

Review of Cases of Uterine Fibroid Managed with Ulipristal Acetate

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Abstract:**Background:** Among the several types of tumors that may develop in the female reproductive system, fibroids account for the vast majority (20-40% of women). But most fibroids don't cause any symptoms, therefore they usually don't need to be treated.**Objective:** The aim of the study was to review individuals with uterine fibroids treated with ulipristal acetate.**Methods:** A prospective interventional trial including 48 premenopausal women who had fibroids causing symptoms was carried out. They had a clinical evaluation for the stated symptoms. Prior to beginning therapy and three months after beginning Ulipristal treatment, each patient had an ultrasound.**Results:** Ulipristal acetate significantly reduced the incidence of symptoms including menorrhagia, pelvic pressure, and pelvic discomfort after three months of treatment. However, urinary frequency remained unchanged. Fibroid volume decreased substantially from $51.0 \pm 46.5 \text{ cm}^3$ to $20.3 \pm 30.2 \text{ cm}^3$, but the change in fibroid diameter appeared inconsistent, raising questions about its accuracy or interpretation.**Conclusion:** Fibroid volume was decreased and fibroid symptoms were improved with ulipristal acetate-based fibroids treatment.**Keywords:** Hemorrhagic control, Hysterectomy, Myomectomy, Ulipristal acetate, Uterine fibroid.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Fibroids are the most prevalent tumors in the female reproductive system, affecting 20–40% of women throughout their reproductive years [1]. Medical intervention is not necessary for fibroids since most of them are painless. Nevertheless, the existence of 'uterine fibroids may result in important medical symptoms such constipation, painful periods, pelvic pressure, heavy menstrual flow, and discomfort in the pelvis [2]. Thyroid growths inside a woman's uterus, or womb, are called uterine fibroids. Often benign, meaning they are not cancerous, these growths do not spread to other parts of the body. It may take a microscope to notice fibroids since they might be so little [3]. They also have the potential to grow rather big. They might weigh several pounds or kilograms and fill the whole uterus. One fibroid may still grow, although multiple fibroid creation is more common. Surgery, either a hysterectomy or a myomectomy, is the cornerstone of therapy for uterine fibroids with symptoms [4]. However, in clinical settings, less invasive options such uterine artery embolization are being used [5]. Additionally, if bleeding is the main problem, hysteroscopic fibroids removal.

Therefore, medication is not recommended for the treatment of uterine fibroids while symptoms are absent (1); instead, surgery has traditionally been the preferred course of action when symptoms, such as pain or bleeding, are present. Four French guidelines for the care of patients with fibroids state that if pregnancy is desired, hysteroscopic excision of submucosal fibroids smaller than 4 cm in length is advised. This advice was based on a thorough evaluation of the literature. Fertility is negatively impacted by interstitial fibroids, sometimes referred to as intramural fibroids, although it is not enhanced by treatment. Therefore, depending on the size and quantity of fibroids, a myomectomy is only recommended for those who are symptomatic. This procedure may be carried either via laparoscopy or laparotomy. The best therapy for symptomatic fibroids for perimenopausal women who are aware of the dangers and other options is a hysterectomy.

Since uterine artery embolization has a low long-term morbidity, Patients should have access to it as a practical therapeutic option for symptomatic fibroids in non-fertility-seeking women. It is also a tried-and-true substitute for hysterectomy and myomectomy. Medical therapy may be used to

manage fibroids' symptoms and enable surgery to be planned under more favorable conditions. Another common treatment for bleeding control is danazol. Moreover, certain negative outcomes have been documented, such as weight gain, hirsutism, acne, and breast shrinkage [6]. All of these symptoms make the medication unsuitable for long-term usage. Young women often utilize oral combination contraceptive tablets to manage dysmenorrhea and menorrhagia. Regrettably, there hasn't been much research done on this kind of treatment for fibroids that cause symptoms.

