

CLINICAL RESEARCH

The clinical effect of Pingxiao capsule as an adjuvant chemotherapy in the treatment of patients with stage III-IV laryngeal cancer and its influence on angiogenesis and tumor markers

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Abstract

Objective To explore the clinical effects of Pingxiao capsule as an adjuvant chemotherapy in the treatment of patients with stage III-IV laryngeal cancer and its influence on angiogenesis and tumor markers. **Methods** A total of 66 patients with stage III-IV laryngeal cancer treated at our hospital from August 2017 to April 2019 were selected as the study subjects, and they were divided into observation group and control group according to random number table method. The control group was treated with TPF regimen, while the observation group was treated with Pingxiao capsule on the basis of the control group. The objective remission rate, vascular endothelial growth factor, matrix metalloproteinase-9, carbohydrate antigen 19-9, cytokeratin 19 fragment, squamous cell carcinoma associated antigen level and the incidence of adverse reactions were compared between the two groups. **Results** The ORR of the observation group was significantly higher than that of the control group. After treatment, the levels of VEGF and MMP-9 in the observation group were greatly lower than those before treatment and in the control group, and the levels of CA19-9, CYFRA21-1 and SCC-Ag in the observation group were noticeably lower than those before treatment and the control group. There was no significant difference in the incidence of adverse reactions between the two groups. **Conclusion** Pingxiao capsule as an adjuvant treatment to chemotherapy showed a high clinical effect in the treatment of stage III-IV laryngeal cancer patients, and it can inhibit angiogenesis factors, reduce the levels of body tumor markers and the occurrence of adverse reactions.

Introduction

Laryngeal cancer is a common malignant tumor

among head and neck tumors, and most of the patients are in the middle to late stage when it is discovered

because the incidence site is hidden and early symptoms are not obvious [1-2]. For patients with intermediate-to-late stage laryngeal cancer, it is difficult to achieve satisfactory therapeutic effects by simple surgery, and therefore radiotherapy and chemotherapy need to be administered simultaneously after surgery [3]. TPF is a newly emerged chemotherapy protocol in recent years, but it can also reduce the number of white blood cells and platelets, leading to adverse reactions such as skin rash and oral ulcers, which is not conducive to patients' prognosis [5-6]. Pingxiao capsule, which is a pure Chinese traditional medicine antitumor preparation, can reduce the toxic side effects caused by radiotherapy and chemotherapy and improve the quality of life of cancer patients. Therefore, this study investigated the clinical effects of adjuvant chemotherapy with Pingxiao capsule in treating patients with stage III-IV laryngeal cancer and its effects on angiogenesis and tumor markers, so as to provide reference for clinical treatment.

Data and Methods

Clinical Data

Sixty-six patients with stage III-IV laryngeal cancer treated at our hospital from August 2017 to April 2019 were selected as the study subjects and divided into an observation group (n=33) and a control group (n=33) according to the randomized numerical table method. In the observation group, there were 19 males and 14 females, aged 51-72 years, with an average age of 61.64 ± 8.21 years; in the control group, there were 18 males and 15 females, aged 49-70 years, with an average age of 59.77 ± 8.46 years. Inclusion criteria: Patients who met the diagnostic criteria of stage III-IV laryngeal cancer [7], who had not recently received other treatment plans, and who were not allergic to the drugs used were enrolled into the study. Exclusion criteria: Patients with other malignant tumors, severe hepatic and renal dysfunction or with psychiatric disorders were excluded. This study was reviewed and approved by the Ethics Committee of our hospital, and all patients signed an informed consent form.

Methods

All the patients were treated with antiemetics, anti-allergy and vitamin supplements. The control group was treated with intravenous docetaxel injection at 75 mg/m^2 for more than 30 minutes (min) on day 1, intravenous cisplatin injection at 40 mg/m^2 on days 1 to 3, and intravenous fluorouracil injection at 750 mg/m^2 on day 1 to 5. The observation group was treated with Pingxiao capsule at 1.84 g a time, three times a day. 21 days were seen as a treatment cycle, both two groups were treated for 3 cycles.

