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Effect of Letrozole on Symptomatology and Health Related Quality of Life in Reproductive Age Group Women with Leiomyomas



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Sarita Goyal, Sanjana Dawra, *Nirmala Duhan, MC Gupta

Department of Pharmacology, Pt. B.D. Sharma, Post graduate institute of medical sciences, Rohtak (Haryana), 124001, India

**Department of Obstetrics and Gynaecology Pt. B.D. Sharma, Post graduate institute of medical sciences, Rohtak (Haryana), 124001, India*

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ABSTRACT

Introduction: Uterine leiomyomas are the most common benign pelvic tumors in women of reproductive age. Abnormal uterine bleeding, pelvic pain and abdominal pressure are the main symptoms which can interfere with daily physical and social activities and negatively affect the well-being and health-related quality of life (HRQOL) of women with fibroids. Aromatase inhibitors such as letrozole have an important role in the treatment of leiomyomas. In spite of advances in the treatment of leiomyomas, one area that has been relatively neglected is the assessment of their impact quality of life.

Objectives: To investigate the effects of letrozole on health-related quality of life and symptom severity in women with uterine leiomyomas.

Material and methods: Thirty two premenopausal women aged 20-50 years, diagnosed with symptomatic fibroids were prescribed tablet letrozole 2.5 mg daily orally for a period of 12 weeks. Health Related quality of life and Symptom Severity were assessed at baseline and at 12 weeks post-treatment using the Uterine Fibroid Symptom Health Related Quality of Life Questionnaire.

Results: Health related quality of life score at baseline was 51.64 ± 3.49 and increased significantly to 74.04 ± 2.58 (43.37%) at 12 weeks with letrozole. Uterine fibroid symptom severity score reduced from 46.14 ± 2.83 at baseline to 23.80 ± 2.24 (48.40%) at the end of 12 weeks.

Conclusion: Letrozole can be a beneficial option for the management of myomas thus having significant improvement in both physical and psychological components of quality of life.

INTRODUCTION

Aim and objective:

To investigate the effects of letrozole on health-related quality of life and symptom severity in women with uterine leiomyomas.

Review of literature:

Uterine leiomyomas are one of the important common health issues in reproductive age group women, with an estimated cumulative incidence of 80% by the age of 50 years.¹ About 50% of women with uterine leiomyomas are symptomatic, majority of the clinical presentations being abnormal uterine bleeding, anemia, abdominal pain, increased urinary frequency and infertility.² Research shows that fibroids are hormone sensitive tumors and other factors such as increasing age, family history, early menarche, genetic alterations, obesity are associated with them.³ Uterine fibroids can have a negative impact on quality of life, leading to personal feelings of anxiety, low self esteem, embarrassment, shame, decreased work productivity and physical activity. It has been observed that chronic illness and recurrence of symptoms create a state of self criticism and discouragement in women having them.^{2,4} Effective treatment can reduce the burden of these symptoms as well as the associated psychological distress and thus improve health-related quality of life (HRQOL). Traditional treatments for symptomatic fibroids includes a wide variety of surgical techniques such as hysterectomy but their cost and impact on fertility remain as the main concerns with them, thus women prefer minimally invasive or non invasive treatment options.⁵ Different medical management options available for myomas are combined oral contraceptives, danazol, GnRH agonists, LNG-IUS. All the above mentioned options can control the symptoms initially but are usually associated with side effects such as hot flushes, acne, weight gain, intermenstrual bleeding, have no or less effect on regression of the size of leiomyomas.⁶ Aromatase inhibitors such as letrozole, anastrozole are widely being utilized in the treatment of myomas due to their contribution in decreased conversion of androgens to estrogens. Letrozole is a reversible, competitive, selective non-steroidal inhibitor of aromatase that is rapidly absorbed from the gastrointestinal tract and has been associated with rapid reduction of menorrhagia and myoma size thus leading to improvement in symptomatology related to fibroids and avoidance of the initial flare-up.^{7,8}

MATERIALS AND METHODS

Study design

This was a prospective, interventional, clinical study carried out at a tertiary care centre in North India after approval by the institutional ethical committee with the objective of evaluation of effects of letrozole on the health related quality of life and symptom severity score in women with uterine fibroids.

Study Population

Thirty two premenopausal women aged between 20 and 50 years, presenting with menstrual symptoms or pressure symptoms on the bowel or urinary system, having either a single or multiple intrauterine myomas of size >2 cm to 10 cm were included in this study. Women with impaired renal function, pregnancy, use of any hormonal medication in the preceding 2 months, previous hormonal or surgical treatment for leiomyomata or a history of previous deep vein thrombosis were excluded. After written informed consent, detailed history and examination, pelvic ultrasonography was conducted to note the size, number and location of myoma. All patients received tablet letrozole 2.5mg per day for a period of 12 weeks. Detailed history and demographic profile were noted in all the cases.

Uterine Fibroid Symptom and Health-Related Quality of Life Questionnaire (UFS-HRQOL)⁹:

The UFS-HRQOL is a questionnaire based score consisting of two parts that are, symptoms severity score and quality of life score. Patients were analyzed for reduction in symptom severity score and improvement in quality of life score at baseline (week 0) and at 12 weeks.

For Symptoms:

assessment was done with symptom severity score which includes questions regarding severity of symptoms such as menorrhagia, urinary frequency, dysmenorrhoea etc. Higher values were indicative of greater symptom severity and lower scores indicated minimal symptom severity.

For HRQOL:

Health-related quality of life included various subscales such as concern, activities, energy/mood, control, self-conscious and sexual function. Higher scores were indicative of better HRQOL.

