ORIGINAL ARTICLE

Evaluation of Xiaoaiping Combined with Oxaliplatin and Capecitabine in the Treatment of Advanced Metastatic Gastric Adenocarcinoma

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Abstract

Objectives: To evaluate the effect of Xiaoaiping combined with oxaliplatin and capecitabine in the treatment of advanced metastatic gastric adenocarcinoma. **Methods:** Seventy patients with advanced metastatic gastric adenocarcinoma in our hospital from January 2018 to March 2019 were randomly divided into the control group treated with oxaliplatin and capecitabine chemotherapy and the observation group treated with Xiaoaiping. Each group has 35 cases. The short-term efficacy of the two groups was compared. **Results:** The total effective rate and disease control rate of the observation group were higher than that of the control group. After treatment, tumor markers, vascular endothelial growth factors and inflammatory cytokines were lower than those in the control group. The quality of life score and peripheral lymphocyte subgroup were higher than the control group. The difference was statistically significant ($P < 0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$). **Conclusions:** Xiaoaiping combined with oxaliplatin and capecitabine is effective in the treatment of advanced metastatic gastric adenocarcinoma. It's worth popularizing.

Keywords

Advanced metastatic gastric adenocarcinoma; Xiaoaiping; oxaliplatin; capecitabine

1. INTRODUCTION

Gastric adenocarcinoma is the most common type of gastric cancer in clinical practice, which is caused by the canceration of gastric glandular cells. It accounts for about 95% of all gastric malignancies^[1]. Due to the lack of specific symptoms in the early stages of gastric adenocarcinoma, they are often in the middle and advanced stages when diagnosed, and the best time for surgery is lost. The prognosis is relatively poor^[2]. Chemotherapy is a commonly used method for the clinical treatment of advanced metastatic gastric adenocarcinoma. XELOX was the preferred treatment, but the short-term efficacy was not very satisfactory^[3]. Xiaoaiping is a traditional Chinese medicine preparation prepared by modern technology, which can inhibit the proliferation of tumor cells and induce apoptosis without damaging normal cells. It is especially suitable for the treatment of various advanced malignant tumors^[4]. Whether the application of Xiaoaiping in the treatment of advanced metastatic gastric

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adenocarcinoma can promote the patients to get more benefits from it has become an important topic of research. Therefore, this study focused on the effect of Xiaoaiping combined with oxaliplatin and capecitabine in the treatment of advanced metastatic gastric adenocarcinoma.

2. MATERIALS AND METHODS

2.1 General Data

Seventy patients with advanced metastatic gastric adenocarcinoma in our hospital from January 2018 to March 2019 were randomly divided into the control group treated with oxaliplatin and capecitabine chemotherapy and the observation group treated with Xiaoaiping. Each group has 35 cases. There were 27 males and 8 females in the control group with the age of 52~69. The average age was (60.34 ± 1.16) years. The duration of disease was 6.5 years to 15 years. The mean duration of disease was (10.77 ± 1.03) years. Metastatic sites: 17 cases of supraclavicular lymph node metastasis, 9 cases of liver metastasis, 5 cases of peritoneal lymph node metastasis, 4 cases of peritoneal metastasis; TNM staging: 22 cases in stage IIIB and 13 cases in stage IV; Karnofsky score: 5 cases with score ≤ 80 and 30 cases with score > 80 . There were 30 males and 5 females in the observation group with age of 50~69 years. The average age was (60.42 ± 1.19) years. The duration of the disease was 6.5 to 15.5 years. The mean duration of disease was (10.82 ± 1.07) years. Metastatic sites: 16 cases of supraclavicular lymph node metastasis, 10 cases of liver metastasis, 6 cases of peritoneal lymph node metastasis and 3 cases of peritoneal metastasis; TNM staging: 24 cases in stage IIIB and 11 cases in stage IV; Karnofsky score: 4 cases with score ≤ 80 and 31 cases with score > 80 . Inclusion criteria: (1) The patient was pathologically diagnosed with advanced metastatic gastric adenocarcinoma; (2) Patients without XELOX plan and/or Xiaoaiping contraindications; (3) Patients with advanced metastatic gastric adenocarcinoma and/or family members sign the Informed Consent Form. Exclusion criteria: (1) The patient is in critical condition and the expected life cycle is less than 4 months. (2) Participating in other clinical trials; (3) Karnofsky score ≤ 60 , with failure of vital organs; (4) Those who do not follow the doctor's advice and take immunological preparations that affect clinical efficacy without authorization. There was no significant statistical difference between the two groups in the general data of patients with metastatic gastric adenocarcinoma.