The effectiveness of an intrauterine device containing levonorgestrel in reducing menorrhagia is well-established; nevertheless, its impact on the growth of uterine fibroids remains controversial. Because of the danger of expulsion and the poor likelihood of symptom relief, its usage is not advised in patients with significant uterine cavity distortion. Prior to the development of SPRMs, GnRH agonists were the most effective medical treatment for both preoperative and conservative conditions. They have the ability to decrease the volume of fibroids and cause significant reductions in the majority of fibroids-related symptoms, including bleeding, anemia, and discomfort [7]. These benefits, however, are temporary, and the fibroids often regain their pre-therapy size a few months after treatment is stopped [8]. Moreover, menopausal symptoms brought on by the chemical castration that GnRH agonists induce restrict the long-term use of these medications.

Recent evidence indicates that SPRMs are useful in reducing the size and symptoms of fibroids. Due to the efficacy of these drugs, surgical intervention will likely be used less often for the treatment of fibroids. Progesterone is crucial for promoting the growth of myomas [9]. The injection of ulipristal acetate reduces the amount of the fibroid, and the selective progesterone receptor modulators like ulipristal acetate that modulate its route provide a novel approach to the medical care and ultrasonography assessment of uterine fibroids [10]. It further facilitates amenorrhea without negatively impacting anti-glucocorticoid activity or estradiol levels [11]. The objective of the research was to review individuals with uterine fibroids treated with ulipristal acetate.

Materials and Methods

Study Design: A prospective observational study to investigate safety of ulipristal acetate in the

management of uterine fibroids undertaken at the 'Department of Obstetrics and Gynecology, Patna Medical College and Hospital, Patna, Bihar, India from November 2017 to October 2018.

Inclusion and Exclusion Criteria: Participants in the study were premenopausal women who had symptoms from at least one fibroid. Patients who had undergone uterine surgery in the past or who did not have any suspected instances of adenomyosis or gynecological cancer (if necessary, an outpatient endometrial biopsy was performed before the patient was included in the research) were not allowed to participate in the study.

Data Collection: The selection of a sample size of 48 was made according to the convenience.

Procedure: For three months, each study participant received five milligrams of ulipristal acetate every day. On the first day of menstruation, treatment started. Every participant in the research gave their informed permission. Transvaginal ultrasonography was used to check trial participants, and clinical assessments were made for symptoms that were reported one month before to beginning Baseline medication and one month after the conclusion of three months of ulipristal acetate treatment. Because every patient who got outpatient therapy matched the selection criteria, the sample size was established.

Statistical Analysis: The statistical analysis was conducted using SPSS software, specifically version 27. The student's t-test was utilized for comparing the mean values of the two categories. Categorical data were analyzed using the Chi-square test. The P-value below 0.05 indicated the statistical significance of result.

Results

The symptoms that 48 individuals experienced before and three months after starting Ulipristal Acetate medication were compared. After treatment, there was a noticeable improvement in several symptoms. Pelvic pressure decreased from 54.17% to 45.83%, and pelvic pain significantly decreased from 58.33% to 35.42%, indicating relief for many patients. Menorrhagia also saw a considerable reduction from 64.58% to 41.67%, suggesting that the therapy was effective in controlling excessive menstrual bleeding. However, urinary frequency remained unchanged at 50%, indicating that Ulipristal Acetate had no effect on this symptom in the study population.

