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COMPARISON BETWEEN LETROZOLE AND SYNTHETIC PROGESTINS IN MANAGEMENT OF UTERINE LEIOMYOMA

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ABSTRACT

Background: Fibroids are considered the most common benign pelvic tumor in women, and they arise at the expense of smooth muscle fibers interspersed with connective tissue. They may be symptomatic or asymptomatic, and the severity and quality of symptoms vary according to the location, size, and number of the fibroids, and they need treatment only if they cause symptoms. **Objective:** Main objective: To compare the clinical and echogenic efficacy of treatment with letrozole and synthetic progestins in the management of fibroids. Second objective: to reduce the use of surgical operations to remove fibroids, and thus reduce the complications resulting from them. **Materials and methods:** This study is a prospective study that included reviews with clinical symptoms of echogenic fibroids, especially with complaints of menstrual bleeding during the period from March 2022 and March 2023, where the women were divided into two groups: the first was treated with letrozole 2.5 mg daily continuously for 12 weeks. the second treated with progestin (medroxyprogesterone acetate) 150 mg as a single dose for 3 months, and studied the clinical improvement through the decrease in the intensity of menstrualbleeding or dysmenorrhoea and the echo change in the size of the fibroid tumer as a result of treatment, and it was compared between the two groups. The letrozole group included 27 patients and the progestin group 23 patients. **Results:** The average age of women in the study was (44.15 years), and the average size of the fibroid tumor in the letrozole group was 3.44 cm compared to 3.32 cm in the progestin group. The size of the echogenic fibroid decreased by 42.1% in 85.2% of the letrozole-treated patients and 24.1% in the progestin-treated patients, of while the size remained constant in 7,4% of the letrozole group and 30,4% of the progestins group, and its volume increased in 7,4% of the letrozole group and 17,4% of the progestins group, with a stst Clinically, menstrual bleeding decreased in 85,2% of the letrozole group compared to 82,6% of the progestin group, without a statistically significant difference. **Conclusion:** Clinical and echogenic improvement was statistically significant in the letrozole and synthetic progestins groups, with letrozole being statistically significantly superior to progestins in echogenic terms. Therefore, it is recommended to conduct more extensive clinical studies on this benefit in preparation for taking it as a conservative treatment in specific cases of fibroids, especially those associated menorrhagia.

KAYWORDS: Fibroids, letrozole, progestin, treatment, bleeding, dysmenorrhoea, menorrhagia.

INTRODUCTION

Fibroids are benign tumors that arise from the smooth muscles of the uterine muscle and are the most common benign tumor that affects the female reproductive system, as it is seen in about 25% of women. They may be symptomatic or asymptomatic, and the severity and type of symptoms vary according to the location of the fibroid, its size, and the number of these tumors. Fibroids need for treatment only if it causes symptoms, and surgery is the traditional and radicaltreatment for it. With the exception of surgery, there are a number of other treatment options, including selective design of the uterine artery and various hormonal therapies.

Letrozole is a non-steroidal aromatase inhibitor that inhibits the conversion of androgens toestrogens in adult neoplastic and non-neoplastic tissues.

Medroxyprogesterone acetate is a synthetic progesterone steroid.

The importance of the study stems from the attempt to reduce the proportion of surgeries toremove fibroids and to resort instead to drug therapy to reduce the size of these tumors andalleviate the clinical symptoms resulting from them, and thus reduce the complications and future risks of these operations.

MATERIALS AND METHODS

The study was conducted in the Department of Obstetrics and Gynecology at Tishreen University Hospital in Lattakia for a full year from (2022 to 2023).

Study design

It Was Prospective Study.

Inclution Criteria

- The patient is of reproductive age.
- The patient desiring medical treatment.
- Non-pregnant and non-lactating patient.
- The patient who is committed to contraception during the treatment period.
- The fibroid is less than 8 cm.

Exclusion criteria

- The patient is in menopause.
- Pregnant or lactating patient.
- The patient who refused to conceive during the treatment period.
- The patient desiring surgery.
- Hepatic insufficiency patients.
- Reviews complain of infertility.
- Large fibrous tumor greater than 8 cm.
- A story of rapid tumor growth over the past months.

