European Review for Medical and Pharmacological Sciences 2023; 27: 10499-10506

The effect of selenium yeast in the prevention of adverse reactions related to platinum-based combination therapy in patients with malignant tumors

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Abstract. – OBJECTIVE: The aim of this was study was to analyze the effect of selenium yeast in the prevention of adverse reactions related to platinum-based combination therapy in patients with malignant tumors.

PATIENTS AND METHODS: A total of 86 patients with malignant tumors treated in Anhui No. 2 Provincial People's Hospital were randomized to receive either platinum-containing combined regimen with selenium yeast at a dose of 200 ug daily (observation group) or platinum-containing combined regimen without selenium yeast (control group), with 43 cases in each group.

RESULTS: The platinum-containing combined regimen exhibited similar total effectiveness either with (25.58%) or without selenium yeast (23.26%) ($p>0.05$). Patients with selenium yeast treatment after chemotherapy had better appetites and more stable body weights than those without selenium yeast ($p<0.05$). The platinum-containing combined regimen significantly improved the quality of life of the patients, as evidenced by the elevated Karnofsky Performance Status (KPS) scores of the two groups, and selenium yeast treatment potentiated this improvement ($p<0.05$). Selenium yeast treatment significantly reduced the incidence of adverse reactions in patients after chemotherapy by 23.26% ($p<0.05$), and patients also experienced milder adverse reactions after selenium yeast administration (Z=-2.438, $p=0.015$). Chemotherapy with selenium yeast treatment provided better pain mitigation for patients vs. without selenium yeast administration (Z=0.854, $p=0.041<0.05$).

CONCLUSIONS: In the clinical treatment of patients with malignant tumors, a 200 ug dose of selenium yeast significantly reduced the adverse reactions related to chemotherapy, improved the patient's post-chemotherapy appetite, prevented weight loss, and provided significant pain mitigation. Therefore, selenium yeast may offer a viable alternative for the management of cancer patients undergoing chemotherapy to enhance treatment effectiveness and reduce adverse events in clinical practice.

Key Words:
Selenium yeast, Tumors, Platinum-based chemotherapy, Adverse reactions.

Introduction

Platinum drugs belong to cell cyclin-specific drugs, which mainly mediate tumor cell necrosis or apoptosis by forming Pt-DNA adducts with DNA and produce anticancer effects[1]. Platinum drugs were developed in the 1960s and have been commonly used for the management of malignancies in clinical practice[2]. However, adverse reactions related to the clinical use of platinum drugs are significant[3-5]. Studies[6,7] have shown that selenium-rich yeast, as one of the main forms of selenium supplement, has the advantages of high bioavailability, safety, and low toxicity, and thus may alleviate adverse reactions related to chemotherapy. Thus, the present study was performed to analyze the effect of selenium yeast in the prevention of adverse reactions related to platinum-based combination therapy in patients with malignant tumors.

Patients and Methods

General Information

A total of 86 patients with malignant tumors treated in Anhui No. 2 Provincial People's Hospital were randomized to receive either platinum-containing combined regimen with selenium yeast at a dose of 200 ug daily (observation group) or platinum-containing combined regimen without selenium yeast (control group), with 43 cases in each group. The conditions of the two groups were consistent with the clinical diag-

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nostic criteria of malignant tumors. There were 25 male patients and 18 female patients in the observation group and 23 male patients and 20 female patients in the control group, with an average age of 61.16±11.78 years. The two groups were well-balanced in terms of baseline patient profiles (p>0.05).

Inclusion criteria: (1) cancer patients were diagnosed by pathological examination; (2) patients without surgery, radiotherapy or chemotherapy; (3) patients signed informed consent.

Exclusion criteria: (1) severe medical diseases; (2) those without self-consciousness and with a history of mental illness; (3) patients with severe intolerance and adverse reactions during chemoradiotherapy; (4) patients who were allergic to the drugs used in this study.