Symptom	Before Treatment n=48 (%)	After Treatment n=48 (%)
Pelvic Pressure	26 (54.17%)	22 (45.83%)
Pelvic Pain	28 (58.33%)	17 (35.42%)
Urinary frequency	24 (50.00%)	24 (50.00%)
Menorrhagia	31 (64.58%)	20 (41.67%)

The diameters and volumes of the fibroids before and after Ulipristal Acetate treatment, together with the observed discrepancies. The average fibroid volume significantly decreased from $51.0 \pm 46.5 \text{ cm}^3$ before treatment to $20.3 \pm 30.2 \text{ cm}^3$ after treatment, showing an average reduction of $-10.7 \pm 28.8 \text{ cm}^3$. Interestingly, the fibroid diameter showed a counterintuitive result, increasing from 37.2 ± 28.6

mm before treatment to 48.4 ± 4.9 mm after treatment, but the difference reported is -18.8 ± 8.6 mm, which suggests an issue with the diameter data presentation or interpretation. This indicates that while the overall fibroid volume reduced, further clarification may be needed on the diameter changes.

Parameter	Before Treatment	After Treatment	Difference
Volume (cm ³)	51.0+46.5	20.3+30.2	- 10.7 + 28.8
Diameter (mm)	37.20+28.6	48.4 + 4.9	-18.8 + 8.6

Discussion

Ligands known as selective progesterone receptor modulators (SPRMs) bind to progesterone receptors and interact with coactivators and corepressors in particular tissues, producing a combination of agonistic and antagonistic effects. Although all synthetic photoperoids (SPRMs) have comparable effects, UPA has shown encouraging efficacy and safety in the treatment of symptomatic uterine fibroids [13, 14]. Two methods by which progesterone promotes the development of fibroids are first, it increases the expression of Bcl-2 protein and epidermal growth factor, and second it reduces the expression of the tumor necrosis factor gene.

A unique class of PR ligands known as SPRMs affect target cells differently depending on the tissue. Orally active and with a tissue-specific progesterone antagonistic action, UPA is a synthetic SPRM. Through upregulating cleaved caspase-3 expression and downregulating Bcl-2 activity, UPA stimulates apoptosis and impedes leiomyoma cell proliferation. On the other hand, UPA inhibits the production of growth factors and receptors that promote angiogenesis. The hypothalamic-pituitary-ovarian axis, which may either delay or prevent ovulation, is another important system that UPA affects. Therefore, neither estrogen deficiency nor the symptoms that go along with it are brought on by UPA. For most women, the main cause of amenorrhea is the interplay between UPA and endometrial PRs. While UPA is certainly helpful in reducing spontaneous fertility during treatment, it is important to remember that it should not be taken as (or in lieu of) a contraceptive. Ulipristal acetate acts by a mechanism that includes effects on the pituitary gland, the endometrium, and specific antiproliferative and proapoptotic actions [15].

Menstrual bleeding is one of the primary reasons people with fibroids see their doctors. In every patient in our study, menorrhagia was the main complaint, and most of them had a decrease in symptoms. The second research compared

leuprolide acetate (LA), a GnRH analogue, with UPA (5–10 mg/day) given intramuscularly once a month at a dosage of 3.75 mg in PEARL II. The third was PEARL III, in which four UPA treatment regimens were given over a three-month period, separated by two menstrual cycles for each regimen. According to our findings, the total fibroid volume was reduced by 33%, which is in line with studies in the literature that suggest fibroid volume reductions of between 21.2% and 36% [16]. According to earlier research by Donnez et al., 60% of women get PAEC after three months of UPA, however this condition is completely reversible six months after the conclusion of therapy [17].

There were several limitations to this investigation the small trial group and the patients' lack of blinding over the three months of ulipristal acetate medication. The successful control of bleeding and shrinkage of fibroids by ulipristal acetate has been shown in many short-term (3 months) randomized clinical investigations (13–16). Following treatment termination, menstruation normally returns within 4–5 weeks, although the decrease of fibroids' volume may last up to 6 months. Furthermore, ulipristal acetate medication decreased discomfort related with fibroid disease, enhanced quality of life, and raised no safety issues.

Conclusion

Ulipristal acetate was a viable option for treating fibroids instead of a hysterectomy. Also helpful in situations when a myomectomy is required. If the goal was only to reduce symptoms, ulipristal acetate was a highly safe and effective substitute for standard medical treatment.

