

## Original Article

# Clinical effect of paclitaxel combined with cisplatin in oral cancer patients and the influence on immune function of patients

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**Abstract:** Objective: We aimed to discuss the therapeutic effect of paclitaxel combined with cisplatin in oral cancer patients and the influence on immune function and prognosis. Methods: Eighty oral cancer patients were selected as subjects of study and divided into an observation group (n=40) and a control group (n=40) according to a random number table method. The patients in the observation group were treated with paclitaxel combined with cisplatin and those in the control group were treated with 5-fluorouracil combined with cisplatin, so as to respectively observe and compare the total effective rates, immune function indexes, serum cytokine indexes, quality of life scores, adverse reaction rates, and 1- and 2-year cumulative survival rates in the two groups. Results: The total effective rate was assessed as 87.50% in the observation group and 62.50% in the control group, which indicated that the difference had statistical significance ( $P<0.05$ ). The tested values of CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> increased after treatment and the tested value of CD8<sup>+</sup>, VEGF and HGF decreased after treatment. The degree of increase and decrease in the observation group were much more apparent than those in the control group, which indicated that the difference had greater significance ( $P<0.05$ ). The adverse reaction rate in the observation group was lower than that in the control group, and the 1- and 2-year cumulative survival rates in the observation group were higher than those in the control group, with statistical significance ( $P<0.05$ ). Conclusion: The application of paclitaxel combined with cisplatin in oral cancer patients who were admitted to hospital, clearly improves the therapeutic effect, increases the level of immune function and enhances the quality of life. Besides, paclitaxel combined with cisplatin, has higher safety, and can achieve a relatively ideal cumulative survival rate, so it has very important promotional value clinically.

**Keywords:** Oral cancer, cisplatin, paclitaxel, total effective rate, immune function

## Introduction

Oral cancer is a multiple pathological form of malignant tumor. According to reports, the incidence of oral cancer is about 5/100,000 in China and is still rising continuously [1, 2]. Every year, about 274,000 patients are diagnosed with oral cancer [3]. Oral cancer, mostly induced by mucosal variation, is related to multiple factors, such as malnutrition, ulceration and smoking, etc. In the past, the oral cancer patients were mostly treated with the combined therapy of primary tumor excision and postoperative chemoradiotherapy [4, 5], but the overall therapeutic effect was poor and the 5-year survival rate of patients was lower than 50% [6]. Therefore, it is of great clinical significance to

actively seek more effective methods to treat oral cancer.

At present, chemotherapy is an important treatment scheme for early oral cancer in clinical practice and platinum drugs are the first-line drugs in chemotherapy. However, due to the wide application of drugs in clinical practice, the susceptibility of oral cancer to these drugs decreases in various degrees, which reduces the therapeutic effect of chemotherapy on patients accordingly [7, 8]. Combined drug application may improve the therapeutic effect of chemotherapy. It was found through research that paclitaxel combined with platinum drugs could clearly enhance the chemosensitivity [9, 10]. This study observed the clinical effects and

# Clinical efficacy of paclitaxel combined with cisplatin in patients

safety of paclitaxel combined with cisplatin in the treatment of oral cancer patients.

## Material and methods

Tissues were collected from 80 oral cancer patients who were admitted to our hospital and divided into two groups according to a random number table. There were 40 patients in the observation group, including 28 men and 12 women, between the age of 23-58 and the average age of (37.4±3.2). There were 40 patients in the control group, including 27 men and 13 women, between the age of 25-59 and the average age of (37.7±3.1). Inclusion criteria: ① The patients were diagnosed with oral squamous cell carcinoma in Stage III-IV according to the staging criteria for oral cancer [11] issued by Union for International Cancer Control (UICC). ② The patients were not suitable for operative treatment due to their disease states or disease relapse after palliative operation. ③ The Karnofsky performance status scores were ≥ 60 and the expected survival time was more than 6 months. ④ The hepatorenal function was normal. ⑤ The patients were not complicated with systemic diseases. ⑥ The patients signed an Informed Consent Form of their own accord. This study was approved by Ethics Committee of Yanan University Affiliated Hospital. Exclusion criteria: ① The patients were complicated with mental diseases. ② The expected survival time was less than 3 months. ③ The patients were diagnosed with immune diseases or treated with immunosuppressors.