The observation group and the control group were given platinum-containing combined regimen for chemotherapy. The patients in the observation group were given 200 ug of oral selenium yeast tablets (Mudanjiang Lintai Pharmaceutical Co., LTD., Chinese Medicine approval number H10940161) during the treatment once daily for a total of 1 month. The frequency and course of chemotherapy in the control group were consistent with those in the observation group.

Observation Indicators and Evaluation Criteria

Clinical efficacy

According to RECIST1.1 criteria, the clinical efficacy of the two groups after treatment was divided into four levels. (1) Complete response (CR): all lesions disappear, and the short diameter of all pathological lymph nodes (including target nodules and non-target nodules) is reduced to less than 10 mm. (2) Partial response (PR): the sum of target lesion diameters is reduced by at least 30% from the baseline. (3) Stable disease (SD): the degree of reduction of target lesions did not reach the level of PR, and the degree of increase did not reach the level of PD, and the minimum value of the sum of diameters can be used as a reference in the study. (4) Progressive disease (PD): the minimum value of the sum of the diameters of all the target lesions measured during the whole experimental study is used as the reference, and the sum relative increase in diameter is at least 20% (if the baseline measurement is the smallest, the baseline value is used as the reference). In addition, an absolute increase of at least 5 mm in the sum of diameters has to be met. The presence of one or more new lesions is considered to be disease progression. The overall response rate was (CR+PR)× 100%.

Appetite and body weight

The changes of appetite and body weight after treatment were compared between the two groups, and the proportion of patients with decreased, unchanged, and increased appetite and body weight was analyzed.

Karnofsy Performance Status (KPS) score

KPS score changes before and after treatment were compared between the two groups. The score was proportional to the quality of life, the higher the score, the better the quality of life.

Adverse reactions

According to the WHO classification standard[8] of adverse reactions to chemotherapy, the adverse reactions of two groups were divided into five grades: grade 0, grade I, grade II, grade III and grade IV according to the common adverse reactions of blood system, gastrointestinal tract, kidney, bladder, heart and nervous system. Grade 0 indicates normal (no reaction), and grade IV indicates the most severe adverse reaction.

Pain evaluation

From the first day of chemotherapy, the same attending physician or chief physician scored the patient's pain according to the patient's description. The grading evaluation criteria were as follows: grade 0 indicates no pain. Grade 1 is mild and tolerable pain that does not affect daily living and sleep. Grade 2 is moderate and intolerable pain that requires analgesics and affects sleep. Grade 3 is severe and intolerable pain that significantly disturbs sleep and may be accompanied by autonomic disturbance or passive posture. The higher the grade, the more severe the pain.

Statistical Analysis

SPSS 15.0 statistical software (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. Measurement data were expressed as (±s), and t-test was used for analysis. Count data were expressed as rate (%) and chi-square test was used for analysis. Rank sum test was used for comparison of categorical data between groups. p<0.05 indicates the difference is statistically significant. GraphPad Prism 9 (La Jolla, CA, USA) was employed to plot the graphics.

Table I. Comparison of basic data between the two groups.

Project	Observation group	Control group	t/χ^2	p
Gender				
Male/Female	25/18	23/20	0.189	0.664
Mean age	61.16 ± 11.78	61.28 ± 9.34	0.003	0.960
Platinum Agents				
Cisplatin	19	18	0.047	0.827
Carboplatin	11	11		
Oxaliplatin	8	11		
Nedaplatin	5	3		
Type of cancers			0.892	0.672
Lung cancer	20	23		
Stomach cancer	21	22		
Liver cancer	17	26		
Colon cancer	23	20		

Results

Comparison of Basic Data Between The Two Groups

The ratio of male to female was 25:18 in the observation group and 23:20 in the control group. There was no significant difference in the sex ratio between the two groups (χ^2=0.189, p=0.664). The average age of the observation group was 61.16±11.78 years old, and the average age of the control group was 61.28±9.34 years old. There was no significant difference in age between the two groups (t=0.003, p=0.960).

