



Comparative study on sex hormone secretion in peripheral blood of women with common hematological tumors before and after chemotherapy

Liying Liu¹, Kexin Zhou¹, Liping Yao¹, Rui Hou², Hui Zhu^{1*}

¹Department of Gynaecology, No.215 Hospital of Shaanxi Nuclear Industry, Xianyang 712000, China

²Department of Hematological Oncology, Baoji People's Hospital of Shaanxi Province, Baoji 721000, China

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ABSTRACT

This study aimed to explore the secretion of sex hormones in peripheral blood of women with common hematological tumors before and after chemotherapy. From January 2019 to April 2021, 100 female patients with common hematological tumors in our hospital were selected as the observation group, and 50 healthy women in our hospital during the same period were selected as the control group. The serum levels of follicle-stimulating hormone (FSH), estradiol (E2) and luteinizing hormone (LH) were detected and compared between the observation group and the control group before chemotherapy, patients with different disease types in the observation group, postmenopausal patients in the observation group, and postmenopausal patients in the observation group. Results showed that the serum FSH, E2 and LH levels of the observation group had no significant changes before chemotherapy ($P > 0.05$). Compared with before chemotherapy, the levels of serum FSH and LH in patients with different disease types in the observation group after chemotherapy were significantly higher, while E2 was significantly lower ($P < 0.05$), and the serum FSH, E2 and LH levels of postmenopausal patients in the observation group did not change significantly after chemotherapy ($P > 0.05$). The levels of FSH and LH in the observation group after chemotherapy were significantly higher, and E2 was significantly lower ($P < 0.05$). In general, the levels of sex hormone secretion in peripheral blood of women with common hematological tumors before and after chemotherapy can change significantly, especially in postmenopausal patients, but not in postmenopausal patients, which has a certain reference value for clinical practice.

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Introduction

Hematological system tumor is a disease occurring in bone marrow and lymphoid tissue, mainly due to the abnormal immune system, which cannot detect and effectively remove abnormal cells in the body in time, resulting in the malignant clonal proliferation of abnormal cells and infiltration of other organs or tissues (1, 2). Common hematological tumors include malignant lymphoma, multiple myelopathies, leukemia, etc., which can cause fever, bleeding, anemia and other clinical symptoms, seriously affecting patients' quality of life and health (3, 4). The clinical treatment of hematological tumors is difficult, and the current treatment methods include molecular targeted therapy, immunosuppression therapy, and glucocorticoid therapy and so on. However, its clinical application is limited by its insignificant clinical therapeutic effect, specific applicable conditions or high price (5, 6). Chemotherapy can

effectively prevent the spread and metastasis of tumors, which is of great significance to improve the clinical treatment effect. Currently, it has become the preferred treatment for hematological tumor diseases (7-9). However, in recent years, some scholars have pointed out that chemotherapy can cause irreversible damage to the function and structure of the female ovary, leading to amenorrhea and infertility, etc., causing certain psychological pressure to patients (10, 11). Studies have shown that chemotherapy-induced amenorrhea and sexual dysfunction are closely related to the secretion of sex hormones (12). Sex hormones are mainly secreted by the placenta and ovary of female animals, which can maintain the normal reproductive function of women, the development of side sex characteristics and induce the maturation of reproductive organs (13). However, few studies have explored the effect of chemotherapy on the secretion of tumor sex hormones in the common blood system of

*Corresponding author. E-mail: zhuhui12A0@163.com
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women, which is worthy of further study. Therefore, this study mainly explored the changes of female peripheral blood sex hormone secretion levels before and after chemotherapy for common hematological system tumors, aiming to provide more reference for clinical treatment of female hematological system tumors.