## Methods

The treatment scheme of 5-fluorouracil combined with cisplatin was used in the control group, with details shown below. The patients were injected with cisplatin at the dose of 30 mg/m<sup>2</sup> through intravenous drip once a day during the first three days, and with 5-fluorouracil at the dose of 750 mg/m<sup>2</sup> through intravenous drip once a day during the first five days. One course of treatment lasted for 21 days and there were 3 courses of treatment in total. The treatment scheme of paclitaxel combined with cisplatin was used in the observation group, with details shown below. The patients were injected with paclitaxel at the dose of 150 mg/m<sup>2</sup> and cisplatin at the dose of 100 mg/m<sup>2</sup> through intravenous drip on the first day. One course of treatment lasted for 21 days and there were 3 courses of treatment in total.

## Observation targets

(1) The total effective rates were compared in the two groups and the therapeutic effect was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST) [12]. If the lesions disappeared completely for 4 weeks successively, this was considered as complete remission (CR). If the total maximum diameter of lesions reduced by more than 30% for 4 weeks successively, this was considered as partial remission (PR). If the total maximum diameter of lesions reduced by 20%-30%, it was considered as stable disease (SD). If the total maximum diameter of lesions increased by more than 20% or if there were new lesions emerging, this was considered as progressive disease (PD). Therefore, the objective remission rate (ORR) = the number of (CR+PR)/the total number of cases × 100%; and the disease control rate (DCR) = the number of (CR+PR+SD)/the total number of cases × 100%. (2) The immune function indexes were compared in the two groups, including CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> levels. Fifty μL of fasting blood from the ulnar vein was taken from patients in the two groups before and after treatment, and then was mixed in a flow tube. Fluorescent labels for CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> monoclonal antibodies were added, 10 μL each, and incubated at 24°C in the dark. Red blood cell lysate and 0.5 mL phosphate buffer (PBS) were added successively and mixed by shaking. Becton Dickinson (BD, USA) was used to detect the levels of CD3<sup>+</sup>, CD4<sup>+</sup> and CD8<sup>+</sup>. (3) Four mL of fasting blood from the ulnar vein was taken in the morning, and the serum was collected by centrifugation. The levels of VEGF, HGF and TNF-α were detected by enzyme-linked immunosorbent assay. (4) The quality of life scores were compared in the two groups through the assessment method of Minnesota Living with Heart Failure Questionnaire, with a total of 105 points. The lower the scores are, the more ideal the quality of life is. (5) The occurrence of adverse reactions were compared in the two groups. (6) The 1- and 2-year survival rates were compared in the two groups.

## Statistical analysis

All the data in this paper were analyzed with SPSS 22.0. The chi-square test was used for enumeration data between groups, which was represented by (%), including total effective rate, adverse reaction rate and cumulative sur-

## Clinical efficacy of paclitaxel combined with cisplatin in patients

**Table 1.** Comparison of clinical data in the two groups

		Observation group (n=40)	Control group (n=40)	$\chi^2/t$	P
Gender	Male	28	12	0.058	0.809
	Female	27	13		
Average age (years old)		37.4±3.2	37.7±3.1	0.426	0.671
Weight (kg)		61.3±7.2	59.3±8.1	1.167	0.247
KPS scoring (scores)		79.7±7.1	79.9±6.9	0.511	0.611
Pathological staging (cases)	Stage III	19	21	0.050	0.823
	Stage IV	18	22		
Pathological pattern (cases)	Squamous cell carcinoma	38	2	0.213	0.644
	Adenocarcinoma	37	3		

**Table 2.** Comparison of total clinical effective rates in the two groups [n (%)]

Group	CR	PR	SD	PD	ORR	DCR
Observation group (n=40)	0 (0)	18 (45.00)	14 (35.0)	8 (20.00)	18 (45.00)	32 (80.00)
Control group (n=40)	0 (0)	11 (27.50)	12 (35.0)	17 (42.50)	11 (30.00)	23 (57.5)
$\chi^2$	-	-	-	-	2.650	4.713
P	-	-	-	-	0.104	0.030

vival rate. The t test was used for the index detection of measurement data and the quality of life scores, which was represented by mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ). A  $P < 0.05$  indicated that the difference had statistical significance.

