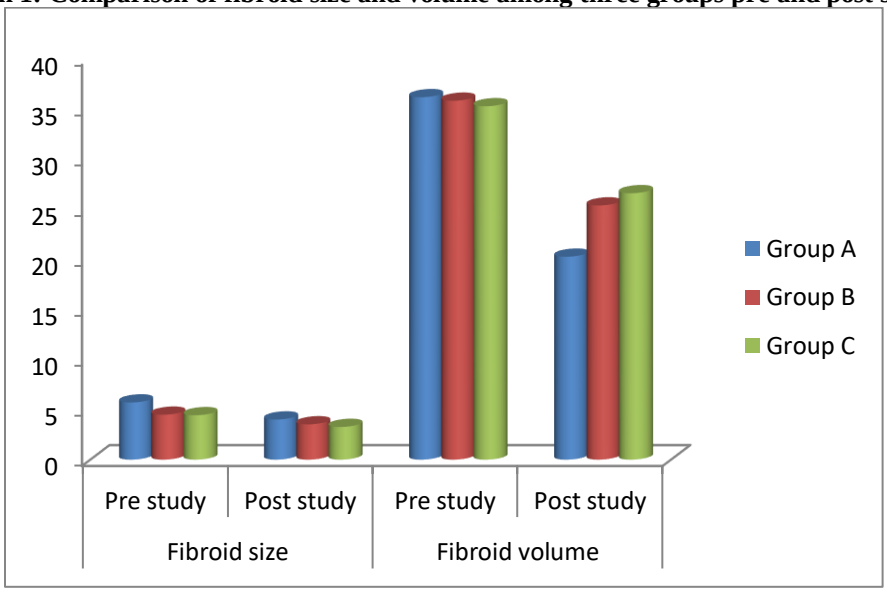
Table 2: Comparison of menstrual blood loss assessment among three group pre and post study.

Variable	Group A	Group B	Group C	P value
Pre study	263.79±48.3	238.34±49.5	247.56±45.9	0.003
Post study	154.22±40.7	134.23±38.5	140.21±41.2	0.006

Table 3: Comparison of fibroid size and volume among three groups pre and post study.

Variable		Group A	Group B	Group C	P value
Fibroid size	Pre study	5.7±1.2	4.48±0.9	4.43±1.2	<0.001
	Post study	4.0±0.6	3.52±0.8	3.26±1.1	0.006
Fibroid volume	Pre study	36.13±13.21	35.78±13.19	35.23±12.67	0.128
	Post study	20.23±11.78	25.34±12.89	26.56±10.98	<0.001

Graph 1: Comparison of fibroid size and volume among three groups pre and post study.



DISCUSSION

Due to their antiproliferative effects on the endometrium and myometrium, medications such as mifepristone, ulipristal acetate, and fibronorm have been used to treat dysfunctional uterine haemorrhage and uterine myomas.[10] Mifepristone was initially reported to be used in 1993 by Murphy et al. to treat uterine fibroids. They demonstrated that uterine fibroids were hormone-dependent tumours that were dependent on steroids and had progesterone and oestrogen receptors (ER and PR).[11]It was suggested that antiprogesterone could shrink uterine fibroids by either preventing progesterone's function or interfering with estrogen's ability to act on fibroids.

In the present study three groups of 50 patients in each were made and results were noted before and after the study of one year duration.

The mean age of patients in our study was between 35 to 45 years among three groups. According to textbooks, the age group that is capable of reproduction has the highest frequency of leiomyoma uteri. The Indian context provides an explanation for the fact that women typically seek medical attention only when their symptoms become severe enough to interfere with their ability to carry out daily tasks and compelling enough for their guardians to take them to the hospital. Furthermore, these fibroids may have been small and symptomless at previous ages, or they may have had just mild symptoms that these women may have

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endured. Due to their great tolerance, they have a propensity to dismiss problems and see the doctor only when it is too late. Furthermore, as people age, the size of these fibroids increases, causing increasingly severe symptoms that require hospitalization.[12]

At the post-study, PBAC reductions were significant in both groups. Donnez J et al have out a number of further investigations with ulipristal acetate that showed comparable outcomes [13].Studies on mifepristone also revealed similar results. For example, Kulshrestha et al.'s study in New Delhi reported a significant decrease in PBAC score ($P<0.001$) following a 6-month course of treatment [14]. Carbonell et al.'s study in Spain also correlated with ours, demonstrating a significant decrease in menorrhagia with mifepristone ($P<0.01$).[15]

Our investigation shows that the three medications significantly reduce the size of the fibroid. The results of two studies using mifepristone were similar to ours. Kulshrestha et al.'s study [14] showed a 35.7% decrease in fibroid size, while Carbonell et al.'s study [15] showed 48.1% and 39.1% reductions in fibroid size with the use of 5 mg and 10 mg mifepristone, respectively.

There was significant reduction in fibroid volume before and at the end of study among three groups. Reinsh RC, Murphy AA, Morales AJ, and Yen SS investigated the effects of 25 mg of mifepristone on fibroid volume over a three-month period in 1995 and discovered a 32% reduction without an increase in hot flushes.[16] The reduction of fibroid size, and volume was associated with improved quality of life in patients receiving Ulipristal acetate as compared to mifepristone and fibronorm.

Numerous more trials have demonstrated the efficacy of Ulipristal acetate in reducing menorrhagia and enhancing the quality of life for uterine fibroid patients. In a recent study, Kalampokas T. et al. discovered that treating patients with Ulipristal acetate was linked to decreased fibroid size and enhanced quality of life measures. They came to the conclusion that treating uterine fibroids with Ulipristal acetate over the short term is a safe and effective option.[17] All of these results were in line with those of our investigation, which shown that administering Ulipristal acetate was linked to reduced blood loss and fibroid size, both of which enhanced quality of life.

One limitation of the study is that it was conducted during a short period of time with a small number of participants. Although further intermittent treatment sessions have been shown to be helpful, we only present outcomes for three of the treatment courses.

CONCLUSION

Mifepristone, fibronorm, and ullipristal acetate treatment of uterine fibroids was linked to decreased fibroid volume, size, and blood loss. Ulipristal acetate was discovered to be more successful. This study leads us to the conclusion that all three medications are effective in treating fibroids; however, if a patient has a high number of fibroids, ullipristal acetate should be taken instead of the other two.

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