

Letrozole, for the Management of Chronic Pelvic Pain Resulting from Endometriosis

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ABSTRACT

Background: Letrozole, an aromatase inhibitor that inhibits the final step of the estrogen biosynthesis pathway to prevent estrogen synthesis, has been utilized in a variety of infertile scenarios. A common gynecological pain problem called endometriosis involves tissue that resembles the tissue that typically lines the inner layer of the uterus. It frequently results in fertility issues. According to the trials, the Letrozole medication continues to reduce the severity of persistent pelvic pain. According to reports, Letrozole therapy relieves pelvic pain brought on by endometriosis.

Objective: In this study, we evaluated Letrozole's effectiveness in treating chronic pelvic discomfort associated with endometriosis.

Study Design: A cross-sectional study

Place and Duration: This study was conducted at Sandeman Provincial Hospital (SPH) / BMCH, Quetta Pakistan from December 2021 to December 2022.

Methodology: A total of 60 patients with endometriosis were taken in this study. Patients with a past history of treatment for endometriosis with varying degrees of improvement were also included. Data was analyzed on SPSS version 24.0. Before starting the treatment, an initial diagnostic laparoscopy was used to diagnose and score endometriosis. Oral administration of Letrozole 2.5mg, celbex 200mg three times a day, calcium citrate 1000 mg, progestin norethisterone acetate 5 mg, and vitamin D (1000 IU) was given for 6 months

Results: The mean age of the participants was 30.9 years. A total of 26 (43.3%) patients presented with dysmenorrhea. Out of 60 patients, 43 (71.6%) were nulliparous. The mean visual analogue scale which was 7.12 at the start of the therapy, dropped to 6.8 (p-value 0.02) in one month and dropped to 3.3 in six months of the therapy.

Conclusion: Letrozole has been shown to be effective in treating pelvic pain related to endometriosis, with notable pain reduction and no recurrence of symptoms.

Keywords: Letrozole, Endometriosis, pain score

INTRODUCTION

Letrozole, an aromatase inhibitor that inhibits the final step of the estrogen biosynthesis pathway to prevent estrogen synthesis, has been utilized in a variety of infertile scenarios. [1] Letrozole is an oral aromatase inhibitor (AI) that is non-steroidal, highly selective, and capable of reversibly binding to the rate-limiting enzyme P450 aromatase in the pathway that produces estrogen. This prevents the conversion of androstenedione to estrone and testosterone to estradiol. [2].

As a feedback mechanism to promote ovulation, the down-regulated estrogen boosts pituitary follicle-stimulating hormone (FSH) release. Letrozole is now frequently used to boost follicle size in ovulatory women and to stimulate ovulation in anovulatory infertile patients. Moreover, Letrozole is utilized as an adjuvant during cycles of intracytoplasmic sperm injection (ICSI) and in vitro fertilization (IVF) [3, 4].

A common gynecological pain problem called endometriosis involves tissue that resembles the tissue that typically lines the inner layer of the uterus. It frequently results in fertility issues [5]. According to the investigations, Letrozole medication continued to reduce the severity of persistent pelvic pain [6]. Between five and ten percent of women of reproductive age have infertility and pelvic pain [7]. Hysterectomy and bilateral oophorectomy are the treatments of choice for a sizable percentage of individuals whose chronic pelvic pain is caused by endometriosis [8].

An aromatase enzyme that was discovered locally in endometriotic implants and found to be predictive of estrogen synthesis has been proposed as a molecular aetiology for endometriosis [9]. Letrozole, a third-generation aromatase inhibitor, is effective at locally and systemically suppressing the production of estrogen. Letrozole medication purportedly resolves endometriosis and associated pelvic pain [10]. They are well tolerated. Letrozole, which currently has only one registered indication, was found to be efficacious in a variety of breast cancer

scenarios. Letrozole was first employed in animal ovulation induction (OI) in 1993. (11). Patients with polycystic ovarian syndrome (PCOS) had a significant rate of ovulation, according to the first pilot trial for the clinical use of Letrozole for OI conducted in 2000 [12]. Subsequently, the purpose of this study is to assess Letrozole's effectiveness in treating endometriosis patients' pelvic pain.