Comparison of Treatment Efficiency Between the Two Groups

The platinum-containing combined regimen exhibited similar total effectiveness either with (25.58%) or without selenium yeast (23.26%) (χ^2=0.063, p=0.802), as shown in Table I.

Comparison of Appetite and Body Weight Changes Between the Two Groups

After treatment, the proportion of patients with appetite and weight loss in the observation group was 25.58% and 16.28%, respectively, which were lower than 51.16% and 34.88% in the control group (p<0.05). After treatment, the proportion of patients with unchanged appetite and body weight in the observation group was 44.19% and 55.81%, respectively, which was not significantly different from 34.88% and 53.49% in the control group, and there was no statistically significant difference (p>0.05). After treatment, the proportion of patients with increased appetite and body weight in the observation group was 30.23% and 27.91%, respectively, which were higher than 13.95% and 11.63% in the control group, but there was no statistically significant difference (p>0.05), as shown in Table III.

Comparison of KPS Scores Between the two Groups

Before treatment, there was no significant difference in KPS score between the observation group (60.72±5.94) and the control group (60.94±6.21) (p>0.05). The platinum-containing combined regimen significantly improved the quality of life of the patients, as evidenced by the elevated KPS scores of the two groups, and selenium yeast treatment potentiated this improvement (p<0.05), as shown in Figure 1.

Table II. Comparison of treatment response rates between the two groups (n, %).

Group	The number of cases	Grade of clinical efficacy				Total effective number
		CR	PR	SD	PD	
Observation group	43	2	9	28	4	11
Control group	43	1	9	28	5	10
χ^2						0.063
p						0.802

Table III. Comparison of appetite and body weight changes between the two groups (n, %).

Group	N	Appetite			Body mass		
		To reduce	The same	Increase	To reduce	The same	Increase
Observation group	43	11 (25.58)	19 (44.19)	13 (30.23)	7 (16.28)	24 (55.81)	12 (27.91)
Control group	43	22 (51.16)	15 (34.88)	6 (13.95)	15 (34.88)	23 (53.49)	5 (11.63)
χ^2		5.949	0.778	3.310	3.909	0.047	3.593
p		0.014	0.377	0.069	0.048	0.828	0.058

Comparison of the Incidence of Adverse Reactions of Different Platinum Drugs Between the Two Groups

Among the 43 cases in the observation group, 15 cases had adverse reactions, including 12 cases of cisplatin, 1 case of carboplatin, 1 case of oxaliplatin, and 1 case of nedaplatin. In the control group, there were 25 cases of adverse reactions, including 17 cases of cisplatin, 3 cases of carboplatin, 4 cases of oxaliplatin, and 1 case of nedaplatin. Selenium yeast treatment significantly reduced the incidence of adverse reactions in patients after platinum-containing combined regimen by 23.26% (χ^2=4.674, p=0.031), as shown in Table IV.

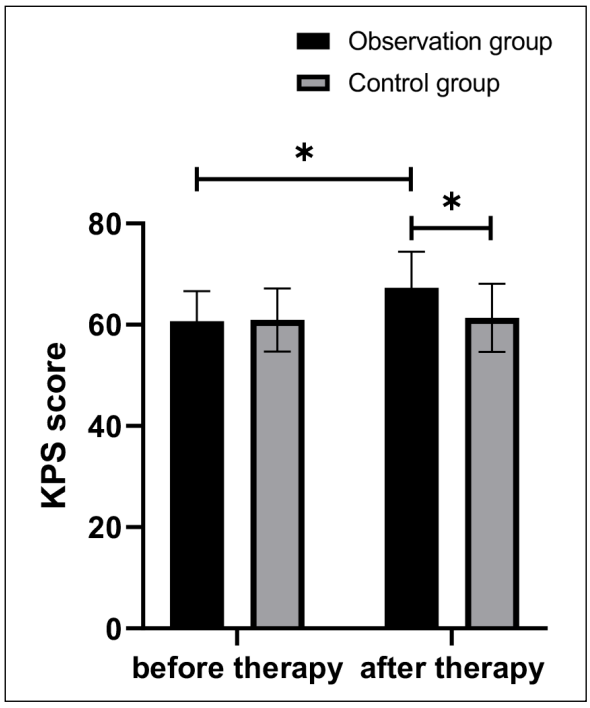

Figure 1. Comparison of KPS scores between the two groups, *p< 0.05.

