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Treatment of Leiomyoma with oral mifepristone in a low resource setting

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Abstract- A common benign tumor of the uterus troubling the women of reproductive age group is fibroids .Primarily it presents with symptoms like menorrhagia, pelvic pain, feeling if heaviness leading to a anemia and discomfort in a women's life. Many women stay asymptomatic and do not seek treatment. The women seeking treatment are primarily treated with symptomatic management with drugs like NSAIDS, hemostatic agents, hematinics, GnRH analogues, Danazol, progesterone oral, depots and IUDs. Minimal invasive procedures like and thermal balloon ablation and uterine artery embolization are expensive and not readily available.The anti-progestin, mifepristone (RU 486) is being now used and studied since the past few decades for its effect on reduction of symptoms of fibroid uterus. This study aims to assess the effect of low dose mifepristone taken for three months on symptomatic patient's leiomyoma over six months. This was a randomized control study done on 100 patients who presented with fibroid, with symptoms, to the department of Obstetrics and Gynecology at SBMCH, Hazaribagh over a period of eighteen months. The study group was given mifepristone 25 mg once a day for 3 months and the control group was given a placebo. Symptoms like menorrhagia, dysmenorrhea, pelvic pain were evaluated in both these groups over six months at interval of one month, three month and six months. Fibroid volume and uterine volume were assessed on ultrasound. Data analysis was done using chi square test. Symptoms like severe menorrhagia, pelvic pain decreased significant in the study group in comparison to the control group. A significant reduction fibroid size was found in the study group. Thus mifepristone is effective in reducing symptoms associated with fibroid uterus.

Key words: Leiomyoma, oral mifepristone, menorrhagia, pelvic pain, dysmenorrhea, Obstetrics, Gynecology

INTRODUCTION

Uterine fibroids are the most common disease in women of reproductive age. Most women with leiomyoma present with symptoms like excessive menstrual bleeding which leads to anemia, pelvic pressure, and increased uterine size[1]. Though there is no definite medical method for complete cure of fibroids, many drugs have been used for medical therapy of fibroids. Drugs like non- steroidal anti-inflammatory drugs, danazol, GnRH analogues show significant reduction in symptoms but they reoccur when the drug in withdrawn. We know from various studies till date that progesterone has a role in fibroid growth. Intrauterine device with progesterone reduces blood loss and uterine size but they cannot be usedwhen the uterus is larger than 12 weeks or cavity is distorted. This led to the introduction of oral antiprogestins for the treatment of fibroid. Mifepristone is a 19 nonsteroid with antiprogesterone and antiglucocorticoid activity.

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Mifepristone is a progesterone receptor antagonist causes the fibroid size to reduce.Reduction in size with mifepristone might be due to reduction in number of progesterone receptors[2]. Wang *et.al.*[3] stated that mifepristone significantly decreases ER and PR in leiomyoma but not in myometrial tissue.

The oral antiprogestin, mifepristone is newly studied treatment for symptomatic fibroids. It has been researched all over the world for symptomatic treatment and for reduction in fibroid size when used in low dose for short interval. The decrease in fibroid volume and improvement of symptoms by mifepristone is similar to GnRH analogues and it has very less side effects. This study done in Sheikh Bikhari Medical College and Hopsital Hazaribag determines the effect of 25 mg of mifepristone on patient symptoms like pelvic pain, dysmenorrhea, menorrhagia and also reduction in uterine size and fibroid volume.

MATERIAL & METHOD

This study was conducted in department of obstetrics and gynecology, SBMCH, Hazaribag from May 2020 to October 202. Patients presenting with symptomatic fibroids were screened and divided into two groups.

Group I: Included 50 patients : mifepristone 25 mg was given once a day for three months. Group II: Included 50 patients : Placebo given for three months.

An informed consent was taken from all 100 patients. Double blinding technique was used.

Inclusion Criteria: symptomatic patients (age 20-50) with fibroid >2cm and uterine volume >150cc on ultrasound.

