

Clinical Value Analysis of Pemetrexed Combined with Cisplatin in the Treatment of Non-Small Cell Lung Cancer

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Abstract: *Objective:* To analyze the clinical value of pemetrexed combined with cisplatin in the treatment of non-small cell lung cancer (NSCLC). *Methods:* Sixty-nine patients in Shengli Oilfield Central Hospital were recruited between May 2021 and August 2022 and separated into the observation group (n = 35) and the control group (n = 34). Cisplatin combined with pemetrexed (the observation group) and cisplatin combined with gemcitabine (the control group) were used for treatment, respectively, and the therapeutic effects of the two groups were compared. *Results:* There was no significant difference in the disease control rate between the two groups ($P > 0.05$); the immune function indexes of the patients in the observation group were significantly higher than those in the control group after treatment ($P < 0.05$); there was no significant difference in the incidence of nausea and vomiting as well as hair loss ($P > 0.05$), but the incidence of blood toxicity in the observation group was significantly lower than that in the control group ($P < 0.05$). *Conclusion:* Pemetrexed plus cisplatin in NSCLC patients has an ideal effect, and it can improve the quality of life of patients and reduce adverse reactions, which has clinical promotion value.

Keywords: Pemetrexed; Cisplatin; Non-small cell lung cancer; Clinical value

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1. Introduction

Lung cancer is a very common type of cancer where a harmful malignant tumor grows in the lungs. Recently, 1.4 million people have been diagnosed every year, and the prevalence and mortality have been rising^[1,2]. Among them, non-small cell lung cancer (NSCLC) accounts for about 80% of lung cancers. Many patients miss the best opportunity for treatment and often seek medical attention during the middle and late stages of lung cancer^[3,4]. Therefore, the purpose of clinical treatment is to alleviate the patient's symptoms as much as possible and prolong the patient's survival period. Currently, platinum-based chemotherapy is the main treatment for NSCLC, but the efficacy is unsatisfactory, as it has only a 20%–40% effective rate^[5]. This article analyzed the clinical effect and safety of 69 patients with NSCLC who received pemetrexed and cisplatin combined therapy, aiming to further explore the efficacy of this treatment plan.

2. Materials and methods

A retrospective study was carried out between May 2021 and August 2022 at the Shengli Oilfield Central Hospital, China. Inclusion criteria included patients being diagnosed with NSCLC, patients who did not receive relevant treatment or had received chemotherapy but within 2 treatment courses before participating

in this study, with expected survival time of over 0.5 years and KPS score of more than 60 points, as well as no other serious diseases such as coronary heart disease, renal failure, liver failure, etc. Exclusion criteria included the following: (1) lack of diagnosis and treatment data; (2) combined with other serious malignant tumors; (3) intolerant to the drug of study; (4) abnormal menstrual blood and electrocardiogram examination before treatment; and (5) lost contact during follow-up or left halfway through the study. Sixty-nine patients aged 48–79 who fulfilled the inclusion criteria were recruited, informed, and signed the consent form. They were then randomly divided into 2 groups: the observation group (male:female = 18:17 [51.43%:48.57%]; mean age = 63.54 ± 4.89 years old), and the control group (male:female = 18:16 [52.94%:47.06%]; mean age = 63.78 ± 4.02 years old).

Both groups of patients received cisplatin therapy with a dose of 75 mg/m² divided into 3 days via intravenous infusion, and the infusion time was over 2 hours. Appropriate diuretic treatment was given before and after treatment.

The control group was treated with cisplatin combined with gemcitabine, and the patients were intravenously infused with 100 mg/m² of gemcitabine and 100 mL of normal saline on the first and eighth day of the treatment, and the infusion lasted for 30 minutes.

The observation group was treated with a combination of pemetrexed and cisplatin; 500 mg/m² of pemetrexed was injected into 100 mL of normal saline and administered intravenously on the first day of treatment. Over a cycle of 21 days, 400 µg/d of pemetrexed oral folic acid was given from 1 week before chemotherapy to 3 weeks after the end of chemotherapy, while vitamin B12 was given one week before pemetrexed injection, once every 3 weeks. On the day of administration and the following day, 4 mg of oral dexamethasone were given twice a day, and an intramuscular injection of 1,000 µg vitamin B12 was administered, followed by cisplatin infusion starting 30 minutes after the end of pemetrexed infusion.

