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Original Article

Role of Ulipristal Acetate in Treatment of Fibroid: A Prospective Study

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Abstract

Background: Uterine fibroids are the most common benign tumours in women of reproductive age group which may present with heavy menstrual bleeding, dysmenorrhea, pelvic pressure and anaemia. Its management depends on the number, size and location of the fibroids, patient's age and desire to preserve fertility. Ulipristal acetate (UPA) is a selective progesterone receptor modulator which selectively inhibits the proliferation of uterine leiomyoma cells and induces their apoptosis. ***Objectives***: The objective of the study was to evaluate the efficacy of ulipristal acetate in reducing the size of a symptomatic fibroid, its effect on menstrual bleeding, dysmenorrhea and its side effects. ***Materials and methods:*** A total of 45 patients were included in this prospective study. Oral ulipristal acetate at a dose of 5 mg per day was given for a period of 3 months. The PBAC Score, Visual Analogue Scale score and ultrasound findings of fibroid were noted. ***Results:*** Ulipristal acetate is an effective drug in reducing heavy menstrual bleeding, pain and fibroid size with minor side effects. ***Conclusion:*** Ulipristal acetate can be a safe, effective and economic option for treatment of symptomatic fibroids in patients.

Keywords: ***Uterine fibroids, myomas, Ulipristal Acetate, selective progesterone receptor modulators.***

Introduction

Uterine fibroids (also known as leiomyomas or myomas) are the most common benign tumor of women of reproductive age which arise from the smooth muscle of the myometrium [1,2]. 5.4 to 77% of women have myomas, depending on the study population and races of the population [3]. The majority of women remain largely asymptomatic; however, they can cause debilitating symptoms in many. Symptomatic fibroids have a considerable impact on women's quality of life as well as their productivity [3,4]. The most common symptoms are heavy menstrual bleeding, dysmenorrhea, pelvic pressure and anaemia resulting in chronic fatigue that adversely affects the women's quality of life and fertility. The management of uterine fibroids depends on the number, size and location of the fibroids, but the choice of treatment is guided by patient's age and desire to preserve fertility or avoid a radical surgery such as hysterectomy. Surgical approaches include myomectomy by hysteroscopy, laparoscopy, laparotomy or hysterectomy. Non-surgical approaches include uterine artery embolization and interventions performed under radiologic or ultrasound guidance to induce thermal ablation of the uterine fibroids. Medical therapy is currently limited to preoperative reduction of symptoms related to uterine bleeding and fibroid size, without providing long term efficacy, acceptable tolerability and safety.

There is growing evidence of the crucial role of progesterone pathways in the pathophysiology of uterine fibroids. The concentration of estrogen and progesterone receptors appears to be significantly higher in uterine fibroids in comparison with healthy myometrium [5] and is positively correlated with the rate of growth of uterine fibroids [6]. Ulipristal acetate (UPA) is a selective progesterone receptor modulator that also exhibits antiproliferative effects on leiomyoma cells and the endometrium [7]. As a progesterone receptor agonist, UPA selectively inhibits the proliferation of uterine leiomyoma cells and induces their apoptosis. Long-term intermittent use of UPA has been demonstrated to be effective in randomized controlled studies. It has effectively shown to control bleeding and shrink fibroids. After treatment cessation, return of menstruation usually occurs within 4 to 5 weeks but fibroid volume reduction is sustained for up to 6 months [8,9]. Alternatives to surgical intervention is the need of the hour, especially for women seeking fertility preservation. In this respect, SPRMs are an option which have been proven to treat fibroid symptoms effectively.

Materials and methods

The study was carried out in the department of Obstetrics and Gynaecology in a tertiary care hospital in eastern India over a period of one year with the objective to evaluate the efficacy of ulipristal

acetate in reduction of size of symptomatic fibroid, improvement in complaints of heavy menstrual bleeding, dysmenorrhea and side effects. A total of 45 patients were included in this prospective study. Premenopausal women with fibroid ≥3 cm and <10 cm in diameter, heavy menstrual bleeding, and uterine size <16 weeks of gestation were included in the study. Eligible women were aged 18–48 years, with body mass index 18-40 kg/m2 and had regular menstrual cycles of 22–35 days. Women with previous uterine surgery, history of or current uterus, cervix, ovarian, or breast cancers, significant finding on Papanikolaou test (PAP) smear within the past 12 months, endometrial hyperplasia or adenocarcinoma within the past 6 months, large uterine polyp (>2 cm), calcified or subserosal fibroids and/or a calcified uterus were excluded from the study. Menstrual bleeding was assessed with the use of the PBAC score. Heavy menstrual bleeding was defined as a PBAC score of more than 100 during one menstrual period, which corresponds to a blood loss of more than 80 ml. Dysmenorrhea was assessed subjectively by a visual analogue scale. The scale is from 0 to 10 with no pain, mild, moderate, severe and worst pain categories. Fibroid volume and endometrial thickness were assessed by ultrasonography. Women received treatment up to 3 months with oral ulipristal acetate at a dose of 5 mg per day. All the cases were called for monthly follow-up for 3 months. At every visit, the PBAC Score, Visual Analogue Scale score and ultrasound findings of fibroid type, volume and endometrial thickness were noted. Hemoglobin and liver function test were done.