Materials and methods

General Information

100 female patients with common hematological tumors who received chemotherapy in our hospital from January 2019 to April 2021 were selected as the observation group, aged 21 to 67 years old, with an average of (49.62±5.83) years old. Body mass index (BMI) ranged from 22 to 28kg/m², with an average of (24.28±1.69) kg/m². Menopause: 12 cases were postmenopausal, 88 cases were not postmenopausal; Type of disease: 12 cases of non-Hodgkin's lymphoma (NHL), 8 cases of multiple myeloma (MM), acute nonlymphocytic leukemia (NHL), 12 cases of non-Hodgkin's lymphoma (NHL), 8 cases of multiple myeloma (MM), 12 cases of non-hodgkin's lymphoma (NHL), 8 cases of multiple myeloma (MM), 12 cases of non-hodgkin's lymphoma (NHL), 8 cases of multiple myeloma (MM), ANLL (51 cases) and acute lymphoblastic leukaemia (ALL) (29 cases). In addition, 50 healthy women who underwent physical examination in our hospital during the same period were selected as the control group, aged from 23 to 68 years old, with an average of (50.21±5.77) years old. BMI ranged from 22 to 28kg/m², with an average of (24.62±1.87) kg/m². Menopause: 5 cases were postmenopausal and 45 cases were not postmenopausal. There was no significant difference in general data between the two groups ($P>0.05$), indicating comparability.

Inclusion and exclusion criteria

Inclusion criteria: Common hematological system tumors were diagnosed according to hematological disease diagnosis and efficacy criteria (14), and all patients were diagnosed as common hematological system tumors. Patients receiving treatment for the first time; the subjects or their families signed informed consent.

Exclusion criteria: Patients with contraindications or intolerance to chemotherapy; Patients with diseases

that affect sex hormone levels; Subjects who had taken drugs affecting sex hormone levels within six months; Pregnant or lactating women.

Treatment methods

VTCP regimen for NHL patients: On the first day, 2mg Vincristine (VCR) (Shanxi Zhindong Taisheng Pharmaceutical Co., LTD., National Drug Approval H14020811) and 60-80mg Pirarubicin (THP) (Shenzhen Wanle Pharmaceutical Co., LTD., National Drug Approval H10930106) and 600~800mg cyclophosphamide (CTX) (Jiangsu Shengdi Pharmaceutical Co., LTD., National drug approval H32020857), orally 60~100mg prednisone (Prednisone, Pred) (Henan Lihua Pharmaceutical Co., LTD., National Drug Approval H41022037).

Patients with MM were given VTD regimen: 0.4mg VCR, 40mg dexamethasone (DX) (tianjin tianyum pharmaceutical co., LTD., state drug approval H20033553) and 20mg THP were intravenated on days 1-4.

TA regimen was adopted for ANLL patients: 40~60mg THP was injected intravenously on the 1st to 3rd day and arabinsyl cytosine (ARA-C) 150~200mg intravenously on the 1st to 7th day (Beijing SeK Pharmaceutical Co., LTD., H11021574).

ALL patients received VTCP regimen: 2mg VCR intravenously on days 1, 8, 15, and 22, 30~40mg THP intravenously on days 1 to 3 and 15 to 17, 600~800mg CTX intravenously on days 1 and 15, and 1mg/kg Pred orally on days 1 to 28.

All patients received supportive treatment: During chemotherapy, the patients were treated with alkalized urine, rehydration, liver protection, antiemetic and other conventional treatments. After chemotherapy, corresponding symptoms were given. If neutrophils were lower than $1.0 \times 10^9/L$, granulocyte colony-stimulating factor (GRANulocyte colony stimulating factor, G-CSF) were used to raise leukocytes; If the patient has fever, a broad spectrum of antibiotics should be given, and antifungal drugs can be added when necessary. If hemoglobin is lower than 70g/L, red blood cells are transfused; if the platelets were lower than $20 \times 10^9/L$, apheresis platelets were given.