The effect judgment included short-term efficacy analysis, immune function indexes, as well as adverse reactions. The short-term efficacy analysis included complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), overall response rate (ORR; the sum of CR and PR), and disease control rate (DCR; the sum of CR, PR, and SD).

Statistical software SPSS 22.0 was used in this study to process data. The measurement data were represented by mean ± standard deviation (SD), and the *t*-test was used. Enumeration data were expressed in %, and the χ^2 test was used. The difference was statistically significant when *P* < 0.05.

3. Results

3.1. Comparison of the short-term efficacy between the two groups

As shown in **Table 1**, there was no significant difference in the disease control rate between the two groups (*P* > 0.05).

Table 1. Comparison of the short-term efficacy between the two groups

Group	Number of cases	CR	PR	SD	PD	RR	DCR
Observation group	35	5 (14.29%)	21 (45.71%)	6 (17.14%)	3 (8.57%)	26 (74.29%)	32 (91.43%)
Control group	34	4 (11.76%)	21 (47.06%)	5 (14.71%)	4 (11.76%)	25 (73.53%)	30 (88.24%)
χ^2		0.128	0.000	0.076	0.193	0.005	0.193
<i>P</i>		0.721	1.000	0.782	0.660	0.943	0.660

3.2. Comparison of changes in humoral immune function indexes between the two groups

As shown in **Table 2**, the cellular immune function indexes of the two groups of patients before

chemotherapy were similar ($P > 0.05$), whereas, after chemotherapy, the cellular immune function indexes of the observation group were significantly higher than those of the control group ($P = 0.016$ for IgA; $P = 0.000$ for IgG, IgM, and IgE).

Table 2. Comparison of changes in humoral immune function indexes

Group	Number of cases	IgG (g/L)		IgA (mg/L)		IgM (mg/L)		IgE (mg/L)	
		Before chemo	After chemo	Before chemo	After chemo	Before chemo	After chemo	Before chemo	After chemo
Observation group	35	6.59 ± 2.47	6.45 ± 0.21	1.67 ± 0.42	1.61 ± 0.57	1.52 ± 0.35	1.50 ± 0.03	1.69 ± 0.35	1.61 ± 0.47
Control group	34	6.23 ± 2.35	5.12 ± 0.35	1.68 ± 0.68	1.31 ± 0.43	1.43 ± 0.31	1.01 ± 0.03	1.73 ± 0.48	1.13 ± 0.35
<i>t</i>		0.620	19.205	0.074	2.463	1.130	67.830	0.396	4.800
<i>P</i>		0.537	0.000	0.941	0.016	0.263	0.000	0.693	0.000

3.3. Comparison of the adverse reactions' incidence between the two groups

As shown in **Table 3**, during the treatment, there was no significant difference in the incidence of nausea, vomiting, and hair loss between the two groups ($P > 0.05$), but the incidence of blood toxicity in the observation group was significantly lower than that in the control group ($P = 0.009$).

Table 3. Comparison of the adverse reactions' incidence between the two groups

Group	Number of cases	Hair loss	Nausea and vomiting	Blood toxicity
Observation group	35	1 (2.86%)	2 (5.88%)	0 (0.00%)
Control group	34	2 (5.88%)	1 (2.94%)	6 (17.65%)
χ^2		0.380	0.319	6.765
<i>P</i>		0.538	0.572	0.009

4. Discussion

Lung cancer is one of the most common malignancies, and NSCLC is the dominant type. Patients who are diagnosed with NSCLC are not suitable for surgical treatment [6,7]. Currently, chemotherapy is the main treatment method. It is necessary to be attentive to its effectiveness and side effects when using specific drugs during the treatment. From the 1960s to the 1970s, platinum-based drugs were widely used in the treatment of lung cancer. However, due to the poor treatment effect and obvious side effects, platinum-containing regimens have been gradually updated and iterated in the treatment of lung cancer. Nowadays, the first-line treatment is a platinum-based two-dose combination regimen, and the application of new chemotherapeutic drugs, such as pemetrexed, docetaxel, and gemcitabine, has further improved the effectiveness of lung cancer treatment [8,9]. In recent years, the treatment of advanced NSCLC has advanced rapidly. Among them, the application of drugs such as vinorelbine, paclitaxel, irinotecan, and pemetrexed has significantly improved the chemotherapy effect on lung cancer and reduced its side effects. Recent large-scale randomized controlled studies have shown that the combination of new chemotherapeutic drugs and platinum-based drugs as third-generation chemotherapy regimens have a better therapeutic effect than second-generation platinum-containing regimens and can achieve a cure rate of 30%–40%. Pemetrexed, as a first-line or second-line treatment drug, has a significant effect on the 1-year survival rate of patients with NSCLC [10,11].