Methods

The research sample included 60 patients, 10 of whom were discharged from the study, where 4 patients resorted to surgery, 4 patients stopped taking Letrozole due to the occurrence of bone and joint pain, and 2 patients stopped taking it also due to the occurrence of menopause (amenorrhea). Also, patients who refused or were unable to use a safe contraceptive method during the period of taking the drug were also excluded from the study, so that the actual number of the sample was 50 patients, divided into 27 patients who took letrozole and 23 patients who took medroxyprogesterone acetate.

All patients were under menopause, and the ages of the entire research sample ranged between22-53 years, with an arithmetic mean of 44.15 years.

For all non-virgin patients, a cervical smear was performed with a sound result, and an investigative uterine curettage was performed for only 10 patients, and the result denied the presence of endometrial malignancy.Five patients underwent a hysterectomy after the end of thedrug application period, due to the lack of sufficient clinical improvement and the result of histopathology of the excised sample showed the presence of a fibroid tumer without the presence of malignancy.

The sample was divided into two groups: the first group included 27 patients who were givenletrozole 2.5 mg for 12 consecutive weeks.

The second group included 23 patients who were given medroxyprogesterone acetate 150 mg asa single dose for 3 months.

The subject of the research was explained, the patient's questions were answered, and herinformed consent was taken, after she had met the criteria for entry into the study.

Data analysis

a This study is a randomized clinical trial Statistical analysis was done using IBM SPSS statistics (version 20). Descriptive statistics: Quantitative variables with measures of central tendency and measures of dispersion.qualitative variables with frequencies and percentages The following tests were used to study the relationship between the two research groups: Independent T Student test to compare the mean of two independent groups. Chi-Square or Fisher exact test to study the relationship between qualitative variables. The results are statistically significant with a p-value >0.05. Adopting the program (IBM SPSS statisticsVersion20) to calculate statistical coefficients and analyze results.

RESULTS

The patients in both groups were subjected to a set of variables, namely age group, reproductive history, smoking prevalence, positive family history of tumor, menorrhagia andfibroid size.

No statistically significant differences were observed between the two groups depending on the age groups, reproductive history, prevalence of smoking, positive family history, and menorrhagia. As for the size of the fibrous tumor, we note that there are no statistically significant differences between the two research groups befor starting The treatment, the average maximum diameter in the progestin group was3.32 cm compared to 3.44 cm in the letrozole group. However, after applying the treatment, there was a decrease in the size of the fibroid in both groups, and the highest decrease was in the letrozole group, where it reached 42.1% compared to 24.1% in the progestin group, with significant statistical differences.

As for the side effects, it included in the letrozole group, the occurrence of cysts on the appendages in two patients with a size of 3 cm and 5 cm, occurrence of amenorrhea in 4 patientsand bone and joint pain in 4 patients.

As for the progestin group, only two cases of cysts on the appendages of 4 cm and 5 cm wererecorded, which were subjected to spontaneous recovery after monitoring.

CONCLUSION

We note from our study that clinical and echogenic improvement was statistically significant inboth groups, with letrozole statistically significantly superior to progestin in echogenicity.

Table (1): Distribution differences between the two research groups according to age groups.

Age group(year)	Synthetic progestins	Letrozole	Total	P-value
20-29	2 (8.7%)	1 (3.7%)	3 (6%)	0.5
30-39	5 (21.7%)	6 (22.2%)	11 (22%)	
40-49	15 (65.2%)	19 (70.4%)	34 (68%)	
≥50	1 (4.4%)	1 (3.7%)	2 (4%)	

Table (2): Distribution differences between the two research groups according to reproductivestory.

Reproductivestory	Synthetic progestins	Letrozole	Total	P-value
Infertility	5 (21.7%)	6 (22.2%)	11 (22%)	0.09
Virgen	8 (34.8%)	4 (14.8%)	12 (24%)	
primigravida	1 (4.4%)	1 (3.7%)	2 (4%)	
Multipara	9 (39.1%)	16 (59.3%)	25 (50%)	

Table (3): Distribution differences between the two research groups according to smoking story.

Smoking story	Synthetic progestins	Letrozole	Total	P-value
Smoking	5 (21.7%)	9 (33.3%)	14 (28%)	0.1
No-smoking	18 (78.3%)	18 (66.7%)	36 (72%)	

Table (4): Distribution differences between the two research groups according to positive familystory.