### Results

#### *Comparison of clinical data in the two groups*

There was no statistical difference in clinical data between the two groups before treatment ( $P > 0.05$ ), including age, gender, weight, pathological staging, KPS scoring, pathological pattern and other baseline information, as shown in **Table 1**.

#### *Comparison of total clinical effective rates in the two groups*

The ORR was assessed as 45.00% in the observation group and 30.00% in the control group, showing no statistical difference ( $P > 0.05$ ). The DCR was assessed as 80.00% in the observation group and 57.50% in the control group, showing a statistical difference ( $P < 0.05$ ). This implied that the overall therapeutic effect of paclitaxel combined with cisplatin in oral cancer patients was better than that of 5-fluorouracil combined with cisplatin, as shown in **Table 2**.

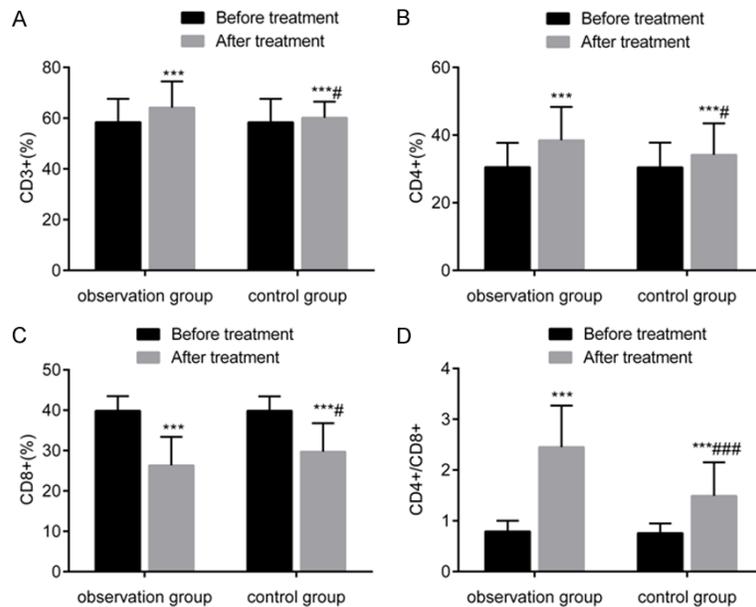
#### *Comparison of immune function indexes in the two groups*

There was no difference in immune function indexes of CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> before treatment in the two groups ( $P > 0.05$ ). The measured values of CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> increased after treatment and the measured value of CD8<sup>+</sup> decreased after treatment. The degree of increase and decrease in the observation group was greater than those in the control group, which indicated that the difference had statistical significance ( $P < 0.05$ ). This implied that paclitaxel combined with cisplatin, had better therapeutic effect in comparison with 5-fluorouracil combined with cisplatin, and can clearly improve the immune functions of oral cancer patients, as shown in **Figure 1**.

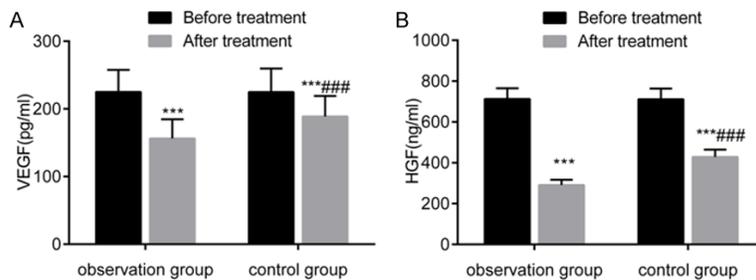
#### *Comparison of serum cytokine levels in the two groups*

There was no difference in the serum cytokines of VEGF and HGF before treatment in the two groups ( $P > 0.05$ ). The test values of all indexes decreased after treatment and the degree of decrease in the observation group was greater than that in the control group, which indicated that the difference had statistical significance ( $P < 0.05$ ). This implied that paclitaxel combined with cisplatin, had better therapeutic effect in

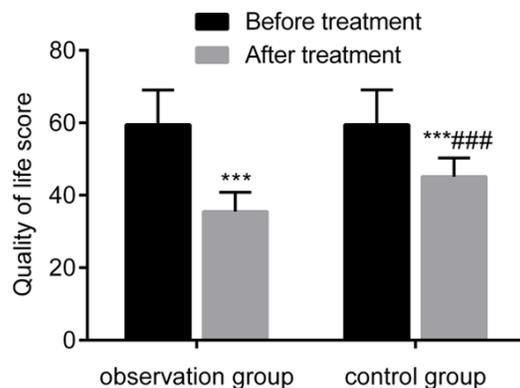
## Clinical efficacy of paclitaxel combined with cisplatin in patients