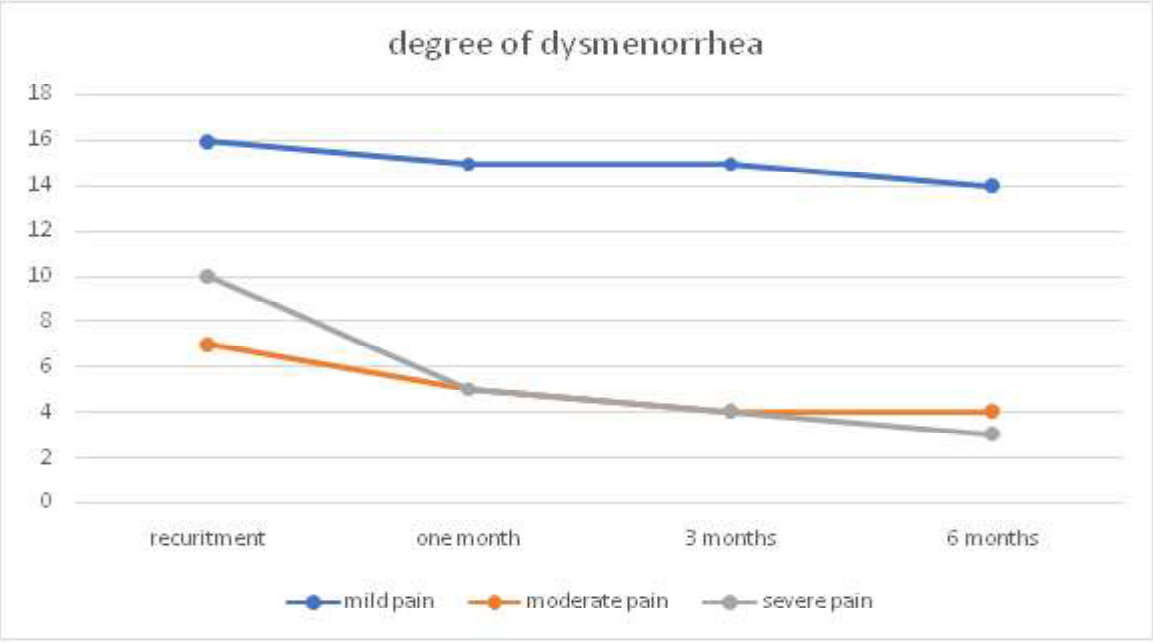
Exclusion Criteria: Patients with PID, adenomyoma, endometriosis, suspected malignancy, bleeding disorders, moderate to severe anaemia, postpartum, on hormonal therapy or contraindications to use mifepristone

After taking detailed medical, surgical and treatment history, patients were evaluated and examined, blood examination was done to rule out anaemia and bleeding disorders and exclude out any other pathological disorder. USG was done to calculate the uterine and the fibroid volume.

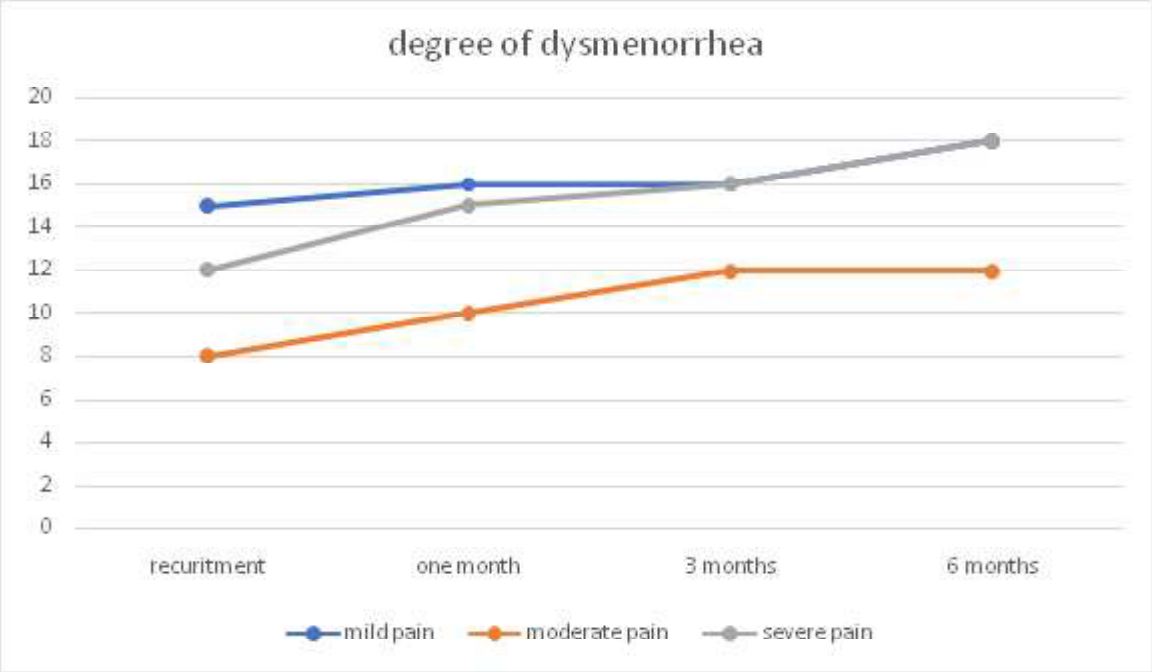
Blood and urine tests were done including thyroid function tests, PAP smear and USG. Formula used was 4/3 π W/2 x L/2 x T/2 (W is transverse width of the fundus; L sagittal length, T is the sagittal thickness. Formula for leiomyoma volume was 4/3π abc, where abc being the radius of the fibroid in three directions. After initial assessment, measurements were taken at one month, three month and six months. At the same time all patients were also assessed for the symptoms as well.