Sex hormone detection method

On the second day after the subjects were enrolled in the study and the end of chemotherapy, 3mL of early

morning fasting elbow venous blood was extracted from the patients and placed in the EP tube. After standing at room temperature for 1 h, the serum was separated by centrifugation method and stored at -80°C for testing. Enzyme-linked immunosorbent assay (ELISA) was adapted to enzyme-linked immunosorbent assay (ENZYme-linked IMmumosorbent assay) to detect follicle-stimulating hormone (FSH), estradiol, E2) and Luteinizing hormone (LH) levels were detected using kits provided by Shanghai Fusheng Industrial Co., LTD.

Observation Indicators

Serum LEVELS of FSH, E2 and LH were compared between the observation group and the control group before chemotherapy. The levels of serum FSH, E2 and LH in patients with different disease types before and after chemotherapy were compared in the observation group. The levels of FSH, E2 and LH in the observation group before and after chemotherapy were compared. Compare the levels of FSH, E2 and LH in the observation group before and after chemotherapy.

Statistical methods

SPSS 18.0 was used for statistical analysis. The measurement data were expressed as mean \pm standard deviation ($\pm S$) and tested by T. Enumeration data were expressed by example (n) or percentage (%) and tested by χ^2 . $P < 0.05$ indicated statistically significant difference.

Results and discussion

Comparison of serum FSH, E2 and LH levels between the observation group and the control group before chemotherapy

There were no significant differences in serum FSH, E2 and LH levels between the observation group and the control group before chemotherapy ($P > 0.05$), as shown in Table 1 and Figure 1.

Comparison of serum FSH, E2 and LH levels in patients with different disease types in the observation group before and after chemotherapy

After chemotherapy, serum FSH and LH levels in patients with different disease types in the observation group were significantly increased, while E2 levels

were significantly decreased, with statistical significance ($P < 0.05$), as shown in Table 2.

Table 1. Comparison of serum FSH, E2 and LH levels in the observation group before and after chemotherapy ($\bar{x} \pm s$)

Indicator s	Observation group (n=100)	Control group (n=50)	t	P
FSH (IU/L)	29.06 \pm 4.12	29.81 \pm 4.15	0.767	0.772
E2 (pmol/L)	221.38 \pm 31.65	220.78 \pm 31.25	0.846	0.569
LH (IU/L)	19.88 \pm 1.85	19.40 \pm 1.97	0.931	0.472

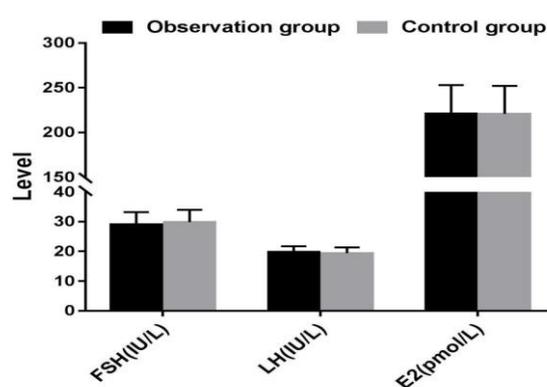


Figure 1. Comparison of serum FSH, E2 and LH levels between the observation group and the control group before chemotherapy

Table 2. Comparison of serum FSH, E2, LH levels before and after chemotherapy in patients with different disease types in the observation group ($\bar{x} \pm s$); A) After chemotherapy, B) Before chemotherapy

Indicators		NHL (n=12)	MM (n=8)	ANLL (n=51)	ALL (n=29)
FSH (IU/L)	B	29.62 \pm 4.00	28.79 \pm 4.11	29.43 \pm 4.06	28.95 \pm 4.19
	A	85.02 \pm 4.43*	84.99 \pm 4.28*	86.14 \pm 4.10*	85.36 \pm 4.22*
E2 (pmol/L)	B	221.56 \pm 30.64	222.82 \pm 29.25	221.68 \pm 30.54	222.43 \pm 30.73
	A	113.07 \pm 7.75*	113.55 \pm 7.84*	112.82 \pm 7.49*	113.29 \pm 7.91*
LH (IU/L)	B	19.98 \pm 2.53	20.12 \pm 2.54	20.64 \pm 2.47	19.85 \pm 2.60
	A	58.89 \pm 3.32*	59.00 \pm 3.33*	59.38 \pm 3.61*	58.47 \pm 3.72*

Note: * represents comparison with before chemotherapy, * $P < 0.05$.

