

Spontaneous Conception Following Ulipristal Acetate on Treating Uterine Fibroid - A Case Report

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Abstract: A case report of a clinical pregnancy after use of ulipristal acetate (UA) to decrease uterine fibroid size. A 35yrs old women, PARA 1, LIVE 1, ABORTION 1, presented with findings of fibroid uterus for which laparotomy myomectomy was done. Following surgery (8 months post surgery) ULIPRISTAL ACETATE 5mg for 13 weeks daily was given as a further management. We measured the shrinkage of fibroids and the morphology of the endometrial cavity in order to study the possibility of pregnancy following treatment. An ultrasound of the endometrium after treatment showed that uterine fibroids had decreased and the morphology of the endometrium had become normal. During the endometrial biopsy, no histological endometrial changes were observed. The patient presented in OPD with amenorrhea for 6 weeks after completing the ulipristal acetate treatment and pregnancy was confirmed by ultrasound four months after end of treatment. After treatment patient underwent a successful pregnancy. After prior myomectomy, a spontaneous pregnancy (by use of UA) which was used in decreasing the size of fibroid which may suggest a potential medical benefit of this selective progesterone receptor modulator in the management of women who desire pregnancy but have uterine fibroids after surgery. The use of UA may be beneficial for patients who do not agree for surgical procedure and/or those planning to undergo Assisted Reproductive Technique (ART). After the treatment is complete, one can immediately try to conceive and avoid the risks of further surgery.

Keywords: Fibroid uterus, Ulipristal acetate, Spontaneous pregnancy, Myomectomy, Endometrium

1. Introduction

Fibroid uterus or leiomyomas, arise from the smooth-muscle tissue are benign neoplasms of uterus. In reproductive age group the most common tumour in women is uterine fibroid. The presenting complaints and symptoms depend on size of the uterine fibroid and location of it. Depending on the location, its divided into submucosal, intramural, subserosal. A decrease in fertility and an increase in miscarriage rates have been associated with the type of fibroid which is likely to be submucosal and intramural fibroids [1]. There is still a lack of evidence regarding the effects of radiologic interventions on fertility outcomes with myomectomy for submucosal and intramural fibroids as the management of uterine fibroid in the reproductive age group is still controversial. Ulipristal acetate, its a selective progesterone receptor modulator (SPRM) which was approved for the treatment of uterine fibroids [2]. It has been demonstrated that the effect of UA at levels of either 5 mg or 10 mg daily for 13 weeks effectively controls profuse bleeding PV, and decreasing the size of uterine fibroids [3]. Leuprolide acetate also has an effect of uterine bleeding. At the end of 13 weeks of treatment with UA, there was a benign histologic endometrial changes noted and was reassured as they had the tendency to get resolved spontaneously within a few months of treatment [4]. After repeated dose of ulipristal acetate 10mg daily given intermittently in span of 3-month, incidence of amenorrhea and further reduce in size of the fibroid (shrinking of fibroid) is been noted, with no evidence of endometrial hyperplasia or malignancy [5]. The evidence for the use of ulipristal acetate to decrease fibroid size in order to avoid its impact on the endometrial cavity prior to pregnancy is still not clear. In order to reduce the size of uterine fibroids successful spontaneous pregnancy after ulipristal acetate use is noted. This method may help a new line of management of fibroids in case of history of infertility.

2. Case Report & Methodology

A 35-year-old patient, para 1, live 1, abortion 1 woman, came to OBG OPD of SBMCH. Patient had come with

- c/o lower abdomen pain not radiating in nature, gradually progressive.
- c/o menstrual irregularities sine 8 months - 3-4 days / 45-50 days cycle, normal flow, changes 2-3 pads/ day not associated with clots, pain +.
- No other significant complaints.

Patient has H/O spontaneous abortion 2 yrs back.

Patient has no significant past history, family history or surgical history. Patient was advised with USG, transvaginal ultrasound done which showed

- Several intramural fibroid with largest measuring- 3.2x2.2x1.4 cm. ▪ Distorted endometrial cavity by the fibroids.
- B/L tubes and ovaries-normal

In view of fibroid uterus, LAPAROTOMIC MYOMECTOMY done and sent for HPE. Myomas were removed and the disrupted endometrium was sutured back. Postoperative period was uneventful.