Statistical Analysis

The results are presented in percentages, frequencies and mean ± SD. The Paired t-test/Wilcoxon rank sum test was used to compare change in the continuous variable for normal/non-normal variables. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Results

Out of the 45 patients, 44.4% patients were >40 years of age (44.4%) followed by 35-40 (37.8%) and <35 (17.8%). The mean age of patients was 39.27±6.37 years ranging from 22 to 48 years. 60% of the patients were multiparous. Heavy menstrual bleeding was present among 86.7% patients, dysmenorrhea among 44.4% patients and infertility was present among 11.1% patients in the present study. There was significant (p=0.0001) change in PBAC from baseline to 1, 2 and 3 months as well as VAS (p=0.0001) (Fig 1&2) Menstrual bleeding was reduced among 84.6% patients. The compliant of dysmenorrhoea improved among 95% patients. There was significant (p=0.0001) change in fibroid volume from baseline to 3 months with mean reduction in fibroid size being 43.62%. (Table 1). Anaemia was corrected and hemoglobin changed significantly (p<0.01) over 3 months. Minor side effects like nausea, hot flushes, breast tenderness and headache were present in 13.2% patients.

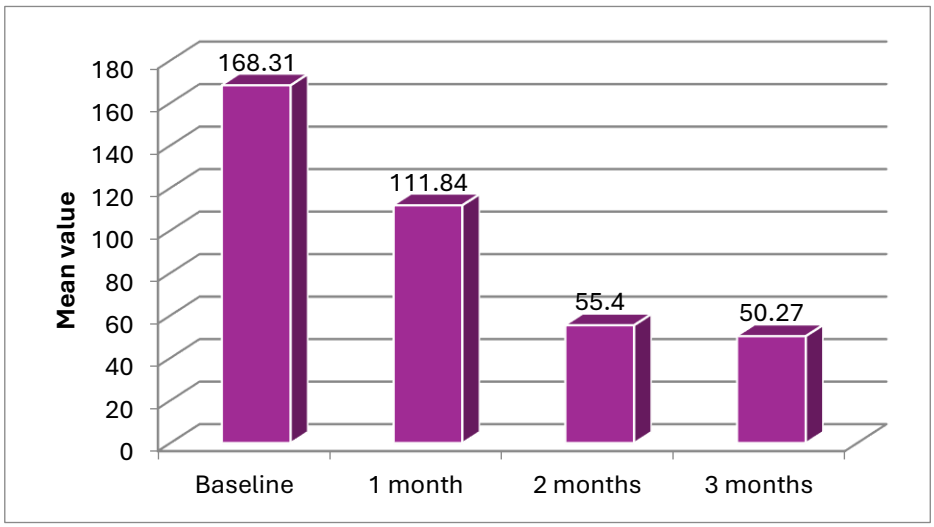

Fig. 1: Distribution of pictorial blood loss assessment chart score from pre to post therapy

