Oncology Treatment Discovery, 2023, Volume 1, Issue 3
http://ojs.bbwpublisher.com/index.php/OTD

Analysis of the Effect of Letrozole on Patients Undergoing Postoperative Endocrine Therapy for Breast Cancer

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Abstracts: *Objective:* To investigate the effect of letrozole on patients undergoing postoperative endocrine therapy for breast cancer. *Methods:* The period of the study was from June 2021 to January 2023, and 40 patients who were undergoing postoperative endocrine therapy for breast cancer were grouped into two groups by randomized numerical table method: the observation group and the control group. The observation group was given letrozole and the control group was given tamoxifen. At the end of the medication, the results of each index of the two groups were compared. *Results:* After medication, The Kupperman score of the observation group was lower and Karnofsky Performance Scale (KPS) score was higher compared to the control group ($P < 0.05$). Besides, the high-density lipoprotein cholesterol (HDL-C) level of the observation group was higher than that of the control group after treatment ($P < 0.05$). Moreover, the adherence to medication and regular follow-up rate of the observation group was higher than that of the control group ($P < 0.05$). Lastly, all liver function indexes of the observation group were lower than those of the control group after treatment ($P < 0.05$). *Conclusion*: Letrozole is more effective in treating breast cancer patients who are undergoing postoperative endocrine therapy, with less impact on blood lipids and liver function. Therefore, it is worthy of further research and application.

Keywords: Breast cancer; Postoperative endocrine therapy; Letrozole; Efficacy

Online publication: December 26, 2023

1. Introduction

Breast cancer is a malignant tumor disease that is highly prevalent among women. It is life-threatening and has a mortality rate, making timely treatment very important. As the population ages, the incidence of breast cancer among the elderly has been increasing. Patients in this demographic often experience a significant decline in bodily functions, resulting in slow cell growth and low invasiveness, coupled with high positive rates of progesterone receptors and estrogen receptors. Surgery is usually the primary treatment option for breast cancer, and it is especially important to provide effective endocrine therapy after the surgery. Endocrine therapy is usually performed at the later stage of the disease, most patients have small subclinical metastatic foci in the early stage of the disease, which leads to the ineffectiveness of the therapy. Neoadjuvant chemotherapy is a

systemic treatment that can reduce the stage of malignant tumors and control local foci to increase the success rate of the treatment. This approach is highly safe as it will damage the patient's body while controlling the progression of the disease, thus prolonging patients' survival and improving their quality of life after surgery. Common endocrine therapy drugs include letrozole and tamoxifen. Letrozole is an effective aromatase inhibitor in endocrine therapy for breast cancer [1]. The purpose of this paper is to investigate the effect of letrozole in patients with postoperative endocrine therapy for breast cancer.

2. General information and methodology

2.1. Baseline data

Patients with postoperative endocrine therapy for breast cancer were selected for this study (admitted between June 2021 and January 2023). The patients were divided into 2 groups, with 20 cases in each group. The study was approved by the Medical Ethics Committee.

Inclusion criteria: (1) diagnosed with hormone receptor-positive breast cancer through postoperative pathological confirmation [2]; (2) all blood lipids and lipid-related data were collected in the fasting state in the morning; (3) patients and their families signed informed consent; (4) hormone levels were in the menopausal state, i.e., aged < 60 years old, with a duration of natural menopause of ≥ 12 months; (5) have not received chemotherapy, tamoxifen, or triamcinolone acetonide therapy recently, FSH and estradiol levels were within the postmenopausal range.

Exclusion criteria: (1) Combined organ failure lesions; (2) cognitive disorders; (3) recently received other anticancer treatments; (4) the presence of other malignant lesions.

The average age of the patients in the observation group was 49.55 ± 2.45 years old, ranging from 42 to 57 years old. The pathological types in this group were 17 cases of invasive lobular carcinoma, 2 cases of invasive ductal carcinoma, and 1 case of mixed type. The TNM stages of the patients were 12 cases of stage IIb, 5 cases of stage IIIa, and 3 cases of stage IIIb. As for the comorbidities, there were 8 cases of diabetes mellitus, 8 cases of hypertension, and 4 cases of coronary artery disease.

The average age of the patients in the control group was 49.63 ± 2.99 years old, ranging from 43 to 57 years old. The pathological types in this group were invasive lobular carcinoma (16 cases), invasive ductal carcinoma (3 cases), and mixed type (1 case). The TNM stages of the patients were stage IIb (11 cases), stage IIIa (6 cases), and stage IIIb (3 cases). As for the comorbidities, there were diabetes mellitus (9 cases), hypertension (7 cases), and coronary heart disease (4 cases).