Family story	Synthetic progestins	Letrozole	Total	P-value
Positive	5 (21.7%)	7 (25.9%)	12 (24%)	0.5
Negative	18 (78.3%)	20 (74.1%)	38 (76%)	

Table (5): Distribution differences between the two research groups according to prevalence ofmenorrhagia.

Research group	Synthetic progestins	Letrozole	Total	P-value
Menorrhagia	17 (73.9%)	21 (77.8%)	38 (76%)	0.3
No menorrhagia	6 (26.1%)	6 (22.2%)	12 (24%)	

Table (6): Mean size of uterine leiomyoma size before and after treatment initiation.

Uterine leiomyomasize	Research group		P-value
	Synthetic progestins	Letrozole	
Before of treatment	3.32±1.1	3.44±1.4	0.7
After of treatment	2.52±0.7	1.99±0.4	0.003

Table (7): Echo changes in patients.

Echo changes	Synthetic progestins	Letrozole	Total	P- value
Reduction in the size of uterine leiomyoma	12 (52.2%)	23(85.2%)	35(70%)	0.004
Increase in the size of uterine leiomyoma	4 (17.4%)	2 (7.4%)	6 (12%)	
No change in the size of uterine leiomyoma	7 (30.4%)	2 (7.4%)	9 (18%)	

Table (8): Distribution differences between the two research groups according to clinicalimprovement.

Clinical improvement	Synthetic progestins	Letrozole	Total	P-value
Yes	19 (82.6%)	23 (85.2%)	42 (84%)	0.1
No	4 (17.4%)	4 (14.8%)	8 (16%)	

DISCUSSION

The current study is a controlled prospective study conducted on 50 patients from Tishreen University Hospital in Lattakia who fulfilled the study conditions.

Pharmacological treatment of fibroids is a necessary recommendation in many previous reports aimed at reducing the need for surgical operations and the complications that follow. There are many drugs used to treat fibroids, including letrozole and synthetic progestins.

This study was conducted to compare the effectiveness of letrozole and synthetic progestins in the management of fibroids. The patients in the study were subjected to the following variables: age group,reproductive history, smoking prevalence, positive family history of tumor, menorrhagia and fibroid size.

No statistically significant differences were observed between the two groups depending on the age groups, reproductive history, prevalence of smoking, positive family history, and menorrhagia. As for the size of the fibrous tumor, we note that there are no statistically significant differences between the two research groups before starting the treatment, the average maximum diameter in the progestin group was 3.32 cm compared to 3.44 cm in the letrozole group. However, after applying the treatment, there was a decrease in the size of the fibroid inboth groups, and the highest decrease was in the letrozole group, where it reached 42.1% compared to 24.1% in the progestin group, with significant statistical differences.

As for the side effects, it included in the letrozole group, the occurrence of cysts on the appendages in two patients with a size of 3 cm and 5 cm, occurrence of amenorrhea in 4 patientsand bone and joint pain in 4 patients.

As for the progestin group, only two cases of cysts on the appendages of 4 cm and 5 cm wererecorded, which were subjected to spontaneous recovery after monitoring.

Our current study focused on the effect of treatment on clinical symptoms, and this agrees with astudy conducted in Turkey 2008 and a study in Iran 2011. The dose of letrozole in our study was 2.5 mg, and this is contrary to the Turkish study 2008, where the dose was 5 mg, as well as the Brazilian study 2008, which used anastrazole 1 mg instead of letrozole. These studies agreed on the duration of treatment, which is 3 months.

CONCLUSIONS

Clinically, menstrual bleeding decreased in 82.6% of the progestin group and 85.2% of theletrozole group without a statistically significant difference.

- The size of the fibroid decreased in 52.2% of the synthetic progestins group and in 85.2% of the letrozole group.
- The size of the fibroid increased in 17.4% of the synthetic progestins group and in 7.4% of the letrozole group.
- The size of the fibroid remained unchanged in 4.30% of the synthetic progestins groupand in 7.4% of the letrozole group.

Recommendations

It is recommended to conduct larger clinical studies on the usefulness of Letrozole as a preludeto taking it as a conservative treatment in specific cases of fibroids, especially those associatedwith menorrhagia.

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