**Figure 1.** Comparison of immune function indexes in the two groups. Notes: \*\*\* $P < 0.001$  in comparison with that before treatment in this group; and # $P < 0.05$  and ### $P < 0.001$  in comparison with those in the control group. A. CD3<sup>+</sup>; B. CD4<sup>+</sup>; C. CD8<sup>+</sup>; D. CD4<sup>+</sup>/CD8<sup>+</sup>.



**Figure 2.** Comparison of serum cytokine levels. Notes: \*\*\* $P < 0.001$  in comparison with that before treatment in this group; and ### $P < 0.001$  in comparison with that in the control group. A. VEGF; B. HGF.



**Figure 3.** Quality of life scores in two groups. Notes: \*\*\* $P < 0.001$  in comparison with that before treatment in this group; and ### $P < 0.001$  comparison with that in the control group.

comparison with 5-fluorouracil combined with cisplatin, and could improve the levels of VEGF and HGF in the serum of oral cancer patients, as shown in **Figure 2**.

### Comparison of quality of life scores in the two groups

There was no difference in quality of life scores before treatment in the two groups ( $P > 0.05$ ). The scores decreased after treatment, and the degree of decrease in the observation group was more clear than that in control group, which indicated that the difference had statistical significance ( $P < 0.05$ ). This implied that the application of paclitaxel combined with cisplatin has better treatment in oral cancer patients and can enhance the quality of life scores, as shown in **Figure 3**.

### Comparison of adverse reaction rates in the two groups

The adverse reaction rate of the observation group was lower than that of the control group, including nausea and vomiting, oral mucositis, myelosuppression and thrombocytopenia, with statistical significance ( $P < 0.05$ ). This implied that paclitaxel combined

with cisplatin had less adverse reactions and higher safety in the treatment of oral cancer patients, as shown in **Table 3**.

### Comparison of 1- and 2-year cumulative survival rates in the two groups

The 1- and 2-year cumulative survival rates in the observation group were higher than those in the control group, with statistical significance ( $P < 0.05$ ), as shown in **Table 4**.

## Discussion

There are many adjuvant chemotherapy schemes used for oral cancer in clinical practice, of which 5-fluorouracil and cisplatin are

## Clinical efficacy of paclitaxel combined with cisplatin in patients

**Table 3.** Comparison of adverse reaction rates in the two groups [n (%)]

Group	Nausea and vomiting	Oral mucositis	Myelosuppression	Thrombocytopenia
Observation group (n=40)	1 (2.50)	1 (2.50)	2 (5.00)	2 (5.00)
Control group (n=40)	9 (22.50)	9 (22.50)	10 (25.00)	10 (25.00)
	7.314	7.314	6.275	6.275
P	0.007	0.007	0.012	0.012

**Table 4.** Comparison of 1- and 2-year cumulative survival rates in the two groups [n (%)]

Group	1-year cumulative survival rate	2-year cumulative survival rate
Observation group (n=40)	36 (90.00)	27 (67.50)
Control group (n=40)	29 (72.50)	18 (45.00)
	4.021	4.114
P	0.044	0.043

used more frequently in clinical application. The overall therapeutic effect is not ideal and the phenomenon of chemotherapy resistance often occurs. It was shown in some research that [13] the ORR of oral cancer patients treated with 5-fluorouracil and cisplatin through intravenous chemotherapy was 23.8% and the DCR was 61.9%, which indicated that the therapeutic effect was not ideal. This study showed that the ORR of oral cancer patients treated with 5-fluorouracil and cisplatin through intravenous chemotherapy was 30.0% and the DCR was 57.5%, which were consistent with other literature reports. This implied that the clinical effect was not ideal in treating oral cancer patients with 5-fluorouracil and cisplatin through intravenous chemotherapy, so we sought out new effective chemotherapeutics.

