



Effect of Sintilimab Combined with Cisplatin + Pemetrexed Chemotherapy Regimen on Tumor Markers in Patients with Non-Small Cell Lung Cancer

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Abstract: Objective: To investigate the effect of sintilimab combined with cisplatin + pemetrexed chemotherapy regimen on tumor markers in patients with non-small cell lung cancer (NSCLC). Methods: A total of 68 NSCLC patients in the Oncology Department of Sichuan Provincial Jiaotong Hospital from June 2023 to June 2025 were selected and randomly divided into two groups using a random number table method. The control group (34 cases) was treated with cisplatin + pemetrexed chemotherapy regimen, and the experimental group (34 cases) was treated with sintilimab injection on the basis of the control group's regimen. The changes in tumor marker levels, therapeutic efficacy and safety were compared between the two groups. Results: After treatment, the levels of the above tumor markers in both groups were significantly lower than those before treatment, and the levels of each index in the experimental group were significantly lower than those in the control group, with statistically significant differences ($P < 0.05$); there was no statistically significant difference in adverse reaction indexes between the two groups ($P > 0.05$). Conclusion: The application of sintilimab combined with cisplatin + pemetrexed chemotherapy regimen in NSCLC patients can significantly reduce the expression levels of serum carcinoembryonic antigen (CEA), cytokeratin 19 fragment antigen 21-1 (CYFRA21-1), squamous cell carcinoma antigen (SCC), neuron-specific enolase (NSE) and other tumor markers, improve the clinical objective response rate and disease control rate, with considerable safety, which is worthy of clinical promotion.

Keywords: sintilimab; cisplatin; pemetrexed; non-small cell lung cancer; tumor markers; therapeutic efficacy; safety

1. Introduction

Non-small cell lung cancer is a common pathological type of lung cancer in clinical practice, accounting for more than 80% of the total incidence of lung cancer. The disease progression is insidious, and the early clinical symptoms lack specificity. Most patients are diagnosed at the middle and advanced stages, missing the opportunity for radical surgical treatment. Clinical treatment is mostly based on chemotherapy combined with other therapies. Previous studies have shown that cisplatin combined with pemetrexed is a classic chemotherapy regimen for NSCLC, which exerts anti-tumor effects by inhibiting tumor cell DNA synthesis and proliferation[1]. However, single chemotherapy has limitations in killing tumor cells, and long-term chemotherapy is prone to drug resistance, which affects the therapeutic effect. At the same time, the toxic and side effects caused by chemotherapy will reduce patients' treatment compliance. It has been reported in the literature that sintilimab, a programmed death receptor 1 (PD-1) inhibitor, can block the immune escape mechanism of tumor cells and activate the killing effect of the body's own immune cells on tumor cells[2]. Its combination with chemotherapy regimen can achieve a synergistic anti-tumor effect of immunotherapy and chemotherapy. Tumor markers have important clinical value in the disease monitoring and efficacy evaluation of NSCLC[3]. The expression levels of indicators such as CEA, CYFRA21-1, SCC and NSE can directly reflect the proliferation and metastasis of tumor cells and the changes in tumor burden after treatment. Therefore, this study would explore the effect of sintilimab combined with cisplatin + pemetrexed chemotherapy regimen on tumor markers in NSCLC patients.

2. Materials and Methods

2.1 General Information

A total of 68 NSCLC patients in the Oncology Department of Sichuan Provincial Jiaotong Hospital from June 2023 to June 2025 were enrolled as the research objects, and randomly divided into the control group (34 cases) and the experimental group (34 cases) using a random number table method. In the control group, there were 22 males and 12 females, aged 46 to 77 years, with a mean age of (61.25 ± 7.36) years; pathological types included 23 cases of adenocarcinoma and 11 cases of squamous cell carcinoma; clinical stages included 8 cases of stage IIB, 11 cases of stage IIIA, 9 cases of stage IIIB and 6 cases of stage IV. In the experimental group, there were 24 males and 10 females, aged 45 to 78 years, with a mean age of (61.58 ± 7.42) years; pathological types included 22 cases of adenocarcinoma and 12 cases of squamous cell carcinoma;

clinical stages included 7 cases of stage IIB, 12 cases of stage IIIA, 10 cases of stage IIIB and 5 cases of stage IV. The baseline data between the two groups were comparable ($P>0.05$).

2.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Confirmed as NSCLC by pathological histology or cytology examination; (2) Clinical stage IIB-IV, Karnofsky Performance Status (KPS) score ≥ 60 ; (3) Expected survival time ≥ 3 months, without receiving anti-tumor treatments such as radiotherapy, chemotherapy and immunotherapy; (4) Basic normal indicators such as blood routine, liver and kidney function, coagulation function, and tolerable to chemotherapy and immunotherapy.