All patients in this study were females. The general information of the two groups showed no statistical difference ($P > 0.05$).

2.2. Methods

Both groups of patients were treated with radical mastectomy for breast cancer (radical mastectomy for breast cancer), and their endocrine therapy was given after the operation, and different drugs were chosen respectively.

Tamoxifen (approval number: H32021472; manufacturer: Yangzijiang Pharmaceutical Group Co., Ltd.) was chosen as the therapeutic drug for the control group; the patients were instructed to take the drug orally at a dose of 20 mg, once a day, for a total of 30 days (1 cycle). For the observation group, letrozole (approval number: H19991001; manufacturer: Jiangsu Hengrui Pharmaceutical Co., Ltd.) was administered at a dosage of 2.5 mg, once a day, for a total of 30 days.

The effect of the drugs was assessed every 2 cycles. A total of 5 assessments were done throughout the study.

2.3. Observation indicators

The Kupperman score and Karnofsky Performance Scale (KPS score), medication adherence and regular follow-up rate, lung function indexes, and blood lipid levels of the two groups after treatment were compared.

The patients' symptoms were evaluated using the modified Kupperman scale, which included nine symptoms: insomnia, skeletal muscle pain, agitation, hot flashes and sweating, fatigue, palpitations, vertigo, headache, depression, and irritability. Scores of 0, 1, 2, and 3 indicated the absence of symptoms, occasional occurrence, frequent but tolerable symptoms, and frequent and insurmountable symptoms, respectively. A lower score reflected a more noticeable improvement in symptoms. Additionally, the patients' quality of life was assessed using the KPS score. The KPS score was employed to gauge the patients' overall quality of life. The scoring scale demonstrated a positive correlation, indicating that higher scores were associated with better quality of life for the patients.

Determination of liver function indexes [3]: Venous blood was drawn from the patient in a fasting state before and after treatment, with a total volume of 5 mL. An automatic biochemical analyzer was utilized to measure the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and direct bilirubin (DBIL). All procedures were conducted in strict accordance with the provided instructions, and the required supporting reagents were employed.

2.4. Statistical treatment

The statistical software used for this study was SPSS 25.00, with $P < 0.05$ indicating statistical significance.

3. Results

3.1. Treatment-related indexes

The Kupperman and KPS scores were compared between the two groups ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of treatment-related indexes (mean ± standard deviation, points)

Group	Cases (*n*)	Kupperman		KPS	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	20	28.22 ± 2.17	20.33 ± 2.41*	72.63 ± 3.45	81.63 ± 3.78*
Control group	20	28.23 ± 2.18	25.63 ± 2.79*	72.65 ± 3.46	73.63 ± 3.01*
t	-	0.015	6.429	0.018	7.404
P	-	0.989	0.000	0.986	0.000

Note: *$P < 0.05$ compared to before treatment.

3.2. Medication adherence and follow-up rate

The medication adherence and regular follow-up rate of the observation group were higher than that of the control group ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of drug treatment adherence and regular follow-up rate in the two groups (n; %)

Group	Cases (*n*)	Medication adherence	Regular follow-up rate
Observation group	20	19 (95.00)	18 (90.00)
Control group	20	12 (60.00)	10 (50.00)
χ^2	-	7.025	7.619
P	-	0.008	0.006

3.3. Liver function indexes

All liver function indexes of the observation group were lower than those of the control group after treatment ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of liver function indexes (IU/L)

Group	AST		ALT		DBIL	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group ($n = 20$)	58.63 ± 3.55	57.36 ± 2.01*	61.39 ± 4.55	61.63 ± 4.01*	11.96 ± 2.02	11.52 ± 1.02*
Control group ($n = 20$)	58.65 ± 3.45	69.52 ± 2.78*	61.38 ± 4.71	79.55 ± 5.78*	11.97 ± 2.93	19.55 ± 1.97*
t	0.018	15.852	0.007	11.392	0.013	16.188
P	0.986	0.000	0.995	0.000	0.990	0.000

Note: *$P < 0.05$ compared to before treatment.

3.4. Blood lipid levels

After treatment, the HDL-C level of the observation group was higher than that of the control group ($P < 0.05$). However, there was no significant difference in the levels of LDL-C, TG, and TC between the two groups ($P > 0.05$), as shown in **Table 4**.

