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Original Research Article

Efficacy of cisplatin in combination with paclitaxel for oral cancer and its effect on cellular immunity

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Abstract

Purpose: *To study the efficacy of cisplatin in combination with paclitaxel in the treatment of oral cancer and its effect on cellular immunity.*
Methods: *A total of 100 patients with oral cancer, treated in the First Affiliated Hospital of Dalian Medical University from May 2018 to April 2020 were included and evenly allocated to study and control groups. The patients in the study group received cisplatin plus paclitaxel, while the patients in the control group received only cisplatin. The serum levels of T lymphocytes, interleukin (IL) -4, IL-2, and interferon gamma (IFN-γ) were determined.*
Results: *After treatment, the study group showed significantly higher levels of CD3+, CD4+ and CD4/CD8, but a lower CD8+ level (26.17 ± 2.14 µL). than those before treatment ($p < 0.05$). The control group was associated with higher post-treatment CD3+, CD4+, CD8+, and CD4/CD8 levels and lower CD8+ levels versus patients in the study group ($p < 0.05$). The study group showed higher levels of IL-2 and INF-γ, (246.77 ± 13.68 and 1194.62 ± 123.15 pg/mL), respectively, but lower IL-4 levels (392.48 ± 13.25 pg/mL) after treatment than before treatment. Control group was associated with higher post-treatment IL-2 and INF-γ levels and lower IL-4 levels compared to patients in the study group ($p < 0.05$).*
Conclusion: *Cisplatin and paclitaxel combination offers a viable treatment alternative for oral cancer, as it enhances patients' immune function and disease prognosis, regulates inflammatory responses, and promotes patients' recovery. Further investigations in larger population settings are, however, recommended.*

Keywords: *Cisplatin chemotherapy, Paclitaxel, Oral cancer, Peripheral blood cells, Immune function*

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INTRODUCTION

Oral cancer is a common malignancy [1], including lip cancer, tongue cancer, jaw cancer, gum cancer, buccal mucosa cancer, etc. [2]. According to epidemiological statistics, there are nearly 300,000 new cases each year in recent years, and the pathogenesis is mainly related to biological and environmental factors [3,4]. The clinical symptoms of oral cancer mostly include pain, leukoplakia, and chronic oral ulcers [5,6]. Presently, surgical resection, radiotherapy, and chemotherapy are the mainstay of treatment for oral cancer [7]. However, the treatment outcome is suboptimal, and patients are still associated

with poor survival and high recurrence and metastasis rates [8].

Cisplatin is a broad-spectrum anti-tumor chemotherapeutic drug that has obtained promising results in treating solid tumors such as ovarian cancer, testicular cancer, and lung cancer [9]. It inhibits the synthesis of DNA and RNA in tumor cells to exert the anti-tumor function and plays a synergistic effect with 5-Fluorouracil (5-FU) [10]. Paclitaxel is a natural secondary metabolite obtained from *Taxus chinensis* and has good antitumor effects for breast cancer, ovarian cancer, and lung cancers [11]. In recent years, neoadjuvant chemotherapy with paclitaxel has achieved good clinical results [12,13]. This study was undertaken to investigate the efficacy of the combination of cisplatin and paclitaxel for oral cancer and its impact on cellular immunity.

METHODS

Study population

A total of 100 patients with oral cancer treated in the First Affiliated Hospital of Dalian Medical University between May 2018 and April 2020 were selected and assigned to the observation and control groups. The study was approved by the ethic committee of First Affiliated Hospital of Dalian Medical University (approval no. 20180230). The study was conducted in line with the protocol of Helsinki Declaration [14]. All the patients consented to participate in the study.

Inclusion and exclusion criteria

Inclusion criteria

Patients with oral squamous cell carcinoma, without allergies to the drugs used in this treatment, and with consciousness that allows normal communication were included.

Exclusion criteria

Patients with systemic diseases such as diabetes and hypertension, with autoimmune disease and use of immunosuppressive drugs, and who revoked their consent were excluded.