Comparison Of Adverse Reaction Grading Between the Two Groups

After treatment, the number of adverse reactions at all levels in the control group was 18 cases of grade 0, 13 cases of grade I, 9 cases of grade II, 2 cases of grade III, 1 case of grade IV, and the incidence of adverse reactions was 58.14%. The number of adverse reactions at all levels in the observation group after treatment was: 28 cases of grade 0, 9 cases of grade I, 6 cases of grade II, and 0 cases of grade III and IV, and the incidence of adverse reactions was 34.88%. The patients experienced milder adverse reactions after selenium yeast administration (z=-2.438, p=0.015). (z=-2.438, p=0.015), as shown in Table V.

Comparison of Pain Between the Two Groups

During the treatment, the incidence of pain degree ≤ I grade in the observation group was 27.91% higher than that in the control group 11.63%, and the incidence of pain degree ≥ II grade was lower than that in the control group. Chemotherapy with selenium yeast treatment provided better pain mitigation for patients *vs.* without selenium yeast administration (Z=0.854, p=0.041<0.05), as shown in Table VI.

Discussion

The incidence and mortality of malignant tumors far exceed that of malaria, and malignant tumors have become the first killer threatening human health. Platinum drugs are currently one of the most widely used anti-tumor drugs in clinical practice. However, due to various adverse reactions, it is of great significance to prevent and reduce the occurrence of adverse reactions to improve the quality of life of patients and reduce additional treatment costs[8-10]. Research[11] has shown that selenium yeast can effectively reduce the adverse reactions of plat-

Table IV. Comparison of the number of adverse reactions of different platinum drugs in the two groups.

Adverse reactions	Cisplatin (n)		Carboplatin (n)		Oxaliplatin (n)		Nedaplatin (n)	
	Observation group (19)	Control group (18)	Observation group (11)	Control group (11)	Observation group (8)	Control group (11)	Observation group (5)	Control group (3)
Gastrointestinal reactions	10	15	1	2	1	3	1	1
Bone marrow suppression	1	2	0	1	0	1	0	0
Allergy	1	0	0	0	0	0	0	0
Drug fever	0	0	0	0	0	0	0	0
Neurotoxicity	0	0	0	0	0	0	0	0
Liver toxicity	0	0	0	0	0	0	0	0
Nephrotoxicity	0	0	0	0	0	0	0	0
Ototoxicity	0	0	0	0	0	0	0	0
A combined	12	17	1	3	1	4	1	1

Table V. Comparison of adverse reactions between the two groups.

Group	The number of adverse reactions of different grades					I-IV
	0	I	II	III	IV	
Control group	18 (41.86)	13 (30.23)	9 (20.93)	2 (4.65)	1 (2.33)	25 (58.14)
Observation group	28 (65.12)	9 (20.93)	6 (13.95)	0 (0.00)	0 (0.00)	15 (74.88)
Z						-2.438
p						0.015

Table VI. Comparison of pain between the two groups.

Group	N	0	I	II	III
Observation group	43	0 (0.00)	12 (27.91)	24 (55.81)	7 (16.28)
Control group	43	0 (0.00)	5 (11.63)	21 (48.84)	17 (39.53)
Z	1.854				
p	0.041				