RESULTS

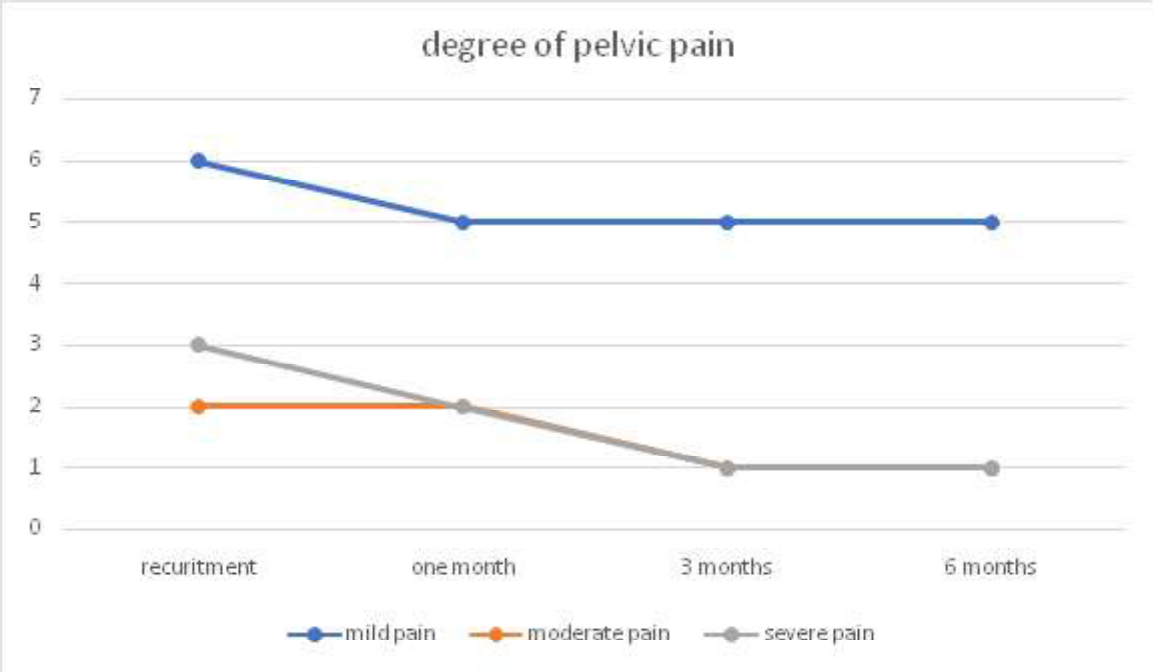
Of total 50 patients in group I, there were 2 dropouts, who were interviewed on phone. Five dropouts were there in-group II.



