CHANGES OF CEA, CYFRA21-1, CA125 AND PLATELET PARAMETERS IN PATIENTS WITH ADVANCED NSCLC BEFORE AND AFTER PLATINUM-BASED CHEMOTHERAPY

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ABSTRACT

Objective*: To study the changes in carcinoembryonic antigen (CEA), CYFRA21-1, CA125, and platelet parameters in patients with advanced non-small cell lung cancer (NSCLC) before and after platinum-based chemotherapy.*

Methods: *A total of 60 patients with NSCLC treated in our hospital from July 2018 to July 2019 were recruited and divided into the control group (n=32) and observation group (n=28) according to the treatment regimen. The control group was given pemetrexed, and the observation group was treated with carboplatin based on pemetrexed. The treatment effect and adverse reactions of the patients in the two groups were observed; 5 ml of fasting venous blood was collected from all patients. The CEA, CYFRA21-1, and CA125 levels in all patients before and after treatment were measured by electrochemical luminescence immunoassay; 2 ml of fasting venous blood was collected from all patients before and after treatment, and the platelet count (PLT), mean platelet volume (MPV), platelet specific volume (PCT), and platelet distribution width (PDW) of all patients were measured using a fully automatic blood cell counter.*

Results: *Before treatment, there was no significant difference between the serum CEA, CYFRA21-1, and CA125 levels of the patients in the two groups (P>0.05). After treatment, the levels of CEA, CYFRA21-1, and CA125 in the serum of the patients in both groups had decreased; the levels of CEA, CYFRA21-1, and CA125 in the serum of the observation group were significantly lower than those of the control group, and the difference was statistically significant (P<0.05). Before treatment, there was no significant difference between the serum PCT, PLT, MPV, and PDW levels of the patients in the two groups (P>0.05). After treatment, the levels of PCT, PLT, and MPV in the serum of the patients in the two groups had decreased; the levels of PCT, PLT, and MPV in the serum of the observation group were significantly higher than those of the control group, and the difference was statistically significant (P<0.05). There was no significant change in PDW level (P>0.05). The effective rate in the observation group was 75.00%, which was significantly higher than the 46.88% in the control group, and the difference was statistically significant (P<0.05). The incidence of adverse reactions in the observation group was 21.43%, which was significantly lower than the 53.13% in the control group, and the difference was statistically significant (P<0.05).*

Conclusion: *Platinum-based chemotherapy can reduce the levels of CEA, CYFRA21-1, and CA125 in patients with NSCLC, but it has a lower effect on the levels of PCT, PLT, MPV, and PDW, reduces the incidence of thrombocytopenia, and has good efficacy and less adverse reactions, and can be widely used in clinics.*

Keywords: *NSCLC, platinum-based chemotherapy, CEA, CYFRA21-1, CA125, platelet parameters.*

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Introduction

Lung cancer is one of the most common malignant tumours worldwide, ranking first as the cause of malignant tumour deaths in urban populations in China[1]. Non-small cell lung cancer (NSCLC) is a type of lung cancer that accounts for about 80% of all lung cancers. Common causes of lung cancer include ionizing radiation, smoking, lung infections, genetic factors, occupations, and the environment[2]. There are no obvious clinical manifestations in the early stage, and symptoms such as blood sputum, low fever, weight loss, decreased appetite, dyspnoea, chest pain, and haemoptysis may occur in the middle and late stages. Most patients are already in the middle and late stages when the disease is discovered, and the 5-year survival rate is only about 15%[3]. Chemotherapy is the main method for the treatment of NSCLC. The currently commonly used chemotherapy regimen is a platinum-based combi-

nation regimen that prolongs life and improves quality of life[4]. There are many reports on the efficacy of platinum-based chemotherapy in the treatment of patients with NSLCL, but there are few studies on its effect on the tumour markers and platelet parameters of patients[5].

The hospital conducted this trial to study the effects of platinum-based chemotherapy on carcinoembryonic antigen (CEA), CYFRA21-1, CA125, and platelet parameters in patients with NSCLC.