Evaluation of clinical effectiveness

Complete remission (CR): all target lesions were gone for at least 4 weeks; partial remission (PR): the largest diameter and largest vertical diameter of the target lesion was reduced by more than 50% for at least 4 weeks; stable disease (SD): the two diameters of the target lesion were reduced by less than 50% or increased by less than 25% for at least 4 weeks; progressive disease (PD): the two diameters of the target lesion were increased by $\geq 25\%$ or a new lesion appeared. Overall response rate (ORR) = (CR+PR) cases/total cases $\times 100\%$.

Observational Indicators

Angiogenic parameters: 5 mL of early morning fasting venous blood was drawn, centrifuged, and then the serum was obtained for the determination of VEGF and MMP-9 by enzyme-linked immunosorbent assay (ELISA).

Tumor markers: Chemiluminescence immunoassay was used to determine the levels of glycogen 19-9 (CA19-9), cytokeratin 19 fragment (CYFRA21-1), and squamous cell carcinoma-associated antigen (SCC-Ag).

Adverse events: the occurrence of adverse events during the course of treatment was recorded. Incidence of adverse reactions = number of cases of adverse reactions/total number of cases $\times 100\%$.

Statistical Methods

SPSS 21.0 was used for statistical analysis, and the mean \pm standard deviation ($\bar{x} \pm s$) was used for

measurement data, t-test was used for comparison, and χ^2 test was used for counting data.

Comparison of clinical outcomes between two groups of patients

Results

Table 1 Comparison of clinical data between two groups of patients

Groups	Cases	Sex		Age (years old)	Clinical stage	
		Male	Female		III	IV
Observation group	33	19	14	61.64±8.21	21	12
Control group	33	18	15	59.77±8.46	23	10
<i>t</i> / χ^2		0.062		0.911	0.273	
<i>P</i>		0.804		0.366	0.602	

Table 2 Comparison of clinical outcomes between two groups of patients

Groups	Cases	CR	PR	SD	PD	ORR
Observation group	33	10	14	6	3	24 (72.73)
Control group	33	4	11	7	11	15 (45.45)
χ^2						5.077
<i>P</i>						0.024

Comparison of angiogenic parameters between two groups of patients

The VEGF and MMP-9 levels of the two groups before treatment were not significantly different ($P>0.05$), and the VEGF and MMP-9 levels of the two

groups after treatment were significantly lower than those before treatment ($P<0.05$), and the VEGF and MMP-9 levels of the patients in the observation group were greatly lower than those in the control group ($P<0.05$), see Table 3.

Table 3 Comparison of angiogenic parameters between two groups of patients

Groups	Cases	VEGF (ng/L)		MMP-9 (ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	33	436.27±42.45	224.67±32.45 ^a	483.64±28.75	241.24±15.38 ^a
Control group	33	429.64±47.31	365.38±39.66 ^a	489.66±26.42	358.63±19.79 ^a
<i>t</i>		0.599	-15.774	-0.886	-26.906
<i>P</i>		0.551	0.000	0.379	0.000

Note: Compared with before treatment, ^a $P<0.05$.

Comparison of tumor marker levels between two groups of patients

The CA19-9, CYFRA21-1, and SCC-Ag levels of the two groups were not significantly different before treatment ($P>0.05$), and the CA19-9, CYFRA21-1, and SCC-Ag levels of the two groups were

significantly lower after treatment than before treatment ($P<0.05$). The levels were significantly lower than those in the control group ($P<0.05$), as shown in Table 4.

Comparison of adverse reactions in two groups of

patients

There was no significant difference in the incidence of

adverse events between the two groups. ($P>0.05$), see Table 5.

Table 4 Comparison of tumor marker levels between two groups of patients

Groups	Cases	CA19-9 (U/mL)		CYFRA21-1 (ng/mL)		SCC-Ag (ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	33	19.75±4.31	13.66±2.39 ^a	4.12±0.65	2.18±0.38 ^a	3.04±0.76	1.35±0.32 ^a
Control group	33	20.25±4.45	17.54±3.13 ^a	4.07±0.71	2.97±0.56 ^a	2.95±0.83	2.21±0.58 ^a
<i>t</i>		-0.464	-5.660	0.298	-6.706	0.459	-7.458
<i>P</i>		0.644	0.000	0.766	0.000	0.647	0.000

Note: Compared with before treatment, ^a $P<0.05$.