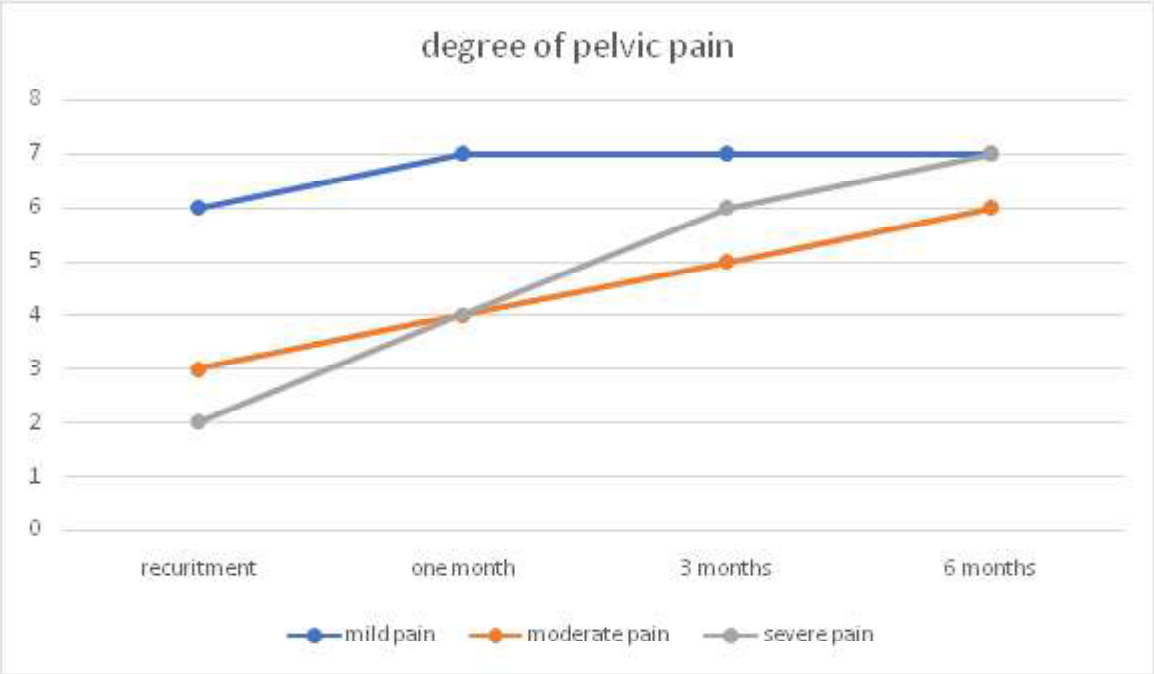
Graph 1: Line graph showing degree of dysmenorrhea



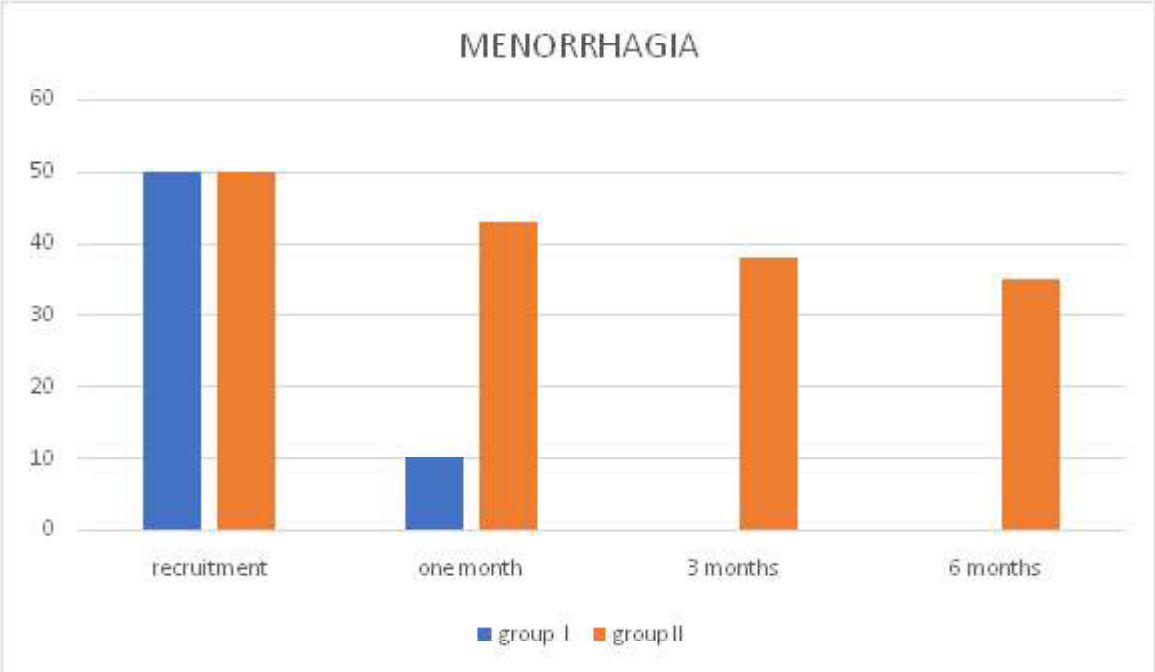
Graph 2: Line graph showing degree of dysmenorrhea