Comparison of FSH, E2 and LH levels in the observation group before and after chemotherapy

There was no significant difference in FSH, E2 and LH levels in the observation group before and after

chemotherapy ($P>0.05$), as shown in Table 3 and Figure 2.

Table 3. Comparison of FSH, E2, LH levels before and after chemotherapy in the observation group ($\bar{x}\pm s$)

Indicators	Before chemotherapy	After chemotherapy	<i>t</i>	<i>P</i>
FSH (IU/L)	71.63 ± 9.15	73.73 ± 12.59	0.756	0.779
E2 (pmol/L)	104.81 ± 27.53	102.79 ± 19.65	0.708	0.830
LH (IU/L)	32.55 ± 4.55	33.50 ± 6.93	0.757	0.778

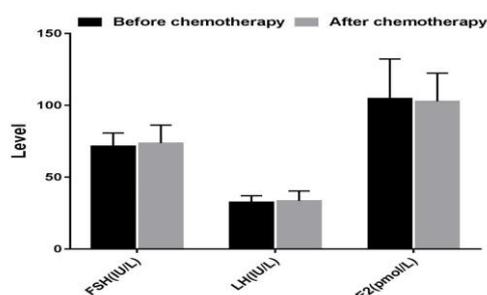


Figure 2. Comparison of FSH, E2 and LH levels in the observation group before and after chemotherapy

Comparison of FSH, E2 and LH levels in pre-menopausal patients before and after chemotherapy in the observation group

After chemotherapy, serum FSH and LH levels were significantly increased and E2 levels were significantly decreased in the observation group before menopause, with statistical significance ($P<0.05$), as shown in Table 4 and Figure 3.

Table 4. The levels of FSH, E2 and LH in the observation group before and after chemotherapy ($\bar{x}\pm s$)

Indicators	Before chemotherapy	After chemotherapy	<i>t</i>	<i>P</i>
FSH (IU/L)	26.59 ± 4.25	86.58 ± 3.51	7.018	0.008
E2 (pmol/L)	237.66 ± 34.19	121.86 ± 7.31	7.632	0.002
LH (IU/L)	19.63 ± 2.88	61.98 ± 3.49	6.522	0.009

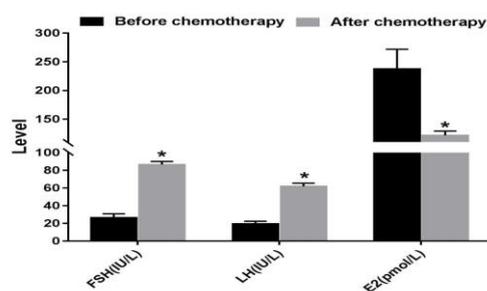


Figure 3. Levels of FSH, E2 and LH in pre-menopausal patients in the observation group before and after chemotherapy. Note: Compared with before chemotherapy, * $P < 0.05$

Hematological system tumor is a disease that occurs when normal cells of hematopoietic tissues such as extramedullary hematopoietic organs and bone marrow undergo malignant transformation into tumor cells (15, 16). Chemotherapy is currently the standard method for the treatment of hematological tumors. However, chemotherapy drugs can not only kill tumor cells but also damage normal tissue cells, resulting in varying degrees of damage, thus affecting the normal physiological functions of the body (17, 18). At the same time, studies have shown that chemotherapy drugs can affect the reproductive function of the body by affecting the level of female sex hormones (19). However, there are few studies on the effect of chemotherapy on sex hormone levels in female patients with common hematological tumors.

