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Research Article

EFFICACY OF ULIPRISTAL FOR TREATMENT OF WOMEN WITH SYMPTOMATIC UTERINE FIBROIDS

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A B S T R A C T

Uterine fibroids or leiomyomas are benign uterine neoplasms that arise from the smooth- muscle tissue.They constitute the most common tumor in women,being present in 20-40% of women of reproductive age.Ulipristal acetate a selective progesterone receptor modulator, is a new ,effective option for medical management of symptomatic uterine fibroids in women of reproductive age.

Aim: The purpose of the study was to study the efficacy of ulipristal acetate for treatment of symptomatic uterine fibroids.

Objectives:

1. To evaluate improvement in symptoms of menorrhagia and dysmenorrhea in women with fibroids after Ulipristal treatment
2. To evaluate reduction in size of fibroid by USG measurements after Ulipristal treatment.
3. Increase in haemoglobin of anemic women at the end of Ulipristal treatment course
4. Assessment of adverse event/side effects.

Study Design: Hospital based observational analytical study/open labeled uncontrolled clinical trial with prospective data collection.

Setting: This study was conducted in Asian Institute Of Medical Sciences,Faridabad

Methods: Women with of uterine fibroid associated symptom were included in the study after obtaining written informed consent.women were administered Ulipristal(5mg) starting from first day of menstrual cycle daily for 90 days and followed up monthly for a period of 6 months,

Result: 90 women were selected for the study out of which 12 dropped out and 2 women got operated in view of increase in size of fibroid and heavy bleeding. During the course of treatment amenorrhoea was achieved in 72 out of 78 patients (92.3%). Dysmenorrhoea was relieved in 47.8% of women,with a much higher relief in menstrual blood loss,94.6% as per PBAC score. The mean volume of the dominant fibroid prior to treatment was 194.29 cc and decreased to 141.53cc after three month treatment period indicating significantly lower volume after treatment. The mean haemoglobin level increased from an initial level of 9.8g/dl(6.7-13g/dl) to 12.7g/dl(10 -13.8g/dl) after three months of ulipristal acetate therapy.No major side effects of the drugs were noticed during the course of treatment.

Conclusions: Three months of ulipristal acetate therapy causes significant reduction in uterine bleeding,fibroid volume with improvement of haemoglobin level without any significant side effect.

INTRODUCTION

Uterine fibroids or leiomyomas are benign uterine neoplasm that arise from the smooth- muscle cells.They constitute the most common tumor in women being present in 20-40% of women of reproductive age [1,2]. Although majority are asymptomatic but they can cause a magnitude of symptoms. The most common symptom being menorrhagia which can lead to iron-deficiency anemia and chronic fatigue[3], that may not be adequately controlled with iron supplementation alone[4,6].

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Other symptoms include pelvic pain, dysmenorrhea , pressure effects ,which may adversely affect quality of life and fertility.[7-10] 53.7% women with fibroids reported a dramatic decline in their quality of life and work productivity [11].

Management strategies are usually individualized based on the severity of the symptoms, the size and location of the fibroid the patient's desire for future fertility, the patient's age and it's chronological proximity to menopause.[10]

Surgical intervention has historically been the mainstay of fibroid treatment and include abdominal hysterectomy, conventional abdominal myomectomy and the radiological interventions like uterine artery embolisation (UAE).Hysterectomy is unacceptable to women wishing to

retain their fertility potential while other surgical modalities require skill and are associated with high rate of morbidity and mortality.[12]

There is there for a need for medical therapy that has efficacy equivalent or superior to surgery; does not interfere with reproduction, has minimal side effects and is relatively cheap.[12]

Selective progesterone receptor modulators (SPRMs) are a relatively new class of synthetic ligands with tissue selective effects of mixed agonist and antagonist activity.[13]

Ulipristal acetate is an orally active synthetic SPRM,characterized by a tissue specific partial progesterone antagonist effect.Ulipristal acetate as a progesterone antagonist inhibits the proliferation of leiomyoma cells and induces apoptosis by increasing cleaved caspase-3 expression and decreasing BCL-2 expression.Moreover Ulipristal acetate down regulates the expression of angiogenic growth factors Thus Ulipristal suppresses neo-vascularization , cell proliferation and survival in leiomyoma cells only but not in normal myometrial cells. Additionally Ulipristal acetate may impair fibroid tissue integrity by reducing the deposition of collagen in the extracellular spaces[14-16].

Besides, it acts on the hypothalamic-pitutary-ovarian axis there by inhibiting or delaying (14,75) ovulation and inducing amenorrhoea. Thus it represents a promising new option for the pre-surgical medical treatment of uterine fibroids.

METHODOLOGY

Necessary approval from the institutional ethical committee was obtained before initiating the study.The study was Hospital based observational analytical study,open labeled uncontrolled clinical trial with prospective data collection study conducted among women who conformed to the specified inclusion and exclusion criteria.