Graph 3: Line graph showing degree of pelvic pain



Graph 4: Line graph showing degree of pelvic pain



Graph 5: bar graph (menorrhagia in patients of both groups on follow up).

Table 1: Showing volume of uterus in group I

Duration	Group I	
	Volume (cc)	Percentage change from baseline
Recruitment	264.2	-------
1 month	232.4	-12.04%
3 months	193.02	-26.94%
6 months	228.04	-13.6%

Table 2: Showing volume of uterus in group II

Duration	Group II		
	Volume (cc)	Percentage change from baseline	P value
Initial	263.92	----------	>0.05
At one month	266.02	+0.7%	<0.001
At three months	270.08	+2.35%	<0.001
At six months	274.10	+3.8%	<0.001

Table 3: Showing volume of fibroid in group I

Duration	Group I	
	Volume (cc)	Percentage change from baseline
Recruitment	138.5	----------
1 month	116.3	-16.42%
3 months	98.7	-28.73%
6 months	104.6	24.4%

Table 4: Showing volume of fibroid in group II

Duration	Group II		
	Volume (cc)	Percentage change from baseline	P value
Initial	132.2	----------	>0.05
One month	135.46	+0.9%	<0.001
Three months	135.23	+2.3%	<0.001
Six months	136.81	+3.5%	<0.001

DISCUSSION

Our study showed patients in the age group of 25-48 years, mostly with the mean age being 34.65 (group I) and 33.78 (group II). This was comparable to observation of Shen *et al.*(2013)[2] and Wang *et al.* (2000)[3]

In this study ,mean parity of patients in group I and group II was 2.56 and 2.88 respectively. This was similar to most of the studies

In-group I, 66% of patients had dysmenorrhea initially with 20% having severe dysmenorrhea. Sixty percent of these women were relieved of severe dysmenorrhea at three months and 70% had relief at six months too. Group II showed increase in patients with severe dysmenorrhea. Kulshrestha *et al.* (2013)[4] reported similar results with 25mg mifepristone with more than 70 percent decrease in dysmenorrhea.

Yang *et al.* (1996)[5] found 100% relief of symptom with 10 and 20mg of mifepristone for 3 months. Shen *et al.*(2013)[2] found significant reduction in dysmenorrhea and menorrhagia in patients with fibroid treated with oral mifepristone .

There was 55% of patients with complete relief from pelvic pain at 3 months and 67% after six months, in group I in our study. Meanwhile, group II showed minor increase in patients with pelvic pain over 6 months. Yang *et al.* (1996)[5] found most patients had relief of pelvic pain.

Eighty percent of patients of patient's in-group I developed amenorrhea and no patient had menorrhagia by six months, in comparison to group II, where menorrhagia persisted.

When we analyzed the mean uterine volume, in group I, the mean uterine volume was 264.2cc initially which decreased by 12.04% (1month) and 26.94% (3 months). After six months it was 228.04cc. Group II showed increase in mean uterine volume increased by 3.8% at the end of six months. The difference in the results of two groups was statistically significant ($p < 0.001$).

Yang *et al.* (1996)[5] found 33% reduction of uterine volume with 20mg mifepristone. Eisinger *et al.* (2005)[6] found 48% and 49% reduction with 5mg and 10mg mifepristone respectively after six months of therapy. Shen *et al.*(2013)[2] also reported significant reduction in uterine and fibroid volume on treatment with mifepristone. Eisinger *et al.* (2005)[6] had similar results.

Most studies demonstrated reduction in fibroid and uterine volume even with difference in the dose and duration of the drug used.

In our study, group I showed mean fibroid volume as 138.5ccinitially,that decreased by 16.42% after 1 month and 28.73% after 3 months. At the same time, group II showed mean fibroid volume initially as 132.2cc which increased by 3.5% after 6 months.