Treatments

Patients in the observation group received 100 mg/m^2 of cisplatin and 150 mg/m^2 of paclitaxel through an intravenous infusion for 5 days, starting from the first day of treatment, and repeated 30 days after first treatment. Patients in the control group received only 100 mg/m^2 of cisplatin through an intravenous infusion 5 days starting on the first day of treatment, and repeated 30 days after first treatment. Approximately 2 mL of venous blood was collected from all participants for the determination of blood indices. All testing methods used were in line with the relevant laboratory diagnostic standards.

Assessment of parameters/outcomes

Treatment efficacy

If the symptoms and signs were significantly mitigated and the test indices were markedly improved after treatment, the treatment was considered markedly effective. After treatment, if the symptoms and signs were mitigated and the test indices were improved, the treatment was considered effective. If aggravations or no changes were observed in the symptoms and test indices after treatment, the treatment was considered ineffective.

Peripheral venous blood test

The blood samples were centrifuged, and the supernatant was collected for assays using the ELISA method. The determination of blood indices was performed as per the kit instructions.

T-lymphocyte measurement

Blood samples collected from each patient was divided into four portions of 100 µL in each group for assay. The first portion was added with FITC-labeled CD3 antibody and PE-labeled CD56 antibody, the second portion was added with FITC-labeled CD4 antibody and PE-labeled CD8 monoclonal antibody, the third portion was added with FITC-labeled CD4 antibody and PE-labeled INF-γ antibody, and the fourth portion was added with FITC-labeled CD4 antibody and PE-labeled IL-2 antibody, with the dose of each antibody sample being 10 µL. The specimens were then incubated for 1 h, added with red blood cell lysate, allowed to react for 10 min, and then centrifuged for 5 min, followed by the collection of the supernatant for assays using flow cytometry.

Statistical analysis

All data analyses were performed with SPSS 22.0 software. The count data (n (%)) are analyzed using the chi-square test. The measurement data (mean ± SD) were analyzed using *t*-test. A *p*-value less than 0.05 was set as the cut-off for statistical significance.

RESULTS

Baseline characteristics of patients

In the study group, there were 35 males and 15 females, 34 cases of clinical stage III, and 16 cases of clinical stage IV, and the participants were aged 51.23 ± 5.18 years. In the control group, there were 36 males and 14 females, 33 cases of clinical stage III, and 17 cases of clinical stage IV, and the participants were aged 51.08 ± 5.37 years. The patient characteristics between the two groups were comparable (p > 0.05) (Table 1).

Treatment effectiveness

After treatment, in the study group, there were 18 cases that were significantly effective, 25 cases were effective, and 7 cases were ineffective; while in the control group, there were 10 markedly effective cases, 20 cases were effective, and 20 cases were ineffective (Table 2).

Expression of T lymphocytes

After treatment, the study group showed higher levels of CD3+, CD4+, CD4/CD8 (66.86 ± 3.14, 39.69 ± 3.12, and 1.52 ± 0.13 µL) and a lower CD8+ level (26.17 ± 2.14 µL) than those before treatment (57.65 ± 2.68, 30.24 ± 3.62, 0.83 ± 0.14, and 39.51 ± 5.62 µL). The control group had a markedly higher post-treatment levels of CD3+, CD4+, CD8+, CD4/CD8 and lower CD8+ levels when compared with patients in the study group (p < 0.05; Table 3).

IL-2, IL-4, INF-γ contents

The study group showed higher levels of IL-2 and INF-γ (246.77 ± 13.68 and 1194.62 ± 123.15 pg/mL) and lower IL-4 levels (392.48 ± 13.25 pg/mL) after treatment than before treatment (156.46 ± 10.33 884.23 ± 102.37, and 429.58 ± 17.35 pg/mL). The control group had higher post-treatment IL-2 and INF-γ contents and lower IL-4 contents versus patients in the study group (p < 0.05). (Table 4)

Table 1: Baseline feature (mean ± SD; n = 45)