As a very important reproductive and endocrine organ for women, ovary can not only effectively maintain female reproductive and physiological functions, but also participate in the regulation process of endocrine and metabolism (20). Once the female ovarian function is lost, it can lead to abnormal changes in hormone levels in the body, which can not only cause menopausal symptoms but also cause sexual pain, loss of sexual desire, hot flashes, night sweats, vaginal atrophy and bad emotions, which seriously affect the quality of life, physical and mental health of women. In addition, relevant studies have shown that ovarian function loss can also induce or aggravate the occurrence and development of osteoporosis, coronary heart disease, hypertension and other diseases (21). Therefore, maintaining ovarian function in women is significantly important in clinical practice. Sex hormone is a steroid hormone synthesized by the body's gonads, adrenal cortex reticular zone, placenta and other tissues, which can maintain the body's sexual function, promote the development of side sex characteristics and the maturity of sexual organs, and can effectively reflect the body's ovarian function (22). In this study, there was no significant difference in the levels of sex hormone secretion between the observation group and the control group before chemotherapy, indicating that common tumors of the blood system will not cause the disorder of the levels of sex hormone secretion in female peripheral blood and have no significant influence on the ovarian function of the body.

FSH, E2 and LH are clinically common sex hormone indicators. FSH is mainly composed of glycoproteins, which can promote the maturation of follicles in the body. When its level changes abnormally, it may indicate ovarian hypoplasia, decreased reproductive function, amenorrhea, etc. (23). E2 is a kind of estrogen and is considered to be the most important sex hormone secreted by the ovary due to its strong sex hormone effect. When its level decreases, it may indicate the body's irregular menstruation and premature ovarian failure (24). LH is a gonadotropin of glycoproteins, mainly secreted from adenohypophysial cells, which can stimulate cholesterol in adenohypophysial cells and then induce its conversion into sex hormones. Abnormal changes in its level indicate decreased reproductive function (25).

A number of studies (26, 27) found that after chemotherapy for breast cancer patients, the levels of FSH and LH in premenopausal breast cancer patients were abnormally increased and E2 significantly decreased after chemotherapy, while E2 levels in postmenopausal breast cancer patients showed no significant change. In this study, observation group of patients with various types of disease after chemotherapy was tied to elevated FSH, LH, E2 were lower, while changes in postmenopausal patients is very significant, and does not change significantly in patients with postmenopausal, consistent with the literature, shows that chemotherapy can seriously affect the common blood system tumor female patients peripheral blood levels of sex hormone secretion, Especially for pre-menopausal women. At present, chemotherapy is one of the effective means to treat common hematological tumors, but the target cells of chemotherapy drugs are not highly selective, which can not only kill cancer cells but also cause different degrees of damage to normal tissue cells of the body. The female ovary is highly sensitive to chemotherapy drugs. In chemotherapy, once the large follicle disappears, the pituitary gland gives feedback and promotes the secretion of gonadotropin. After the small follicle is supplemented, it will be destroyed by chemotherapy drugs. Over time, the number of small follicles decreases, eventually leading to an ovarian failure (28, 29).

FSH and LH secretion from the anterior pituitary basophilic cells, E2 is directly produced by the body

ovarian secretion of a kind of estrogen, and E2, FSH and LH in peripheral blood was a significantly negative correlation of gonadotropin-releasing hormone by the hypothalamus and ovarian estrogen regulation together, thus constituted the hypothalamus-pituitary - ovarian axis a complete control system (30-33), But after the organism menopause, its ovarian function declines gradually, disappear completely finally. Therefore, chemotherapy has no significant impact on menopausal women, suggesting that it can be safely treated with chemotherapy for menopausal women with common hematological tumors.

In conclusion, abnormal secretion of peripheral blood sex hormone levels in common female patients with hematological system tumors after chemotherapy, especially in pre-menopausal women, has no significant effect on pre-menopausal women, which is worthy of clinical reference.

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None.

Interest conflict

The authors declare no conflict of interest.

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