This showed a significant change in the fibroid volume after 3 and 6 months.

Eisinger *et al.* (2003)[7] found decrease in fibroid volume (49%) at six months with 10mg mifepristone whereas Yang *et al.* (1996)[5] reported 33% reduction in fibroid volume. Liu *et al.* (2017)[1] in their comparison study also have stated that there is significant reduction in uterine as well as fibroid volume with use of mifepristone.

Rita *et al.* (2015)[8] found similar results with 25 mg mifepristone used for three months. They found reduction in pelvic pain, dysmenorrhea, menorrhagia and also a significant reduction in fibroid and uterine volume.

The side effects of mifepristone were nausea, vomiting, hot flushes and ocassional diarrhea.

In our study, patients who received mifepristone, 5.6% had nausea and 2% had hot flushes. After 3 months, 6% patients complained of nausea and 4% had hot flushes.

The side effects stopped on stopping the therapy. Similar reports on the side effects were seen on the other studies.

CONCLUSION

Fibroids are the most frequent cause of menorrhagia leading to significant morbidity in women. Due to trouble some symptoms many women prefer to go for surgery. What is needed is an effective, non-expensive and readily available medical treatment. Mifepristone can be used to treat symptomatic fibroids. It can also be a good option other than GnRH analogues for use in pre-operative period. It can reduce fibroid size to decrease the blood loss during surgery. It can be useful in perimenopausal women in whom fibroid would generally decrease in size after menopause and also in nulliparous or unmarried women who do not prefer hysterectomy or myomectomy. Its role in non surgical of fibroid uterus has been studies and is getting preference in the past few years. Our study shows that treatment of fibroids with 25mg mifepristone is useful in symptomatic treatment of fibroids and also causes a significant decrease in uterine and leiomyoma size. These findings suggest valuable role of mifepristone in medical management of fibroid and also in indirectly treating and decreasing the incidence of anemia in women and improving their general well being

REFERENCES

1. **Liu, Chongdong MD; Lu, Qi MM; Qu, Hong MD; Geng, Li MD; Bian, Meilu MD; Huang, Minli MD; Wang, Huilan MD; Zhang, Youzhong MD; Wen, Zeqing MD; Zheng, Shurong MD; Zhang, Zhenyu MD. 2017.** Different dosages of mifepristone versus enantone to treat uterine fibroids. *Medicine*: **96(7):** e6124

2. **Shen Q, Hua Y, Jiang W, Zhang W, Chen M, Zhu X. 2013.** Effects of mifepristone on uterine leiomyoma in premenopausal women: a meta-analysis. *FertilSteril.* Dec;100(6):1722-6.e1-10. doi: 10.1016/j.fertnstert. 2013.08.039. Epub 2013 Oct 2.

3. **Wang H, Jin J. 2000.** Effects of mifepristone on estrogen and progestin receptors in human uterine leiomyoma. *Zhonghua Fu Chan Ke Za Zhi.* **35(2):**79-81.

4. **Kulshrestha V, Kriplani A, Agarwal N, Sareen N, Garg P, Hari S, Thulkar J. 2013.** Low dose mifepristone in medical management of uterine leiomyoma - an experience from a tertiary care hospital from north India. *Indian J. Med Res*. **137(6):**1154-62.

5. **Yang Y, Zeng s, Li K.1996.** Treatment of leiomyoma by two different doses of mifepristone (in chinese). *Zhonghua Fu Chan Ke Za Zhi.* **31:** 624-6.

6. **Eisinger SH, Bonfiglio T, Fiscella K, le roux HD, Guzick DS. 2005.** Twelve month safety and efficacy of low dose mifepristone for uterine myomas. *J. Minim Invasive Gynecol.* **12:**227-233.

7. **Eisinger SH, Meldrum S, Fiscella K, le Roux HD, Guzick DS.2003.** Low dose mifepristone for uterine leiomyomata. *Obstet Gynaecol.* **101:** 243-50.

8. **Rita Lal, Akriti Ashwini, Sweta Lal. 2015.** Role of Low Dose Mifepristone in the Treatment of Symptomatic Fibroid Uterus: A Double Control Randomized Control Trial. *Journal of Evolution of Medical and Dental Sciences*. **4(57):** 9990-10000

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