inum and other drugs. Selenium yeast is a selenium supplement drug, which is mainly used for the management of patients with tumors, liver diseases, cardiovascular and cerebrovascular diseases, or other diseases caused by low selenium[12,13]. Selenium is an essential trace element for human body and plays an important role in the decomposition of peroxides, removal of free radicals, regulation of body immunity, and antagonism of toxic elements[14,15]. Proper intake of selenium can increase the level of selenium and activity of glutathione peroxidase (GSH-PX). GSH-PX can protect the integrity of cell membranes, eliminate free radicals, and enhance immune function[16-18]. In the present study, the significantly higher treatment efficacy of the observation group compared with the control group may be related to the addition of selenium yeast tablets. Many chemotherapy drugs induce apoptosis by upregulating the generation of intracellular reactive oxygen species (ROS)[19], while the mechanism of selenium-induced cytotoxicity is oxidative stress response caused by excessive ROS, so selenium compounds have synergistic effects with chemotherapy[20,21]. Furthermore, patients with selenium yeast treatment after chemotherapy had better appetites and more stable body weights than those without selenium yeast ($p<0.05$). The platinum-containing combined regimen significantly improved the quality of life of the patients, as evidenced by the elevated KPS scores of the two groups, and selenium yeast treatment potentiated this improvement. These results suggested that selenium yeast tablets can control the patient's appetite and weight loss, and can improve the quality of life of patients with advanced malignant tumors.

Selenium yeast treatment significantly reduced the incidence of adverse reactions of patients after platinum-containing combined regimen by 23.26% ($p<0.05$), and patients also experienced milder adverse reactions after selenium yeast administration ($z=-2.438$, $p=0.015$). It suggested that the drug can reduce the risk of adverse reactions during chemotherapy. Selenium supplementation has a significant inhibitory effect on the occurrence of gastrointestinal reactions, bone marrow suppression, and liver and kidney toxicity caused by radiotherapy and chemotherapy, indicating that selenium yeast tablets are safe for tumor treatment. Consistent with a study[22], selenium yeast tablets can effectively alleviate the toxic effects of chemotherapy drugs on leukocytes and neutrophils. In addition, the incidence of gastrointestinal reactions and bone marrow suppression caused by cisplatin was the highest in this study. The main clinical manifestations of gastrointestinal damage were nausea, vomiting and diarrhea, and the main manifestations of hematopoietic system damage were leucopenia, thrombocytopenia and anemia, which were consistent with the main adverse reactions of platinum drugs[23,24].

Though several strategies to prevent neurotoxicity have so far been investigated, we failed to evaluate the risk of interactions in this study. To overcome this life-threatening side effect, while taking advantage of the antineoplastic activities of oxaliplatin, Francia et al[25] described in detail recent findings on the underlying mechanisms

of genetic variants associated with toxicity and resistance to oxaliplatin-based chemotherapy in colorectal cancer. A comprehensive panel of eight polymorphisms, previously validated as significant markers related to oxaliplatin toxicity, is proposed and discussed. In addition, the most common available strategies or methods to prevent/minimize the toxicity were described in detail. Moreover, an early outline evaluation of the genotyping costs and methods was taken in consideration. In addition, the authors team revealed the results of allelic status from 7 validated polymorphism assays, allowed the stratification of the patients who are most likely to respond to FluOx treatments. Also, they took in consideration the usefulness and costs of the methods used to detect these polymorphisms. With these pharmacogenomics markers, we will have new means based on the genetic profile of the individual, to make treatment decisions for their patients in order to maximize benefits and minimize toxicity[26].

Conclusions

In the clinical treatment of patients with malignant tumors, a 200 ug dose of selenium yeast significantly reduces the adverse reactions related to chemotherapy, improves the patient's post-chemotherapy appetite, prevents weight loss, and provides significant pain mitigation. Therefore, selenium yeast may offer a viable alternative for the management of cancer patients undergoing chemotherapy to enhance treatment effectiveness and reduce adverse events in clinical practice. However, this study has the following limitations, such as single center and small sample size, which may lead to certain deviations in the accuracy of the results. Therefore, more studies with larger sample size and more centers are needed for further discussion.

Conflict of Interest
The authors declare that they have no conflict of interests.

Ethics Approval
The study was approved by the Ethics Committee of Anhui No. 2 Provincial People's Hospital (20102308/234).

Informed Consent
The informed consent was signed with the patients and their families.

Availability of Data and Material
All data are available upon request to the corresponding author.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contribution
All authors contributed equally to the study.

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