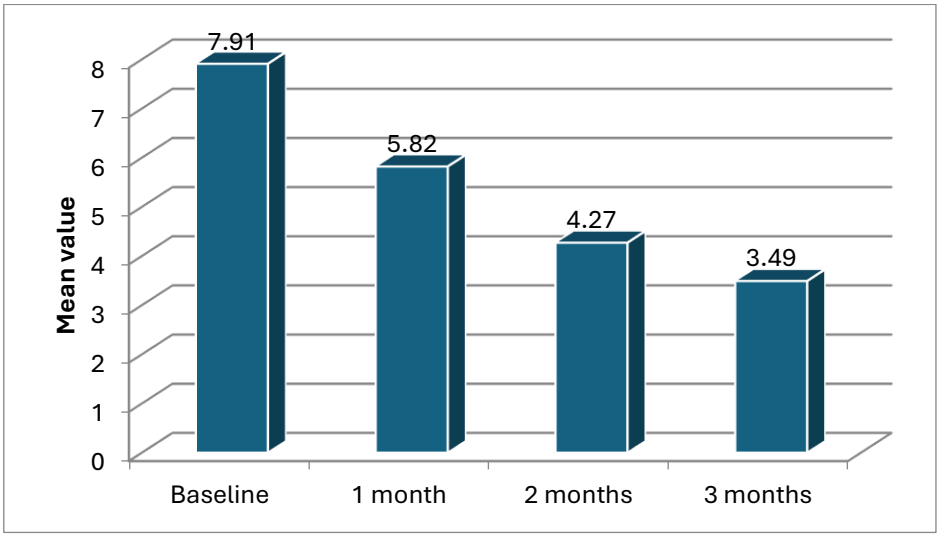

Fig. 2: Distribution of VAS from pre to post therapy

Table 1: Comparison of fibroid volume from pre to post therapy

Time period	Fibroid (Mean± SD)
Baseline	121.24±97.55
3 months	73.72±79.84
Mean change	49.96±41.87
Percentage reduction	43.62±33.87
p-value[1]	0.0001*

[1]Wilcoxon rank sum test, *Significant

Discussion

In the present study, there was significant (p=0.0001) change in PBAC from baseline to 1, 2 and 3 months which is similar to the study by Donnez *et al.* (2014) [10] where PBAC was progressively reduced from medians of >200 at the start of the first course to <100 at the end. In the present study, menstrual bleeding was reduced in 84.6% patients similar to the PEARL I trial where uterine bleeding was controlled at week 13 in 91% women receiving UPA (5 mg). (Donnez *et al.*, 2012) [11]. Amenorrhea was achieved in 42.2% patients in the present study within 10 days of treatment. In the PEARL I trial, amenorrhea occurred in 50% patients within the first 10 days of treatment. In PEARL III trial amenorrhea was achieved by 79% of the women after the first course of ulipristal and 90% after four courses. The present study reported significant change (p=0.0001) in VAS which is similar to the study by Donnez *et al.* (2014) [10] where VAS score decreased substantially from baselines of 39.5 to 6.0 at the end of course in patients receiving 5 mg of ulipristal acetate. The present study showed significant improvement in dysmenorrhea (95%). Nalini *et al.* (2017) [9] and Fernandez *et al.* (2017) [12] also reported the effectiveness of Ulipristal Acetate in decreasing pain. The present study reported 43.62% reduction in mean fibroid volume. PEARL I (2012) [10] demonstrated reduction in fibroid size, as measured at week 13 by 21%. Nalini *et al.* (2017) [9] found that after the end of course 3 out of 50 patients, 48 patients had fibroid volume reduction ≥25%. 33.3% of patients had ultrasound findings suggestive of fibroid shrinkage in the study conducted by Singh and Rai (2018) [13]. In the study by Woodhead *et al.* (2018) [14] reduction in size of fibroid was 34%. In the present study, side effects like hot flushes, headache, breast tenderness and nausea were present in 13.2% patients. However, Donnez *et al.* (2015) [15] reported side effects in 44% of patients, headaches and hot flushes being the most common. Nalini *et al.* (2017) [9] also reported no serious side effects of UPA. Liu, *et al.* (2017) [16] reported in their study, common adverse effects (≥5% in any UPA group) during course 1 and 1st off-treatment were hot flush (9.5%), headache (7.3%), fatigue (4.4%) and nausea (5.4%). Fauser *et al.* (2017) [17] also reported a higher percentage of adverse events, the most frequent being headache and hot flushes.

Conclusion

The treatment of symptomatic fibroid by Ulipristal acetate was associated with reduction in menstrual bleeding, fibroid volume and pain, with amenorrhea occurring in more than 40% patients and correction of anemia after 3 months of therapy with minor side effects. Thus, Ulipristal acetate is a very effective drug for management of symptomatic fibroids and can be given at a dose of 5mg for 3 months. It is an economic option to surgeries with decreased morbidity.

List of abbreviations

UPA: Ulipristal acetate
PAP smear: Papanikolaou smear
PBAC: Pictorial blood loss assessment chart
VAS: Visual Analogue Scale

Declarations

Ethical approval

The study was approved by the Institutional Ethics Committee of Tata Main Hospital.

Ethical Committee Approval document no.
TMH/FRM/QMS/ALL/17

Consent

Written and informed consent was obtained from all the participants of the study.

Data Availability

Can be accessed on request from the corresponding author.

Conflicts of Interest

None

Funding Statement

None

Authors' contributions

PB: Study design, data collection.
SW: Supervised the project and verified the data collection
MS: Preliminary draft
OS: Supervised, final draft.

All the authors have read and approved the final manuscript.

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