Information and methods

General information

Patients with NSCLC admitted to our department of respiratory medicine from July 2018 to July 2019 were selected.

The inclusion criteria were:

• The tumour stage of all patients was between stage III and IV;

• All patients were aged ≥18 years, and there were no restrictions on gender or race;

• No patients had previous tumour treatment;

• All patients had an estimated survival time of more than six months;

• All patients were confirmed by pathology;

• Routine blood analysis, liver and kidney function, and ECG were normal in all patients;

• All patients and their family members were informed and signed informed consent forms.

The exclusion criteria included:

• Drop-out due to serious adverse reactions;

• Patients who had severe liver and kidney dysfunction;

• Patients who had severe cardiovascular and cerebrovascular diseases;

• Patients who had other malignant tumours;

• Patients who were allergic to treatment drugs;

• Patients who had contraindications to chemotherapy;

• Patients who refused the trial or who had poor compliance.

The treatment group was divided into the control group and the observation group. There were 32 patients in the control group, including 18 males and 14 females, with an average age of (52.16±5.16) years, an average disease duration of (5.86±2.15) months, and an average BMI of (20.05±1.33) kg/m^2, 15 cases of adenocarcinoma, 17 cases of squamous cell carcinoma; there were 28 patients in the observation group, including 16 males and 12 females, with an average age of (52.09±5.34) years, an average treatment course of (5.75±2.26) months, and an average BMI value of (20.11±1.21) kg/m^2, with 12 cases of adenocarcinoma and 16 cases of squamous cell carcinoma. There were no significant differences in the age, gender, and BMI of subjects in the two groups (P>0.05).

Methods

The control group

Patients were given pemetrexed (produced by Lilly France; approval number: H20110035; specification: 0.5 g/bottle) 500 mg/m^2, intravenous infusion for 30 min, once/day, treatment for 30 d.

The observation group

The patient was given pemetrexed 500 mg/m^2, once/day, for 30 min by intravenous infusion. Meanwhile, 0.3–0.4 g/m^2 carboplatin (produced by Qilu Pharmaceutical Co., Ltd.; approval number: H20020181; specification: 10 ml/bottle) was administered intravenously for 3 h, once during the treatment of 30 d. A routine blood examination was performed twice a week for all patients, and liver and kidney function, electrolytes, blood glucose, electrocardiogram, and urine tests were performed before each cycle.

Observation indexes

Platelet parameter detection

2 ml of fasting venous blood was collected from all patients before and after treatment, and anticoagulation was conducted with 15% dipotassium ethylenediamine tetraacetate. The platelet count (PLT), mean platelet volume (MPV), platelet specific volume (PCT), and platelet distribution width (PDW) of patients before and after treatment were measured using an automatic blood cell counter.

Detection of tumour markers

5 ml of fasting venous blood was collected from all patients before and after treatment, and serum was separated at a low temperature of 4 °C. The levels of CEA, CYFRA21-1, and CA125 of the patients were measured before and after treatment by electrochemical luminescence immunoassay.

Efficacy

With reference to the relevant efficacy evaluation criteria, where the tumour completely disappeared, and this was maintained for more than 4 weeks, this was defined as a complete remission

(CR); where the tumour was reduced by more than 50%, and this was maintained for more than 4 weeks, it was defined as a partial remission (PR); where the tumour was reduced by 50%, or was unchanged or even worsened, this was defined as no remission (NP). PR + CR=valid.

Adverse reactions

During the treatment, adverse reactions such as anaemia, nausea and vomiting, neutropaenia, and thrombocytopaenia of patients were observed and recorded.

Statistical methods

The data in this study were analysed using the SPSS 20.0 software package for statistical data analysis. All measurement data comparisons were expressed as ($\bar{x}\pm s$), comparisons between groups were performed using a t-test; enumeration data were expressed as percentages, and comparison between groups was performed using a χ^2 test. Ranked data comparison was performed using a ridit test. Statistical results were statistically significant for $P<0.05$.