Group	Gender *Male/Female*	Age (years)	Stage		Disease site			
			III	*IV*	*Tongue*	*cheek*	*gums*	*floor of mouth*
Study	35/15	51.23±5.18	34	16	13	12	12	13
Control	36/14	51.08±5.37	33	17	12	14	11	13
T/X^2	0.049	0.315	0.045				0.086	
P-value	0.826	0.893	0.832				0.776	

Table 2: Effectiveness of treatment in the observation group (n = 50)

Group	Markedly effective	Effective	Ineffective
Study	18	25	7
Control	10	20	20
X^2		8.574	
P-value		0.003	

Table 3: Comparison of T lymphocyte expression (mean ± SD; n = 50)

Group		CD3 (µL)	CD4 (µL)	CD8 (µL)	CD4/CD8
Study	Before treatment	57.65±2.68	30.24±3.62	39.51±5.62	0.83±0.14
	After treatment	66.86±3.14*	39.69±3.12*	26.17±2.14*	1.52±0.13*
Control	Before treatment	57.82±2.89	32.42±2.59	37.48±5.99	1.35±0.16
	After treatment	68.96±3.53*	42.69±3.14*	29.47±2.64*	1.92±0.43*
T		14.966	13.265	14.881	24.228
P-value		<0.001	<0.001	<0.001	<0.001

Note: *Significant difference between pre- and post-treatment within the group (p < 0.05)

Table 4: Comparison of changes in IL-2, IL-4 and INF-γ levels between the two groups (mean ± SD, n = 50)

Group		IL-2 (pg/mL)	IL-4 (pg/mL)	INF-γ (pg/mL)
Study	Before treatment	156.46±10.33	429.58±17.35	884.23±102.37
	After treatment	246.77±13.68*	392.48±13.25*	1194.62±123.15*
Control	Before treatment	155.46±11.23	430.58±16.35*	885.03±112.37
	After treatment	233.72±12.58*	382.38±11.45*	1124.32±113.15*
T		35.341	11.400	13.002
P-value		<0.001	<0.001	<0.001

Note: * indicates a significant difference between pre- and post-treatment within the group (P < 0.05)

DISCUSSION

Oral cancer is clinically treated with surgical resection, supplemented with radiotherapy and chemotherapy [15], yet both have a high degree of recurrence and metastasis. Cisplatin is a clinical anticancer drug [16] with cell cycle non-specificity. It inhibits the synthesis of DNA and RNA to exert anti-tumor effects. Research has reported that cisplatin is effective in various solid tumors such as ovarian cancer and prostate cancer, testicular cancer, lung cancer, nasopharyngeal cancer, esophageal cancer, malignant lymphoma, head and neck squamous cell carcinoma, thyroid cancer and osteosarcoma [10]. Paclitaxel is a common drug in neoadjuvant chemotherapy with good antitumor activity [17].

In the present study, patients in the study group showed treatment effectiveness of 95.56 %, indicating that the combination of cisplatin and paclitaxel are effective for oral cancer. Moreover, the study group showed higher levels of CD3+, CD4+, CD4/CD8 after treatment and a lower CD8+ level than those before treatment suggesting that cisplatin and paclitaxel improve patient immunity and promote the recovery of patients. The results were consistent with the previous studies [18,19]. Additionally, the study group showed higher levels of IL-2 and INF-γ and lower IL-4 levels after treatment than before treatment and the differences in the three indices between the two groups were also statistically significant, suggesting alleviated inflammatory responses in the patients and enhanced secretion of cytokines after the use of cisplatin and paclitaxel. This outcome is similar to the previous research results that reported that inflammatory factors in peripheral blood increased significantly, and the immune function of peripheral blood cells was improved, resulting in diminished tumor volume [20].

CONCLUSION

The combination of cisplatin and paclitaxel offers a viable treatment alternative for oral cancer, as it enhances patients' immune function and improves disease prognosis, regulates their inflammatory responses, and promotes their recovery. However, further studies in larger population groups are recommended.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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