Table 4. Comparison of changes in blood lipid levels (mmol/L)

Group	HDL-C		LDL-C		TG		TC	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group ($n = 20$)	1.53 ± 0.32	1.48 ± 0.32*	2.89 ± 1.64	2.61 ± 1.02*	1.85 ± 1.04	1.74 ± 0.03*	4.88 ± 1.64	4.51 ± 1.34*
Control group ($n = 20$)	1.54 ± 0.21	1.22 ± 0.21*	2.91 ± 1.57	2.58 ± 1.24*	1.86 ± 0.21	1.75 ± 0.34*	4.89 ± 1.54	4.99 ± 1.31*
t	0.117	3.038	0.039	0.084	0.042	0.131	0.020	1.146
P	0.908	0.004	0.969	0.934	0.967	0.869	0.984	0.259

Note: *$P < 0.05$ compared to before treatment

4. Discussion

Breast cancer is a common malignant tumor among females that is usually treated by surgery. However, the surgical procedure is prone to complications, so it is necessary to strengthen the postoperative treatment. It is very important to carry out endocrine therapy after surgery, and the commonly used drugs include aromatase inhibitors, tamoxifen, etc. As a hormone-dependent systemic disease, breast cancer can be managed and treated effectively through endocrine therapy. This treatment approach works by reducing the levels of estrogen in the body and blocking the progression of the hormone-signaling pathway. By altering the environment necessary for tumor growth, endocrine therapy aims to control and treat breast cancer effectively [4,5].

According to the National Comprehensive Cancer Network (NCCN) guidelines, endocrine therapy should be preferred for hormone receptor-positive patients. The study results revealed that the observation group exhibited higher adherence to drug treatment and a more consistent follow-up rate compared to the control group. Additionally, the observation group had a lower Kupperman score and a higher KPS score than the control group. These findings suggest that postoperative endocrine treatment with letrozole not only

enhances patients' adherence to drug treatment but also improves their regular follow-up rates. As a typical third-generation aromatase inhibitor, letrozole is different from other drugs in that it can irreversibly inhibit the combination of aromatase and androgen substrate. By permanently deactivating aromatase, it disrupts the conversion process of androgen into estrogen, effectively lowering estrogen levels in patients' bodies. This contributes to the accelerated improvement of symptoms with a high level of safety and minimal adverse effects. The drug's safety profile and low incidence of adverse reactions enhance patient compliance, leading to a significant improvement in follow-up rates. This suggests that the application of postoperative letrozole not only enhances clinical efficacy but also improves the overall quality of life for patients [6,7]. As a new type of directional enzyme inhibitor, its mechanism of action is to inhibit the synthesis and production of aromatase, thereby effectively reducing the level of estrogen and eliminating the stimulating effect of estrogen on tumor growth. According to relevant studies, letrozole exhibits greater activity in the human body compared to amiloride. This class of drugs also demonstrates higher selectivity towards its active target. Notably, letrozole's impact on human thyroid function, saline corticosteroids, and glucocorticoids remains limited. Even at large doses, it does not inhibit the secretion of adrenal cortical steroids, so it is believed that letrozole may have a more favorable therapeutic effect [8].

With prolonged endocrine medication, various side effects may arise. Foreign studies indicate that long-term use of AIs can predominantly lead to menopausal symptoms due to decreased estrogen levels, such as irritability and hot flashes. Additionally, adverse events may include issues like abnormal bone events, cardiovascular events, and disturbed lipid metabolism. Among these, abnormal lipid metabolism is a commonly observed condition in menopausal women and represents an independent risk factor for cardiovascular disease. It is crucial to consider the side effects and prognosis of endocrine therapy for patients on long-term treatment to enhance clinical efficacy while minimizing adverse events associated with endocrine therapy. In the observation group, the HDL-C level decreased after treatment, but it was higher than that of the control group ($P < 0.05$). This is because letrozole can inhibit aromatase in peripheral and tumor tissues and also reduce plasma estrogen levels, which can cause an increase in lipid levels [9]. Aromatase inhibitors not only inhibit aromatase's effects on androstenedione and testosterone but also influence the prognosis of endocrine therapy. By inhibiting the conversion of androstenedione and testosterone to estrone and estradiol, aromatase inhibitors reduce estrogen levels, hindering estrogen's positive effects on blood lipids. This inhibition slows down the clearance of chylomicron remnants in the liver and reduces LDL uptake by the liver, the anabolic metabolism of HDL, and bile acids' secretion, leading to a decrease in cholesterol elimination from the body. Consequently, blood lipid levels increase [10]. Compared to the control group, the changes in blood lipids in the observation group were lesser, indicating that letrozole has less effect on blood lipids.