Results

Comparison of tumour marker levels in serum between two groups of patients before and after treatment

Before treatment, there was no significant difference in the serum CEA, CYFRA21-1, and CA125 levels of patients between the two groups ($P>0.05$). After treatment, the serum levels of CEA, CYFRA21-1, and CA125 of patients in both groups decreased; the levels of CEA, CYFRA21-1, and CA125 in the serum of the observation group were significantly lower than those of the control group, and the difference was statistically significant ($P<0.05$), as shown in Table 1.

Group	Case		CEA (ng/ml)	CYFRA21-1 (U/ml)	CA125 (ng/ml)
The control group	32	Before treatment	21.45±20.16	92.86±52.11	12.56±8.56
		After treatment	18.45±15.23[a]	76.25±36.89[a]	7.31±5.06[a]
The observation group	28	Before treatment	21.43±21.33	93.11±50.74	12.85±7.98
		After treatment	13.46±10.22[ab]	46.75±26.21[ab]	4.28±3.04[ab]

Table 1: Comparison of tumour marker levels in serum between two groups of patients before and after treatment ($\bar{x}\pm s$).

Note: a means [a]P<0.05 compared with the same group before treatment, b means [b]P <0.05 compared with the control group after treatment.

Comparison of patient platelet parameters before and after treatment

Before treatment, there was no significant difference in the serum PCT, PLT, MPV, and PDW levels between the two groups of patients ($P>0.05$). After treatment, the levels of PCT, PLT, and MPV of patients in the serum in both groups decreased; the levels of PCT, PLT, and MPV in the serum of the observation group were significantly higher than those of the control group, and the difference was statistically significant ($P<0.05$). There was no significant change in PDW level ($P>0.05$), as shown in Table 2.

Group	Case		PCT (%)	PLT (×109/l)	MPV (fl)	PDW (fl)
The control group	32	Before treatment	0.26±0.11	286.49±53.48	13.46±5.13	16.20±2.14
		After treatment	0.19±0.05[a]	203.16±48.16[a]	9.18±0.43[a]	15.33±1.77
The observation group	28	Before treatment	0.27±0.12	287.43±52.52	13.45±0.81	16.23±2.15
		After treatment	0.21±0.06[ab]	220.46±52.42[ab]	9.96±2.46[ab]	15.46±1.43

Table 2: Comparison of patient platelet parameters before and after treatment ($\bar{x}\pm s$).

Note: a means [a]P<0.05 compared with the same group before treatment, b means [b]P <0.05 compared with the control group after treatment.

Comparison of efficacy of patients between two groups

The effective rate in the observation group was 75.00%, which was significantly higher than the 46.88% in the control group, and the difference was statistically significant ($P<0.05$), as shown in Table 3.

Group	Case	CR	PR	NP	Invalid
The control group	32	0 (0.00%)	15 (48.88%)	17 (53.13%)	15 (46.88%)
The observation group	28	4 (14.29%)	17 (60.71%)	7 (25.00%)	21 (75.00%)
χ^2					4.922
P					0.026

Table 3: Comparison of efficacy of patients between two groups (case, %).

Comparison of adverse reactions of patients between two groups

The incidence of adverse reactions in the observation group was 21.43%, which was significantly lower than the 53.13% in the control group, and the difference was statistically significant ($P<0.05$), as shown in Table 4.

Group	Case	Anaemia	Nausea and vomiting	Neutropaenia	Thrombocytopaenia	Total adverse reactions
The control group	32	5 (15.63%)	4 (12.50%)	5 (15.63%)	3 (9.38%)	17 (53.13%)
The observation group	28	2 (7.14%)	1 (3.57%)	2 (7.14%)	1 (3.57%)	6 (21.43%)
χ^2						6.347
P						0.012

Table 4: Comparison of adverse reactions of patients between two groups (case, %).