Administration of Ulipristal Acetate:

It is specifically highlighted for shrinkage of Fibroid. After treatment of fibroid, patient was anxious to conceive. Following Eight months of post surgery, the patient resumed her normal menstrual cycles. however, repeat ultrasound done showed, 3 intramural fibroids with largest measuring 2.6x2cm and 2.5x1.8cm, respectively located in the posterior wall of uterus and with slight distortion of the endometrial cavity. Hence, the patient was given ulipristal acetate 5 mg

daily for 13 weeks. Advantage and disadvantage of UA for treatment was well explained to the patient and consent obtained.

Follow-Up

Patient was advised to have a monthly follow-up. The patient had H/O amenorrhea persistently since the start of the treatment. One month later, after the completion of the treatment, patient resumed her menstrual cycles regularly. Follow up with ultrasound (TVS) showed a decrease in size of the fibroids and endometrial cavity with normal structural morphology. Pipelle endometrial sampling done which was done on the day 22 of cycle (premenstrual to next cycle) and was found to have normal secretory endometrium.

3. Results

Three months after the end of ulipristal acetate, the patient to the OPD with c/o 6 weeks of amenorrhea. Using USG TVS, both pregnancy and fibroid uterus was noted. The antenatal period during pregnancy was uneventful and the follow up obstetric USG showed an increase in size of the two uterine fibroids, with diameters of 3.2x2.3cm and 4.5x3.8 cm, respectively, on 30 weeks of gestational age. The endometrial cavity appears to be normal without any distortion by fibroids. As the pregnancy progressed successfully with proper uterine contraction and with history of previous myomectomy, the patient was taken up for elective LSCS at around 36 weeks of gestation. An alive term male new born with weight of 2734kgs. Immediate postoperative period was uneventful. On POD # 4 following LSCS, mother along with the new born was discharged.

4. Discussion

Fibroids are benign, monoclonal tumors of the smooth muscle cells of the myometrium and contain large aggregations of extracellular matrix composed of collagen, elastin, fibronectin, and proteoglycan.

Symptoms that are commonly seen includes Abnormal uterine bleeding (profuse bleeding p/v during menstruation) leading to anemia, lower abdomen pain, pain during menstruation (dysmenorrhea), bleeding and pain affecting daily activity, and infertility. The desire for conceiving following treatment of fibroid is still high [6]. In the reproductive age group the treatment for fibroid depends on the parity and symptoms. As increase in size of fibroid depends on oestrogen and progesterone, medical therapies have been noticed to have disadvantage in treating the cause and preserving fertility. The medical management available are oral progestin, IUCD (intrauterine device containing progestin), gonadotropin releasing hormone. Other medical management that helps In reducing size of the fibroid includes aromatase inhibitors, mifepristone, danazol and raloxifene.

Ulipristal acetate (UA) is a selective progesterone receptor modulator with pure antagonist activity. UPA modulates the progesterone signalling pathway and promotes remodelling of the extracellular matrix and reduction of collagen synthesis. UPA is effective for controlling profuse bleeding and reducing the size of uterine fibroids, while increasing

the quality of life. The largest study included 451 women with symptomatic uterine fibroids, uterine size less than 16 weeks, and profuse bleeding PV during menstruation. Women received four repeated 12-week treatment courses of daily UPA, 5 or 10 mg, given orally. Both doses led to amenorrhea, usually within 1 week, in $\geq 70\%$ of women and bleeding was controlled in $\geq 73\%$. Haemoglobin levels increased over the first two treatment courses and were maintained during follow-up. By the fourth treatment course, approximately 80% of women had more than 25% reduction in the volume of the three largest fibroids. Patients had significant improvement in pain and quality of life and reached scores reported for healthy individuals. Six cases of hyperplasia were observed, all of which returned to normal endometrium during the study. Adverse events included headache and hot flushes in 11% of women, almost all of which were mild or moderate. Levels of E2 remained well above postmenopausal levels, suggesting that bone mineral density will not be adversely affected by ulipristal.

Surgical intervention include, myomectomy in case of submucous and intramural fibroid for those who have not completed family and young age group, other procedure hinders with fertility hence not discussed in this case report. other methods like, intervention radiology also helps In preserving fertility in case of symptomatic fibroids. The most effective treatment for symptomatic fibroid are gonadotropin releasing hormone analogues.

Oral progestin - cause increase in size of fibroid and abnormal uterine bleeding, IUCD is not helpful in distorted endometrial cavity though it helps in reducing bleeding p/v and in treating infertility.