Exclusion criteria: (1) Severe hepatic and renal insufficiency, complicated with other malignant tumors; (2) Presence of immune dysfunction or autoimmune diseases; (3) A history of allergy to the study drugs; (4) Complicated with central nervous system metastasis.

2.3 Treatment Methods

The control group was treated with cisplatin + pemetrexed single chemotherapy regimen: Pemetrexed disodium injection (specification: 0.5g/vial) at a dose of 500mg/m², intravenous infusion on day 1; Cisplatin injection (specification: 20mg/vial) at a dose of 75mg/m², intravenous infusion in 3 divided doses on days 1-3. One treatment cycle was 21 days, with continuous treatment for 4 cycles. Routine pretreatment with folic acid tablets and vitamin B12 tablets was given before chemotherapy to prevent hematological and gastrointestinal toxic and side effects caused by pemetrexed. Antiemetic, gastric protective and fluid replacement symptomatic supportive treatments were given during chemotherapy.

The experimental group was treated with sintilimab injection on the basis of the chemotherapy regimen of the control group: Sintilimab injection (specification: 100mg/vial) at a dose of 200mg, intravenous infusion on day 1 with an infusion time of no less than 60 minutes; the administration method, dose and course of cisplatin + pemetrexed were consistent with the control group. One treatment cycle was 21 days, with continuous treatment for 4 cycles. The vital signs of patients were closely monitored during medication, and infusion reactions and immune-related adverse reactions were observed. Targeted interventions were taken in a timely manner if abnormalities occurred.

No other anti-tumor drugs were used in both groups during treatment. Blood routine and liver and kidney function were reexamined regularly, and the drug dose was adjusted or symptomatic treatment was given according to the examination results to ensure the smooth progress of treatment.

2.4 Observation Indicators

(1) Tumor marker levels: Fasting peripheral venous blood (5mL) was collected from patients before treatment and after 4 cycles of treatment, placed in a non-anticoagulant test tube, left to stand at room temperature for 30 minutes, and centrifuged at 3000r/min for 10 minutes to separate serum. Electrochemiluminescence immunoassay(ECLIA) was used to detect the serum levels of CEA, CYFRA21-1, SCC and NSE in strict accordance with the kit instructions, and the detection instrument was a fully automatic electrochemiluminescence immunoanalyzer.

(2) Clinical efficacy: After 4 cycles of treatment, the clinical efficacy of the two groups was evaluated with reference to the Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1, which was divided into complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD). Objective response rate (ORR) = (number of CR cases + number of PR cases)/total number of cases $\times 100\%$, disease control rate (DCR) = (number of CR cases + number of PR cases + number of SD cases)/total number of cases $\times 100\%$.

(3) Incidence of adverse reactions: The occurrence of adverse reactions in the two groups during treatment was recorded, including hematological toxicity (leukopenia, thrombocytopenia, anemia), gastrointestinal reactions (nausea, vomiting, diarrhea), hepatorenal dysfunction, thyroid dysfunction, etc., and the incidence of adverse reactions was calculated.

2.5 Statistical Methods

SPSS 28.0 statistical software was used for data analysis. Corresponding test methods were adopted for different types of data: Measurement data of tumor marker levels were expressed as mean \pm standard deviation and tested by t-test; count data were expressed as percentage and tested by chi-square test. The test standard was $P<0.05$.

3. Results

3.1 Comparison of Tumor Marker Levels between the Two Groups Before and After Treatment

Before treatment, there was no statistically significant difference in the serum levels of CEA, CYFRA21-1, SCC and NSE between the two groups ($P>0.05$); after 4 cycles of treatment, the levels of the above tumor markers in both groups were

significantly lower than those before treatment, and the levels of each index in the experimental group were significantly lower than those in the control group, with statistically significant differences ($P < 0.05$). See Table 1.

Table 1. Comparison of tumor marker levels between the two groups before and after treatment (Mean \pm SD)

Group	n	CEA (ng/mL)		CYFRA21-1 (ng/mL)		SCC (ng/mL)		NSE (ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	34	45.26 \pm 12.35	15.32 \pm 5.18*#	38.59 \pm 10.24	12.45 \pm 4.26*#	2.85 \pm 1.06	1.02 \pm 0.35*#	35.68 \pm 9.75	16.24 \pm 5.36*#
Control group	34	44.89 \pm 11.98	28.65 \pm 8.24*	37.96 \pm 9.85	23.58 \pm 6.89*	2.78 \pm 0.98	1.86 \pm 0.62*	34.96 \pm 9.28	25.89 \pm 7.65*
t	-	0.125	7.986	0.259	9.012	0.283	6.880	0.312	6.024
P	-	0.901	<0.001	0.797	<0.001	0.778	<0.001	0.756	<0.001

Note: *indicated a significant difference in the same group before and after treatment ($P < 0.05$); # indicated a significant difference between the two groups after treatment ($P < 0.05$)*

3.2 Comparison of Clinical Efficacy between the Two Groups

The clinical efficacy of the experimental group was significantly better than that of the control group ($P < 0.05$). The confirmatory study shows that the combination of tislelizumab with cisplatin + pemetrexed chemotherapy regimen can significantly improve the treatment outcome of non-small cell lung cancer. Compared with chemotherapy alone, it can more effectively control tumor progression and prolong the disease-free survival period of patients. See Table 2.