Discussion

NSCLC is one of the most common of the many solid tumours. It is more prone to metastasise in the blood system, lymph node system, and distant multiple organs in the early stage, and the mortality rate of patients with this tumour is high[6]. Currently, the methods for treating advanced NSCLC include systemic chemotherapy, targeted therapy, biological therapy, physical ablation, radiotherapy, and radioactive particle implantation. Of these, platinum-based chemotherapy is the most common[7]. Platinum drugs are indispensable for lung cancer chemotherapy. Carboplatin is a second-generation platinum anticancer agent with good stability and high solubility[8]. Studies have found that carboplatin has less gastrointestinal toxicity and renal toxicity than cisplatin, which is a first-generation platinum drug. It is commonly used in ovarian cancer, NSCLC, and head and neck squamous cell carcinoma[9]. In this study, the effective rate in the observation group was 75.00%, which was significantly higher than the 46.88% of the control group, and the difference was statistically significant (P<0.05). The incidence of adverse reactions in the observation group was 21.43%, which was significantly lower than the 53.13% of the control group, and the difference was statistically significant (P<0.05), suggesting that platinum-based chemotherapy for NSCLC is more effective than non-platinum single-agent chemotherapy, and has fewer adverse reactions than non-platinum single-agent chemotherapy, and is well-tolerated and highly safe.

CEA is a tumour-associated antigen that is commonly found in malignant tumours such as lung cancer, oesophageal cancer, and colorectal cancer, and plays a significant role in detecting tumours, prognosis after surgery or chemotherapy, recurrence, and metastasis[10]. CYFRA21-1, as a soluble tablet of cytokeratin 19 and a tumour marker, is of great significance in the diagnosis of lung cancer[11]. CA125 is a glycoprotein detected from epithelial ovarian cancer antigen[12], and it is abnormally elevated in the serum of patients with malignant tumours such as ovarian, lung, intestinal, and breast cancers[13]. In this study, there was no significant difference in the levels of CEA, CYFRA21-1, and CA125 in the serum of patients in the two groups before treatment (P>0.05).

After treatment, the levels of CEA, CYFRA21-1, and CA125 in the serum of patients in both groups was decreased, and the levels of CEA, CYFRA21-1, and CA125 in the serum of the observation group were significantly lower than those of the control group, and the difference was statistically significant (P < 0.05), suggesting that platinum-based chemotherapy can reduce the levels of CEA, CYFRA21-1, and CA125 in the serum of patients with NSCLC, further indicating better efficacy.

Malignant tumours can accelerate tumour growth, invasion, and metastasis by disrupting the body's coagulation and anticoagulation balance[14]. The normal cells of the body may also be damaged during chemotherapy. Platelet quality and quantity reflect the body's bone marrow haematopoiesis and coagulation function to a certain extent, and due to the expense of bone marrow examination and the high risk of infection, the bone marrow function is assessed indirectly through the measurement of platelet parameters. PLT shows the number of platelets in circulating blood, which reflects the proliferation and metabolism of megakaryocytes in the bone marrow and can also reflect platelet production[15]. PCL refers to the percentage of platelets in a volume of whole blood. MPV can reflect platelet activity and size, and indirectly reflects bone marrow hyperplasia. PDW is a parameter that indicates a difference in the width of platelets. In this study, there were no significant differences in serum PCT, PLT, MPV, or PDW levels between the two groups of patients before treatment (P>0.05).

The levels of PCT, PLT, and MPV in the serum of patients in the two groups decreased after treatment; the levels of PCT, PLT, and MPV in the serum of the observation group were significantly higher than those of the control group, and the difference was statistically significant (P<0.05).

There was no significant change in PDW level (P>0.05), suggesting that platinum-based chemotherapy has a low effect on platelet parameters of NSCLC patients, reduces the damage to bone marrow function, and greatly reduces the incidence of thrombocytopaenia. The insignificant change in PDW may be related to the small number of experimental samples.

In conclusion, platinum-based chemotherapy can reduce the levels of CEA, CYFRA21-1, and CA125 in NSCLC patients, but it has a lower impact on PCT, PLT, MPV, and PDW levels, reduces the incidence of thrombocytopenia, and has a better effect, better efficacy, and fewer adverse reactions, and can be widely used in clinics.

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