The advantage of medical management of fibroid over fertility is still unclear. Treatment with UA 5 mg or 10 mg of the SPRM continuously for 13 weeks controls profuse bleeding p/v and reduces the size of the fibroid. These regimens are as effective as leuprolide acetate in controlling uterine bleeding and induce significantly fewer hot flashes. Ulipristal acetate and leuprolide acetate has a significantly greater effect on decreasing the volume of uterine fibroid as SPRM has the same effect even after the discontinuation of treatment. It has been noted that repeated dose of ulipristal acetate 10mg has an higher effect on reducing the size of volume of fibroid and increased rate of amenorrhea than a single dose of ulipristal acetate. Treatment with 5mg or 10mg ulipristal acetate has been associated with benign changes of endometrium that are resolved within 6 months of treatment [7]. It has been reported that trans abdominal myomectomies have an risk of adhesions in the pelvic region which has an impact on fertility. Due to damage of endometrial cavity there is always an chance of spontaneous abortion in any trimester (high rate being the 1st trimester) [8, 9] and on the other hand can lead to elective LSCS hence it is always best to plan pregnancy after 3 months of myomectomy and as it may also lead to LSCS in following pregnancy. However, there is still a lack of information on improving fertility following myomectomy. In this case report, Patient underwent elective LSCS due to distorted endometrium following laparotomic myomectomy. After treatment with ulipristal acetate there was an spontaneous conception with decrease in size of fibroid. Use of ulipristal

acetate can be suggested in women who have desires and plans for pregnancy with uterine fibroid at young age group. As it not only symptomatically helps in reducing the size of fibroid but also by promoting pregnancy as early as possible and by avoiding surgical intervention. It is also noted that conception following ulipristal acetate has no effects on the foetus like teratogenicity or anomaly, further series are required in order to establish the safety of ulipristal acetate as a treatment of symptomatic fibroids prior to pregnancy. Hence can also be used in patients with history of infertility who are managed by assisted reproductive techniques.

5. Conclusion

Patient who have fibroid uterus, still desire to conceive UPA may be effective treatment option. Larger studies on the subject are required, UPA may, in a near future, play a role in the management of fibroids in the infertility context.

References

- [1] Kroon B, Johnson N, Chapman M, Yazdani A, Hart R, Australasian CREI Consensus Expert Panel on Trial Evidence (ACCEPT) Group Fibroids in infertility—consensus statement from ACCEPT (Australasian CREI Consensus Expert Panel on Trial evidence) Australian and New Zealand Journal of Obstetrics and Gynaecology. 2011; 51 (4): 289-295. [Google Scholar]
- [2] Electronic Medicines Compendium. Esmya 5mg tablets (ulipristal acetate) [http://www.medicines.org.uk/EMC/medicine/26068/SPC/Esmya+5+mg+Tablets+\(ulipristal+acetate\)/3](http://www.medicines.org.uk/EMC/medicine/26068/SPC/Esmya+5+mg+Tablets+(ulipristal+acetate)/3). Scholar.] [Google Scholar]
- [3] Donnez J, Tatarchuk TF, Bouchard P, et al. Ulipristal acetate versus placebo for fibroid treatment before surgery. The New England Journal of Medicine. 2012; 366 (5): 409-420. [Abstract] [Google]
- [4] Williams ARW, Bergeron C, Barlow DH, Ferenczy A. Endometrial morphology after treatment of uterine fibroids with the selective progesterone receptor modulator, ulipristal acetate. International Journal of Gynecological Pathology. 2012; 31 (6): 556-569. [Google Scholar]
- [5] Donnez J, Vázquez F, Tomaszewski J, et al. Long-term treatment of uterine fibroids with ulipristal acetate. Fertility and Sterility. 2014; 101 (6): 1565. e1-1573. e18. [Abstract] [Google Scholar]
- [6] Metwally M, Cheong YC, Horne AW. Surgical treatment of fibroids for subfertility. Cochrane Database of Systematic Reviews. 2012; 11CD003857
- [7] Fiscella K, Eisinger SH, Meldrum S, Feng C, Fisher SG, Guzick DS. Effect of mifepristone for symptomatic leiomyomata on quality of life and uterine size: a randomized controlled trial. Obstetrics and Gynecology. 2006; 108 (6): 1381-1387. [Google Scholar].
- [8] LiTC, MortimerR, Cooke ID. Myomectomy: a retrospective study to examine reproductive performance before and after surgery. Hum Reprod 1999; 14: 1735-1740. Google Scholar Crossref PubMed.
- [9] KhaundA, Lumsden MA. Impact of fibroids on reproductive function. Best Pract Res Clin Obstet Gynaecol 2008; 22: 749-760.