Statistical Analysis

Data was recorded and entered into a Microsoft Excel Sheet. For all descriptive and analytical analysis, Statistical Package for Social Sciences (SPSS) Version 23 was used. Data was expressed as Mean \pm SEM, number (%) depending on nature of data. The outcomes of quality of life and symptom severity score was compiled and analyzed using parametric test. p-value < 0.05 was considered significant.

RESULTS

A. Uterine fibroid symptom severity score

The uterine fibroid symptom severity score was evaluated in all the patients before drug administration (baseline) and at the end of 12 weeks. As shown in **Figure 1**, baseline symptom severity score with letrozole was **46.14 \pm 2.83** which reduced to **23.80 \pm 2.24 (48.40%)** at 12 weeks and this decrease was statistically significant ($p < 0.05$). These observations indicate that letrozole was efficacious in improving the symptoms associated with fibroids.

B. Uterine fibroid health related quality of life score

The improvement in health related quality of life score was recorded in all the patients at the end of 12 weeks. As shown in **Figure 1**, baseline quality of life score with letrozole was **51.64 \pm 3.49** which increased to **74.04 \pm 2.58 (43.37%)** at week 12 and this increase was statistically significant. ($p < 0.05$).

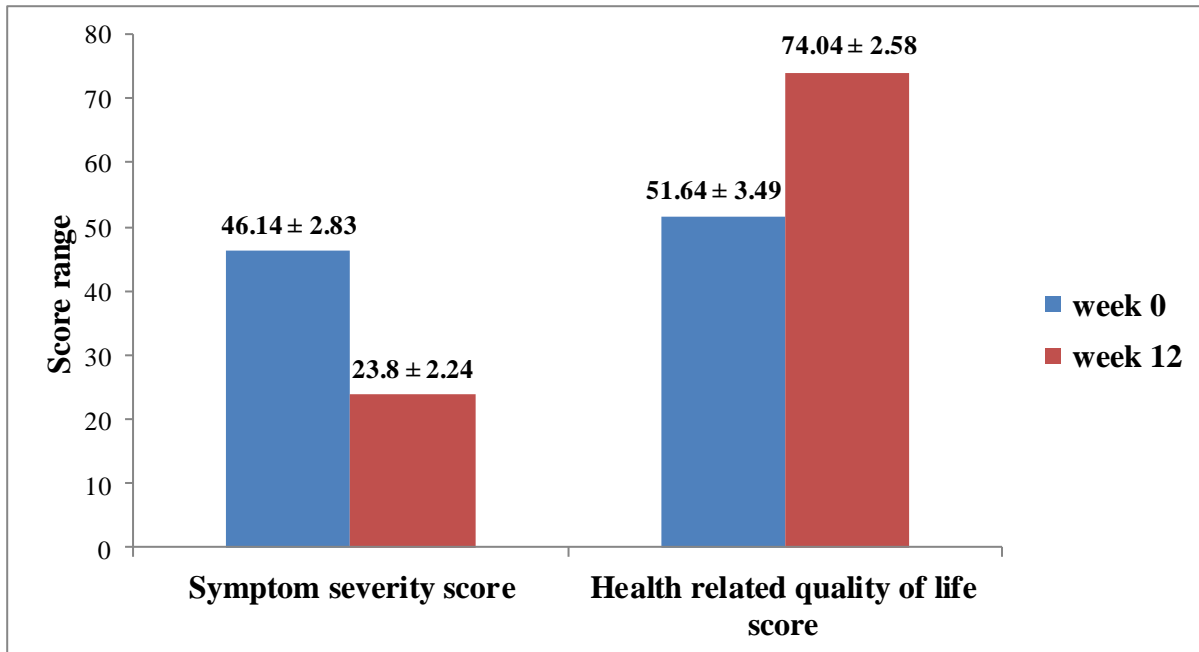


Figure No. 1: Symptom severity score and health related quality of life score at week 0 and at 12 weeks after treatment

DISCUSSION

Menorrhagia along with dysmenorrhoea, fatigue associated with fibroids creates an environment of mental and physical distress in the life of women having them due to the severity of symptoms, common misbeliefs regarding menstruation and association of such symptoms with malignancies. In an online survey, conducted in around 20000 women diagnosed with symptomatic fibroids, Zimmermann et al, reported severe, moderate and mild negative impact on their quality of life in 14.8%, 18.3% and 20.6% respectively, in the last 12 month on their daily lives. They also reported a dramatic decline in quality of life of up to 27.7%, 27.2% and 42.9% of women due to general impairment in work productivity, family life and sexual life, respectively.¹⁰

Duhan et al,¹¹ conducted a study on 30 premenopausal women aged between 30 and 55 years with menstrual or pressure symptoms and having a single intrauterine myoma of size 4 cm or more with or without one or more additional myoma each of size 2 cm or less, who received letrozole 2.5 mg for a duration of 3 months, and reported that mean myoma size reduced from 5.4 ± 1.3 cm to 4.3 ± 0.9 cm ($p < 0.05$) and the myoma volume exhibited a reduction of 52.45% ($p = 0.00$), with nausea and hot flushes as main adverse effects observed.

Parsanezhad et al,⁸ compared letrozole 2.5 mg per day and triptorelin (3.75 mg/month) for 12 weeks in premenopausal women with leiomyomas. A total of 70 subjects were taken with myoma of size more than 5 cms. Myoma volume reduction was 45.6% with letrozole as compared to 33.2% with triptorelin.

In this study, letrozole showed a statistically significant improvement in symptom severity score and quality of life score at 12 weeks. This improvement can be related to the amelioration of the symptoms such as menorrhagia and dysmenorrhea and myoma size by letrozole.

CONCLUSION

Treatment with letrozole was associated with significant improvement in both physical and psychological components of quality of life suggesting that letrozole can be promising, non invasive treatment option for the management of myomas.

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