The liver function indexes of the observation group were better compared to the control group. This is because letrozole can inhibit peroxidative stress disorders in the body and enhance aromatase activity, which leads to a smaller impact on liver function. Over a 6-month drug administration period, abnormalities in liver function may occur with letrozole. Patients may experience loosening of hepatocyte cytoplasm around the lobule, mild hepatocyte edema, occasional hepatocyte point necrosis, and congestion in part of the region surrounding interlobular blood vessels and the central vein of the lobule. Additionally, eosinophilic changes may be observed. These findings suggest that prolonged endocrine treatment with letrozole may lead to liver damage. However, letrozole, by inhibiting estrogen biosynthesis, avoids the accumulation of androgen precursors. Therefore, compared to anti-estrogen drugs, letrozole exhibits a more significant anti-tumor effect. It does not affect luteinizing hormone, progesterone levels, thyroid function, or follicle-stimulating hormone in the body. Clinical studies indicate that letrozole has no potential toxicity to various target organs and systems in

the human body. Importantly, it remains unaffected by the patient's liver and kidney function, age, and gender. Dose adjustment is unnecessary according to clinical findings.

5. Conclusion

In conclusion, the application of letrozole in postoperative endocrine therapy of breast cancer can significantly improve the efficacy of the treatment and also enhance the quality-of-life level of patients. Therefore, it is worthy of further application and research.

Disclosure statement

The author declares no conflict of interest.

References

[1] Peng C, Chen J, Li S, et al., 2023, Evidence-Based Pharmacoeconomic Evaluation of Piperacillin in Combination with Letrozole Versus Docetaxel in Combination with Epirubicin for the First-Line Treatment of Advanced Breast Cancer. Chinese Pharmacology (English Edition), 32(3): 214–222.

[2] Chinese Anti-Cancer Association International Medical and Communication Branch, Breast Cancer Group of Oncologists Branch of Chinese Physicians Association, 2023, Expert Consensus on the Application of Multigene Testing in the Postoperative Adjuvant Treatment of Hormone Receptor-Positive Human Epidermal Growth Factor Receptor 2-Negative Early-Stage Breast Cancer (2023 Edition). Chinese Journal of Oncology, 45(10): 863–870.

[3] Liu Y, Qi Y, Mao X, 2022, Assessment of Adherence to Endocrine Therapy in Breast Cancer. Evidence-Based Medicine, 22(5): 303–308.

[4] Kang X, Zhao L, Lu C, 2022, Clinical Observation on the Treatment of Hormone-Dependent Breast Cancer by Combining Hassun Thirteen Flavor Pills with Letrozole Tablets. West Chinese Medicine, 35(8): 66–69.

[5] Zhang Z, Liu Y, Ding L, 2022, Efficacy and Safety of Perphenazine in the Treatment of Hormone Receptor-Positive Human Epidermal Growth Factor Receptor 2-Negative Advanced Breast Cancer. Chinese Journal of Clinical Pharmacology, 38(21): 2545–2549.

[6] Zhang W, Kong J, Cui Y, 2023, Analysis of a Clinical Study of Perphenazine in the Treatment of Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Advanced/Metastatic Breast Cancer. Chinese Journal of Clinical Pharmacology, 39(4): 573–577.

[7] Meng C, Zhang F, Su Y, 2021, Research Progress of Letrozole in Adjuvant Endocrine Therapy for Breast Cancer. Cancer Progress, 19(5): 438–441.

[8] Jiang Y, Jin C, Xia W, 2022, A Case of Osteoporotic Vertebral Fracture Due to Bone Microstructure Damage by Aromatase Inhibitor Treatment in Postmenopausal Breast Cancer. China Cancer Clinic, 49(11): 593–594.

[9] Pang H, Wang W, Li Y, 2022, Progress of Research on the Application of Endocrine Therapeutic Agents After Breast Cancer Surgery. China Prescription Drugs, 20(10): 189–191.

[10] Wang C, Cao F, Wang P, et al., 2023, A Study of Body Component Changes During Endocrine Therapy in Breast Cancer Patients Assessed by Quantitative CT. China Medical Equipment, 20(1): 47–50.