Inclusion Criteria

- Age >18yrs
- Diagnosed and radiologically confirmed cases of uterine fibroids
- BMI 18-40kg/m2
- Symptomatic cases with menorrhagia or dysmenorrhoea/pressure symptoms.
- Fibroid size >3cm<12cm
- Fibroid related anemia Hb<10gm/dl

Exclusion Criteria

- Pregnancy
- Fibroid size to >12cm or <3cm
- Malignancy
- Submucosal fibroid
- Hypersensitivity to ulipristal acetate
- Renal hepatic insufficiency

Study Procedure: Women were included in the study after written informed consent and were subjected to detailed history taking and clinical examination. An ultrasound evaluation of the pelvic organ and routine investigation was performed in all the participants of the study at the begining of the therapy

Ulipristal 5 mg daily was started during first week of a menstrual cycle ,for 90 days.The study group was followed in outpatient for clinical monitoring.At the end of the study subjects were enquired about the symptoms and assessment of fibroid size by usg tvs and increase in haemoglobin level.

RESULTS

90 women were included in the study out of which 12 dropped out and 2 women got operated in view of heavy bleeding. During the course of treatment complete cessation of menstrual bleeding was observed in 72 out of 78 treated patients (92.3%) [fig 1].

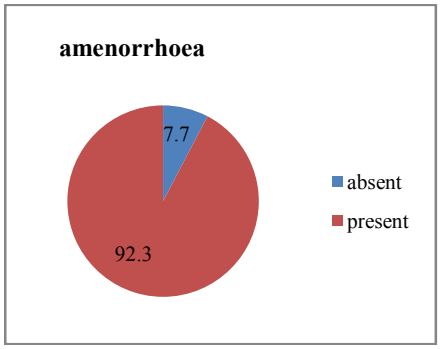

Fig 1

71.7%(56 out of 78) of women had menorrhagia(PBAC score >100) prior to the onset of treatment and 53 patients out of 56(94.6%) had significant reduction in uterine bleeding after three months of ulipristal acetate treatment Pain associated with fibroids persisted in 13 out of 51 patients who complained of dysmenorrhoea (47.4% decrease)

Table 1 Relief in Dysmenorrhoea

Dysmenorrhoea	Frequency	Percent
No relief	13	25.5
Relief	38	74.5
Total	51	100

The mean volume of the dominant fibroid prior to treatment was 194.29 cc and decreased to 141.53cc after three month treatment period, indicating significantly lower volume(P<0.005) after treatment [fig2].

Fibroid volume and size was assessed in following USG TVS.

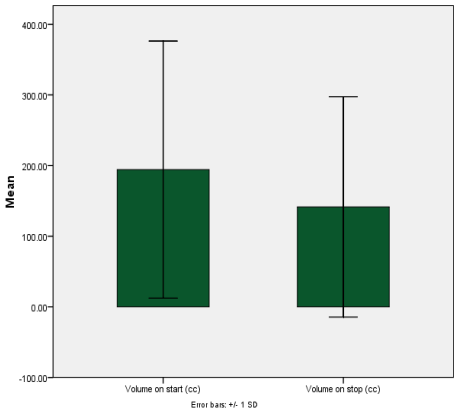

Fig 2 Fibroid volume and size as assessed by TVS

The mean haemoglobin concentration prior to treatment was 9.8g/dl(6.7-13g/dl) in our group and after 90 days of treatment with ulipristal acetate rose to 12.7g/dl(10 -13.8g/dl). Comparision of haemoglobin level before and after study

(total 2)

Hemoglobin (gm%)	Number of women before study	Number of women after treatment
Normal (>11)	26	34
Mild(10-11)	17	29
Moderate (7-10)	32	15
Severe (4-7)	3	0
Very severe(<4)	0	0

No major side effects of the drugs were noticed during the course of treatment.1.3% of women (1 out of 78) complained of headache or breast tenderness[fig 3].

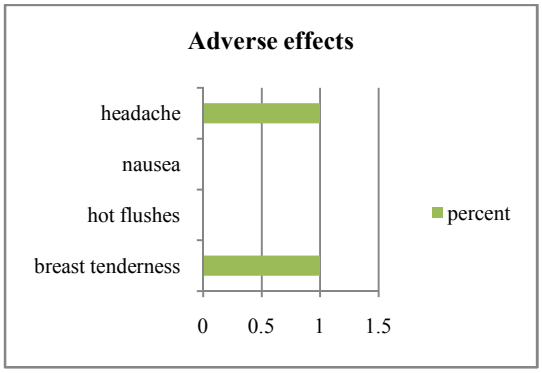

Fig 3

DISCUSSION

In our study bleeding was controlled in 94.6% and there was significant shrinkage in size of fibroid.

J.Donnez et al.[(2)] in 2012 reported that treatment with ulipristal acetate 5mg or 10mg for 13 weeks controls excessive bleeding and reduce fibroid volume.

In PEARL II [(17)] after 13 weeks uterine bleeding was controlled in 89-98% and volume shrinkage from baseline was (-37.7 to -5.6%). Most common side effect in their study was headache , pain/discomfort in breast and hot flushes.

Slawomir et al. in 2014 in their study reported a 45.6% mean decrease in fibroid volume , cessation of menses in 77% and mean haemoglobin increased from 10.1g/dl (prior to UPA) to 12.6g/dl after 12 weeks of UPA therapy.[(18)]

In our study the increase in mean haemoglobin concentration was from 9.8g/dl to 12.7 g/dl at the end of 90 days of treatment .

CONCLUSION

Ulipristal acetate 5mg/day for 90 days may be a good option for women with symptomatic uterine fibroids. However, more studies preferably in Indian scenario are required before the safety of this drug can be fully established.

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