References

1. Wallach EE, Vlahos NF. Uterine myomas: an overview of development, clinical features and management. *Obstet Gynecol* 2004;104(2):393-406.
2. Hirst A, Dutton S, Wu O, et al. A multi-centre retrospective cohort study comparing the

- efficacy, safety and cost effectiveness of hysterectomy and uterine artery embolization for treatment of symptomatic uterine fibroids. The HOPEFUL study. *Health Technical Asses* 2008;12(5):1-248, iii.
3. Dolan MS, Hill CC, Valea FA. Benign gynecologic lesions: vulva, vagina, cervix, uterus, oviduct, ovary, ultrasound imaging of pelvic structures. In: Gershenson DM, Lentz GM, Valea FA, Lobo RA, eds. *Comprehensive Gynecology*. 8th ed. Philadelphia, PA: Elsevier; 2012:chap 18.
 4. Matcher DB, Myers ER, Barber MW, et al. Management of uterine fibroids. *Evid Rep Technol Asses (Summ)* 2001;(34):1-6.
 5. Tropeano G, Amoroso S, Scambia G. Non-surgical management of uterine fibroids. *Human Repr Update* 2008;14(3):259-74
 6. Manyonda I, Belli AM, Lumsden MA, et al. Uterine-artery embolization or myomectomy for uterine fibroids. *N Engl J Med*. 2015 ;383(5):440-451.
 7. Lelhaby A, Vollenhoven B, Sowter M. Pre-operative GnRH Analogue therapy before hysterectomy or myomectomy for uterine fibroid. *Cochrane Database Syst Rev* 2001;(2):CD000547.
 8. Stovall TG, Munneyirci-Delale O, Summit RL Jr, et al. GnRH agonist and iron versus placebo and iron in the anaemic patient before surgery for leiomyomas: a randomized controlled trial. *Leuprolide Acetate Study Group. Obstet Gynecol* 1995;86(1):65-71.
 9. Kim JJ, Sefton EC. The role of progesterone signalling in the pathogenesis of uterine leiomyoma. *Mol Cell Endocrinol* 2012;358(2):223-31.
 10. Donnez J, Vazquez F, Tomaszewski J, et al. Long-term treatment of uterine fibroids with ulipristal acetate. *Fertil Steril* 2014;101(6):1565-73.e1-18.
 11. Attardi BJ, Burgenson I, Hild SA, et al. In vitro antiprogesterone/ antiglucocorticoid activity and progesterone and glucocorticoid receptor binding of the putative metabolites and synthetic derivative of CDB2914, CDB-4124 and mifepristone *J Steroid Biochem Mol Biol* 2004;88(3):277-88.
 12. Prostag SmPC. <http://www.medicines.org.uk/EMC/medicine/2237/SPC/Prostag+3+Leuprolin+Acetate+Depot+Injection+11.25mg/>
 13. Donnez J, Donnez O, Matule D, et al. Long-term medical management of uterine fibroids with ulipristal. *Fertil Steril* 2016;105(1):165-73.e4.
 14. Courtoy GF, Donnez J, Marbaix E, et al. In vivo mechanisms of uterine myoma volume reduction with ulipristal acetate treatment. *Fertil Steril* 2015;104(2):426-34.e1
 15. Collins J, Crosignani PG, ESHRE Capri Workshop Group. Endometrial bleeding. *Hum Reprod Update* 2007;13(5):421-31.
 16. Tafi F, Scala C, Maggiore ULR, et al. Drug Safety evaluation of ulipristal acetate in the treatment of uterine fibroids. *Expert Opin Drug Safety* 2015;14(6):965-77.
 17. Donnez J, Tatarchuk TF, Bouchard P, Puscasiu L, Zakharenko NF, Ivanova T, et al. Ulipristal acetate versus placebo for fibroid treatment before surgery. *N Engl J Med* 2012;366:409-20.