Table 5 Comparison of adverse reactions in two groups of patients

Groups	Cases	Nausea	Vomiting	Diarrhea	Incidence of adverse events
Observation group	33	3	0	3	6 (18.18)
Control group	33	2	2	4	8 (24.24)
χ^2					0.363
<i>P</i>					0.547

Discussion

In recent years, the treatment options for advanced laryngeal cancer are still undergoing continuous improvement, and at present, total laryngectomy is often used to treat laryngeal cancer patients clinically, but the larynx, as an important organ of the common passage between the respiratory tract and the digestive tract, plays a critical role in maintaining the functions of vocalization and swallowing [8-9]. Therefore, it is increasingly important to preserve laryngeal function in the treatment of laryngeal cancer. Studies have shown that TPF chemotherapy regimens have strong effects on preserving the laryngeal function and improving the quality of life of laryngeal cancer patients [10]. At the same time, the adjuvant chemotherapy with Pingxiao capsule can effectively improve the effect of chemotherapy and reduce the occurrence of adverse reactions. Therefore, in this

study, patients with stage III-IV laryngeal cancer were treated with Pingxiao capsules combined with TPF chemotherapy, and the results showed that the clinical efficacy of patients treated with Pingxiao capsules was significantly better than that of non-users.

The TPF regimen mainly includes docetaxel, cisplatin and fluorouracil, which are paclitaxel-based antitumor drugs with antitumor role by inhibiting cell mitosis [11-12]. Cisplatin is a cell cycle non-specific antitumor agent that cross-links DNA strands and affects the synthesis of cellular DNA to inhibit cancer cells [13]. Fluorouracil can inhibit the activity of thymine nucleotide synthase, which in turn can inhibit DNA biosynthesis and prevent the proliferation of cancer cells [14-15]. Pingxiao capsule is a Chinese medicine preparation, the main components of which are Yu Jin, Citrus aurantium, alum, Xian He Cao, dried lacquer, powder of horse chestnut, Wu Ling

Lipid, nitrate, etc. It can strengthen the body resistance to eliminate pathogenic factors, promote blood circulation and remove stasis, clear heat and remove toxins, relieve pain and disperse stagnant, etc. It can also improve the immunity of the body and relieve the pain of cancer patients.

VEGF, which is an important angiogenic factor in the body, not only promotes the formation of tumor new blood vessels, but also induces lymphangiogenesis and helps tumor metastasis [17]. MMP-9 is a matrix metalloproteinase that can decompose tumor extracellular matrix and promote tumor invasion and metastasis [18]. In this study, the VEGF and MMP-9 levels of the patients in the observation group were significantly lower than those in the pre-treatment and control groups, indicating that the combination of Pingxiao capsule and TPF chemotherapy can more effectively inhibit the formation of new blood vessels and tumor invasion. This may be due to the fact that the active ingredient of *Hovenia Citrus aurantium dulcis* can inhibit the expression of matrix metalloproteinases and the polymerization of microtubule proteins, thus reducing the ability of tumor cells to migrate and invade.

CA19-9 is a glycoprotein tumor marker that plays an important role in the diagnosis and prognosis of cancer patients [20-21]. CYFRA21-1 is a soluble fragment of cytokeratin 19 expressed in malignant tumor cells [22]. SCC-Ag is a human squamous cell carcinoma-related antigen that is often distributed in the cytoplasm of squamous cell carcinoma [23-24]. The CA19-9, CYFRA21-1, and SCC-Ag levels of the patients in this study were obviously lower than those in the pre-treatment and control groups, indicating that the combination of Pingxiao capsule and TPF chemotherapy was more effective in reducing tumor markers and inhibiting tumor recurrence. At the same time, alum has the effect of eliminating pain and heat and resolving stubborn phlegm, and wulingin has the effect of eliminating stasis and subduing accumulation, thereby they can reduce the toxic side effects brought by chemotherapy and improve patients' prognosis. In the course of treatment, the occurrence of adverse reactions in the two groups of patients was statistically

evaluated, and the results showed that there was no significant difference in the incidence of adverse reactions between the two groups of patients, but the number of adverse reactions in the observation group was relatively low.

In summary, the adjuvant chemotherapy of Pingxiao capsule for patients with stage III-IV laryngeal cancer has a strong clinical effect, and it can inhibit the generation of angiogenic factors, reduce the level of tumor markers and the occurrence of adverse reactions.

Declaration of conflict-of-interest

The authors declare no conflict-of-interest.

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