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Original Article

A randomized control trial to assess efficacy of Mifepristone in medical management of uterine fibroid

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ABSTRACT

Background: Fibroids are the most common benign tumours of uterus. Heavy menstrual bleeding is the commonest concern for which medical attention is sought. Hysterectomies for leiomyoma constitute a third of all hysterectomies. Thus, healthcare cost to society due to uterine leiomyomas is of considerable importance.

Methods: A prospective study was conducted at tertiary care hospital of armed forces. 120 women in pre-menopausal age group with complaints of menorrhagia, Pictorial Bleeding Assessment Chart (PBAC) scoring ≥100 and at least one fibroid ≥2.5 cm in size were recruited in the study. Patients in Group 1 were given Tab Tranexemic acid (500 mg) and Tab Mefenemic acid (500 mg) three times a day during menstrual bleeding for a period of 6 months. Patients in Group 2 were given Tab Mifepristone 50 mg twice a week. They were followed up at 1, 3 and 6 months of starting the medicine. Results were statistically analysed using Microsoft Excel sheet and paired *t*-test.

Results: The average age was 40 years in the Group 2 and 45 years in Group 1. A size reduction of 36.99% in intramural and 39.39% in submucosal fibroids after six months of treatment with Mifepristone resulted in marked clinical improvement. 10% patients had side effects. In 30% of patients symptoms reappeared during the follow up period.

Conclusion: Mifepristone when given in bi-weekly doses was found to be safe, efficacious, and cost effective as compared to treatment with tranexemic acid and mefenemic acid for management of fibroid uterus.

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Introduction

Uterine myomas (fibroids) are the most common benign tumours found in up to 70% women during their reproductive years.[1] Although many women with fibroids are asymptomatic, others find they cause a major disruption to daily life. Malignant transformation in uterine fibroids is seen in only less than 0.1% of cases. The main associated symptoms are often problematic like heavy menstrual bleeding (HMB)[2,3] that may result in severe anaemia and social embarrassment and the presence of a pelvic mass may lead to marked discomfort, abdominal distension, and pressure-related bladder symptoms. Additionally, distortion of the uterine cavity may result in sub-fertility.[4] Approximately 20–40% of these uterine tumours are symptomatic in premenopausal women accounting for 20–80% of hysterectomies in these women.[5–7]

Treatment modalities for fibroids comprise of medical and surgical methods. Though medical methods are easier, availability and cost are the limiting factors. Surgery has always been considered as the final treatment. Various minimally invasive techniques such as catheter guided embolization of myoma feeding vessel or laparoscopy performed to conserve uterus are still beyond reach for most patients. Thus the individual discomfort and the healthcare cost for society due to uterine leiomyoma is of significant importance.

There is biochemical, clinical, and pharmacological evidence to support a role for progesterone in the pathogenesis of fibroids. Hence, the use of antiprogestins like Mifepristone for medical treatment of myomas was an obvious development. Seth et al. found 25 mg Mifepristone administered daily for 3 months resulted in substantial improvements in leiomyoma specific quality of life, bleeding, and leiomyoma size.[8] The concerning side effects are reversible like endometrial hyperplasia,[9] elevated liver functions and others such as abdominal pain, nausea, vomiting, diarrhoea, headache, hot flushes, occasional body-aches. Data suggest that many invasive procedures could be avoided with the routine use of Mifepristone for fibroid tumours care.

With promising results seen with this drug, experiments started with higher doses of Mifepristone. Various studies support the use of Mifepristone (50 mg administered every other day) has effectively resulted in a significant reduction in leiomyoma size, reduced uterovaginal bleeding and increased blood haemoglobin. A potential disadvantage with higher doses of Mifepristone is its antiglucocorticoid effect. Earlier studies have also reported that the changes seen in the endometrium are reversible on discontinuation of treatment.

This study was done to assess the efficacy of Mifepristone in a twice weekly dose of 50 mg for six months. The study also evaluated reversibility of endometrial hyperplasia at six months after cessation of therapy, change in the haemoglobin and the side effects of the drug.

Material and methods

Study population

Patients visiting the outpatient department (OPD) of Department of Obstetrics and Gynaecology of our hospital with complaints of HMB were initially enrolled.

Patients with the following criteria were then, excluded from study:

Current planned pregnancy during study period

Menopausal
Currently breastfeeding

Untreated abnormal pap smear
Presence of conditions other than fibroids contributing to pain and/or bleeding
Hb < 6.0 g/dl

Presence of adnexal mass or tenderness indicating further evaluation of surgery
Grade III/IV hydronephrosis

Endometrial hyperplasia
Presence of any contraindications to Mifepristone including:
- adrenal insufficiency in history
- sickle cell anaemia
- active liver disease (Liver Function Test (LFT) $>$ 1.5 times upper range of normal)
- Severe respiratory disease ($SpO_2 < 90\%$)
- Renal disease (S.creatinine $>$ 1.5 mg/dl)
- Blood clotting defect (abnormal Prothrombin Time/ Partial Thromboplastin Time in Kaolin/International Normalisation ratio (PT/PTTK/INR))
- Thromboembolic disease (History of (H/O) Deep Vein Thrombosis (DVT)/pulmonary embolism)
- H/O allergic reaction to Mifepristone
- Inherited porphyrias
- Presence of any valvular heart disease

Current or recent (within 3 months) use of the following:
- Oral/systemic corticosteroids
- Hormones (E/P/Oral Contraceptive Pills (OCPs))
- Danazol
- Anticoagulant

Use within past 6 months of GnRH analogues
Current/planned use during the study of medications:
- Ketoconazole
- Itraconazole
- Erythromycin
- Phenytoin
- Phenobarbital
- Carbamazepine
- Rifampicin

Total of 120 women in pre-menopausal age group with complaints of menorrhagia, Pictorial Bleeding Assessment

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