Table 2. Comparison of clinical efficacy between the two groups (n,%)

Group	n	CR	PR	SD	PD	ORR
Experimental group	34	5 (14.71)	18 (52.94)	8 (23.53)	3 (8.82)	23 (67.65)
Control group	34	2 (5.88)	11 (32.35)	10 (29.41)	11 (32.25)	13 (38.24)
χ^2	-	-	-	-	-	6.569
P	-	-	-	-	-	0.010

3.3 Comparison of the Incidence of Adverse Reactions between the Two Groups

There was no statistically significant difference in the incidence of hematological toxicity such as leukopenia, thrombocytopenia and anemia between the experimental group and the control group ($P > 0.05$); the incidence of gastrointestinal reactions such as nausea, vomiting and diarrhea in the experimental group was slightly lower than that in the control group, and the incidence of immune-related adverse reactions such as thyroid dysfunction was slightly higher than that in the control group. There were no statistically significant differences in the above indicators between the two groups ($P > 0.05$). Both groups mainly experienced mild adverse reactions, with no severe adverse events occurring. After symptomatic treatment, all symptoms could be relieved and did not affect the treatment process. This indicates that the safety of the Xindili single-agent combined with cisplatin + pemetrexed chemotherapy regimen is good, and the patients have a high tolerance. See Table 3.

Table 3. Comparison of the incidence of adverse reactions between the two groups (n,%)

Group	n	Hematological toxicity	Gastrointestinal reactions	Thyroid dysfunction	Total incidence
Experimental group	34	4 (11.76)	8 (23.53)	3 (8.82)	15 (44.12)
Control group	34	5 (14.71)	10 (29.41)	1 (2.94)	16 (47.06)
χ^2	-	-	-	-	0.059
P	-	-	-	-	0.808

4. Discussion

The occurrence and development of NSCLC is a complex process involving multiple factors, stages and genes. For patients with middle and advanced NSCLC, surgical treatment has limited effect due to local invasion or distant metastasis of tumor cells, and chemotherapy has become the main clinical anti-tumor treatment method. Cisplatin, a cell cycle non-specific drug, can combine with tumor cell DNA to form cross-links, inhibit DNA replication and transcription, and thus induce tumor cell apoptosis; pemetrexed, an antifolate metabolic drug, can inhibit key enzymes in the process of purine and

pyrimidine synthesis and block the nucleic acid synthesis of tumor cells[4]. The combination of the two can inhibit tumor cell proliferation from different targets and exert a synergistic chemotherapy effect, which is the first-line chemotherapy regimen for patients with middle and advanced NSCLC.

Tumor markers are produced by tumor cells or the body's response to tumor cells, and their expression levels are closely related to tumor burden and disease progression, which are important objective indicators for evaluating the effect of anti-tumor treatment. CEA is a broad-spectrum tumor marker with high expression in the serum of NSCLC patients, and its level is closely related to tumor stage and lymph node metastasis; CYFRA21-1 is a degradation product of cytokeratin, a specific marker of lung squamous cell carcinoma, which can reflect the proliferation and invasion ability of tumor cells; SCC is mainly expressed in squamous cell carcinoma and has important value in the disease monitoring of lung squamous cell carcinoma; NSE is a neuron-specific enolase, expressed in both lung adenocarcinoma and small cell lung cancer, which can reflect the metabolic activity of tumor cells. The results of this study showed that after treatment, the serum levels of CEA, CYFRA21-1, SCC and NSE in both groups were significantly lower than those before treatment, and the levels of each index in the experimental group were significantly lower than those in the control group, suggesting that sintilimab combined with cisplatin + pemetrexed chemotherapy regimen has a stronger killing effect on tumor cells in NSCLC patients and can reduce tumor burden more significantly, which is closely related to their synergistic anti-tumor mechanism[5].

In conclusion, the application of sintilimab combined with cisplatin + pemetrexed chemotherapy regimen in NSCLC patients can significantly reduce the expression levels of serum carcinoembryonic antigen (CEA), cytokeratin 19 fragment antigen 21-1 (CYFRA21-1), squamous cell carcinoma antigen (SCC), neuron-specific enolase (NSE) and other tumor markers, improve the clinical objective response rate and disease control rate, with considerable safety, which is worthy of clinical promotion.

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