As shown in many reports, the application of paclitaxel and cisplatin to chemotherapy could achieve an ideal effect in many departments [14, 15]. Cisplatin, is a nonspecific drug with cell cycle applications and may interact with appropriate bases in the DNA of tumors, which will inhibit the replication progress of tumor cells [16, 17]. Paclitaxel, with unique antitumor mechanisms, can inhibit the growth and diffusion of cancer cells effectively. It can also promote microtubule polymerization to keep the microtubule structure stable and thus inhibit microtubule depolymerization. Therefore, paclitaxel plays an important role in regulating the balance of microtubule dynamics and thus inhibits cancer cells significantly [18, 19]. The

results of this study show the ORR of oral cancer patients in the observation group was 45.0% and the DCR was 80.0%. Also, the DCR level of the observation group was much higher than that of control group. Meanwhile, the 1- and 2-year cumulative survival rates in the observation group were much higher than those in the control group. Furthermore, the quality of life scores decreased after treatment in the two groups, and the degree of decrease in the observation group was enhanced over that in control group, which implied that paclitaxel combined with cisplatin, had better overall therapeutic effects in comparison with 5-fluorouracil combined with cisplatin, which could prolong the survival time of patients and improve the quality of life of oral cancer patients.

It was found in research that [20] immune function may be reduced in different degrees during the pathogenetic processes of tumor patients and that disease progression of oral cancer patients was closely related to the reduction of immune function. Therefore, T cells are a key marker that reflects the changes of immune function during the anti-tumor process of cancer patients. The number of CD3<sup>+</sup> cells is mainly used to evaluate the changes of cellular immune function. CD4<sup>+</sup> cells are mainly used to evaluate the resistance ability of the human body to tumor cells. CD8<sup>+</sup> cells mainly reflect immunosuppression. The ratio of CD4<sup>+</sup>/CD8<sup>+</sup> reflects the development and progress of tumors. This study indicated that the measured values of CD3<sup>+</sup>, CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> increased after treatment, and the measured value of CD8<sup>+</sup> decreased after treatment. Besides, the degree of increase and decrease in the observation group was enhanced over those in the control group. This implied that paclitaxel combined with cisplatin, had better therapeutic effects in comparison with 5-fluorouracil com-

bined with cisplatin, in improving the immune function in oral cancer patients.

HGF, primarily for synthesis and secretion of mesenchyma, plays a crucial role in the growth, regeneration and remodeling of histocytes. It can also mediate cell migration and invasion and plays an important role in tumor metastasis and invasion. VEGF is a cell growth factor which, with the strongest effect and the highest specificity, is generated and secreted by vascular endothelial cells. With high expression, it can promote the occurrence and development of tumors. As shown in research, HGF can activate the phosphoinositide 3-kinase pathway, promote the synthesis and secretion of VEGF, mediate the formation of tumor vessels and promote the progress of tumors. Some scholars proposed that [21] the levels of HGF and VEGF in serum from oral cancer patients is clearly increased, which showed the progress state of tumors. However, after treatment, HGF and VEGF levels were reduced, which indicated that tumor invasion functions were reduced after the tumor lesions were controlled. This implied that HGF and VEGF levels could be regarded as important indexes to judge the severity of oral cancer patients and evaluate the therapeutic effect. This study showed that the tested values of the serum cytokines VEGF, HGF and TNF- $\alpha$  decreased after treatment and the degree of decrease in the observation group was greater than that in the control group. This implied that paclitaxel combined with cisplatin, had better therapeutic effect in comparison with 5-fluorouracil combined with cisplatin, and can improve the levels of VEGF, HGF and TNF- $\alpha$  in the serum of oral cancer patients.

What's more, this study also showed that the adverse reaction rate in the observation group was lower than that in the control group, which implied that paclitaxel combined with cisplatin had less adverse reactions and higher safety in the treatment of oral cancer patients.

In conclusion, the application of paclitaxel combined with cisplatin for the treatment of oral cancer in patients who were admitted to our hospital could enhance the total effective rate, improve the level of immune function, inhibit tumor cells, and strengthen the quality of life. Moreover, with higher safety and a relatively ideal cumulative survival rate, paclitaxel com-

bined with cisplatin has a very important value clinically. However, as this is a preliminary study with a short research period and few cases, the specific mechanism of action of paclitaxel chemotherapy on oral cancer has not been discussed. In the next step, animal and cell experiments will be carried out to explore the specific mechanisms of drug action.

### Disclosure of conflict of interest

None.

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## Clinical efficacy of paclitaxel combined with cisplatin in patients

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