METHODOLOGY

In this study, 60 patients with endometriosis were included, to evaluate the effect of Letrozole in the treatment of endometriosis-related chronic pelvic pain. Patients with a past history of treatment for endometriosis with varying degrees of improvement were also included. Before starting the treatment, an initial diagnostic laparoscopy was used to diagnose and score endometriosis. Oral administration of Letrozole 2.5mg, celbex 200mg three times a day, calcium citrate 1000mg, progestin norethisterone acetate 5mg, and vitamin D (1000 IU) was given for 6 months. During each visit, pain levels were recorded using a 0–10 visual analogue scale (0: no pain; 10: maximum pain), Pelvic discomfort and all other reported adverse effects were documented and graded using a visual analogue scale following a three-month course of therapy.

SPSS version 24.0 was used for the statistical analysis. To determine significance, Student's t-test and chi-square test were employed. The significance threshold was conventional set at $p < 0.05$.

RESULTS

The findings of the present study revealed that the mean age of the participants was 30.9 years. A total of 26 (43.3%) patients presented with dysmenorrhea. Out of 60 patients, 43 (71.7%) were nulliparous. Out of 60, 22 (36.7%) had previously received oral contraceptives, 21.7% received GnRH agonists and 11(18.3%)

received medroxyprogesterone acetate or 07(11.7%) under went laparotomy with ovarian cystectomy. (As shown in Table I)

In response to treatment, the patient's pelvic pain score considerably decreased. The mean visual analogue scale which was 7.12 at the start of the therapy, dropped to 6.8 (p-value 0.02) in one month and dropped to 3.3 in six months of the therapy. The most important adverse effects thought to be associated with treatment were headache and depression. (As shown in Table II).

Table 1: Characteristics of the Study's Patient Population

Variable	Yes	%	No	%
Dysmenorrhea	26	43.3	34	56.7
Nulliparous	43	71.7	17	28.3
Oral contraceptives	22	36.7	38	63.3
GnRH agonists	13	21.7	47	78.3
Medroxyprogesterone acetate	11	18.3	49	81.7
Ovarian cystectomy.	7	11.7	53	88.3
Age	Range 18-43 mean, SD (27.4 , 3.06)			

Table 2: Complaints of Side Effects during the Treatment

Adverse events	No of patients	%
1. Headache	7	11.6667
2. Depression	6	10
3. Body ache	4	6.66667
4. Mood Swings	2	3.33333
5. Bone, joint pain	2	3.33333

DISCUSSION

Five to ten percent of women of reproductive age suffer from pelvic pain and infertility. The studies have observed that the intensity of chronic pelvic pain continued to decrease during treatment with Letrozole [6, 7]. Therefore, as the most important finding of the study, the present study evaluated the efficacy of Letrozole in the treatment of endometriosis-related chronic pelvic pain.

In our study, it was observed that the pain of the study subjects improved over time during taking Letrozole, consistent with the findings of our study, a similar study, conducted in China by Yi Zhao, reported that the intensity of chronic pelvic pain and deep dyspareunia was significantly decreased at both 1-month after treatment and 6-month follow-up [6].

In our study, certain side effects of Letrozole were reported by the patients during the course of treatment. The most common adverse effect in this study was headache, in line with our findings, Mejia et al reported that headache, hot flashes, abdominal bloating, and abdominal pain including cramps were the most common adverse effects [13].

Furthermore, a small number of investigations revealed that Letrozole can pass the blood-brain barrier, obstruct the hippocampus estrogen synthesis, and cause cognitive impairment in addition to other neurological symptoms (14–16). According to certain research, receiving treatment with AI has been linked to a variety of side effects, including mood swings, somnolence, anxiety, lethargy, and hot flashes (17). (18, 19, 20).

In the present study, the mean visual analogue scale which was 7.12 at the start of the therapy, dropped to 6.8 (p-value 0.02) in one month and dropped to 3.3 in six months of the therapy. In line with these findings, endometriosis and the resulting pelvic pain are said to be resolved as a result of Letrozole therapy. Laparoscopic grading utilizing ASRM scoring sheets can identify the stage of the disease and the level of its severity [10, 21].

CONCLUSION

With significant pain reduction and no recurrence of symptoms, Letrozole has been shown to be effective in treating pelvic pain associated with endometriosis, according to the study's overall findings.

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