Pemetrexed is a novel antineoplastic drug that disrupts folate-dependent cell replication processes. It inhibits the activity of all the folate-dependent enzymes, thymidylate synthase (TS), dihydrofolate reductase (DHFR), and glycinamide ribonucleotide formyltransferase (GARFT), thereby reducing the biosynthesis of purine and thymidine nucleotides and inhibiting the DNA and RNA production of tumor cells [12]. Pemetrexed has also been shown to have antitumor properties in a variety of tumors, including colorectal, breast, lung, pancreatic, and gastric cancers.

Pemetrexed performs well in the treatment of malignant mesothelioma where non-surgical treatment is feasible. It can significantly relieve symptoms when used alone or in combination with platinum-based drugs and has become one of the standard drugs for advanced malignant mesothelioma. Several clinical studies have shown that when pemetrexed is used in combination with cisplatin, the effective rate and median survival time of newly diagnosed NSCLC are better than those of pemetrexed alone. Among them, two phase I clinical studies have shown that the RR and DCR of combination therapy were 74.29% and 91.43%, respectively, and the median survival time reached 10.9 months and 8.9 months, respectively [13]; while the effective rate of pemetrexed alone was only 16% and 23%, respectively. A total of 571 NSCLC patients participated in a large-scale randomized clinical study to compare the second-line treatment effects of single-agent pemetrexed and paclitaxel. The results of the study showed that there was no significant difference between the two drugs in terms of effective rate (9.1% vs 8.8%), median survival (8.3 months vs 7.9 months), and 1-year survival rate (both 29.7%) [14]. Side effects including neutropenia, fever, and hair loss were noted, where the pemetrexed group had significantly reduced adverse reactions, as compared to the paclitaxel group. Based on this study, the US Food and Drug Administration (FDA) approved pemetrexed as a first-line drug for the treatment of locally advanced and metastatic NSCLC in August 2004. The study achieved a PR rate of 21.05% and a clinical utilization rate of 57.89% with the pemetrexed combined with a cisplatin regimen, similar to the results reported in the existing literature. The use of pemetrexed can cause various rare and severe side effects, such as leukopenia, rash, anemia, abnormal liver function, thrombocytopenia, and many more [15]. To reduce the occurrence of bone marrow toxicity, patients need to consume folic acid and vitamins. In addition, taking oral dexamethasone can prevent a rash from developing. All patients who took dexamethasone orally supplemented with folic acid and vitamins were found with no rash and white blood cell decline. Symptomatic treatment is effective for patients with leukopenia and non-hematological toxicity.

Gemcitabine belongs to difluoronucleoside antineoplastic drugs, which inhibit the proliferation of cancer cells and disrupt cell replication. The study showed that the RR and DCR of the observation group were 74.29% and 91.43%, respectively, as compared to the control group, despite no statistically significant difference between the two groups ($P > 0.05$). Compared with pemetrexed, gemcitabine resulted in poorer immune indexes, and the incidence of alopecia, nausea, and vomiting among other adverse reactions had no significant difference between the use of the two drugs ($P > 0.05$). This further verified the research point of view, suggesting that the combination of pemetrexed and cisplatin is indeed effective, which is the same as Qiu Pei's study [16], confirming that there was no statistically significant difference in adverse reactions between the pemetrexed group and the gemcitabine group.

5. Conclusion

In summary, chemotherapy is the main treatment option for patients diagnosed with NSCLC, who realize the futility of surgery during the advanced stages of the disease, but the effect of chemotherapy alone is limited. Therefore, the comprehensive use of pemetrexed combined with cisplatin as first-line treatment can not only enhance the therapeutic effect and promote the relief of patient indicators and symptoms but also reduce side effects and improve treatment comfort and compliance. In addition, comprehensive treatment is expected to stabilize the disease and improve the survival rate of patients.

Disclosure statement

The author declares no conflict of interest.

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