2.2 Methods

The control group received oxaliplatin and capecitabine chemotherapy. The specific scheme is as follows: Oxaliplatin (Nanjing Pharmaceutical Factory Co., Ltd., Chinese Medicine Standard H20000686) $130 \text{ mg/m}^2 + 5\%$ glucose solution was dripped into 250 mL or 500 mL intravenously, and it was administered on the first day. Capecitabine (Shanghai Roche Pharmaceutical Co., Ltd., Chinese Medicine Standard H20073024) 1000 mg/m^2 , twice a day, oral, 1d~14d. 21d is a treatment cycle, with 6 consecutive cycles.

The observation group was treated with Xiaoaiping. Xiaoaiping (Beijing Sanlian Pharmaceutical Co., Ltd., national drug approval Z20060351) was taken orally, 8 to 10 pills each time, three times a day.

2.3 Observed Indicator

Total effective rate, disease control rate, tumor markers, vascular endothelial growth factor, inflammatory cytokines, quality of life score, peripheral lymphocyte subsets and incidence of adverse reactions were used as the observation indicators. Tumor markers include CA19-9, CA72-4, and carcinoembryonic antigen. The detection instrument is the AU5800 automatic biochemical analyzer produced by Beckman Coulter Company. Inflammatory cytokines include interleukin-6, interleukin-10 and tumor necrosis factor α . The detection instrument is the same as tumor marker. The detection instrument of vascular endothelial growth factor (VEGF) was the same as tumor marker. Peripheral lymphocyte subsets include CD4^+ and $\text{CD4}^+/\text{CD8}^+$. The detection instrument was a cytoflex flow cytometer produced by Beckman Coulter Company. The quality of life score was determined using the World Health Organization Quality of Life Scale Shortlist, with a total of 24 items. It is divided into four dimensions: physiological field (7 items), psychological field (6 items), social relationship field (3 items), and environmental field (8 items), and evaluated on a scale of 0 to 4. The higher the value, the higher the quality of life. Tumor markers, vascular endothelial growth factor, inflammatory cytokines, quality of life score, and peripheral lymphocyte subsets were measured before and after treatment. Adverse reactions include nausea/vomiting, loss of appetite, leukopenia, and diarrhea. The total effective rate, disease control rate and adverse reactions were calculated after treatment.

2.4 Criterion of Therapeutical Effect

The efficacy evaluation criteria for solid tumors (RECIST)^[5] were divided into complete remission, partial remission, stable condition and disease progression. The total effective rate (%) = complete response rate+partial response rate. Disease control rate (%) = complete response rate+partial response rate+stable disease rate.

2.5 Statistical Methods

SPSS22.0 statistical software was used for processing. The measurement data were expressed as mean±standard deviation ($\bar{x} \pm s$). Independent t-tests were used between groups and paired t-tests were used within groups. The counting data were expressed by rate (%), and χ^2 test was used. $P < 0.05$ indicates that the difference is statistically significant.

3. RESULTS

3.1 Comparison of Total Effective Rate and Disease Control Rate Between the Two Groups

The total effective rate and disease control rate in the observation group were higher than those in the control group. The difference was statistically significant ($P < 0.05$). Table 1 shows the comparison of total effective rate and disease control rate between the two groups.

Table 1 Comparison of total effective rate and disease control rate between the two groups [n(%)]

Group	n	Complete remission	Partial remission	Stable condition	Disease progression	Disease control rate (%)	Total effective rate (%)
Observation group	35	7 (20.00)	11 (31.43)	7 (20.00)	10 (28.57)	71.43	51.42
Control group	35	4 (11.43)	9 (25.71)	7 (20.00)	15 (43.86)	57.14	37.14
χ^2		-	-	-	-	4.253	3.977
P		-	-	-	-	0.039	0.046

3.2 Comparison of Tumor Markers Between Two Groups

There was no significant difference in tumor markers between the two groups before treatment ($P > 0.05$). After treatment, they were significantly lower than those before treatment in this group, and the difference was statistically significant ($P < 0.05$). In the comparison between the groups, the observation group was lower than the control group, and the difference was statistically significant ($P < 0.05$). Table 2 shows the comparison results.

Table 2 Comparison of tumor markers between two groups ($\bar{x} \pm s$)

Group	CA19-9 (mg/L)		t	P	CA72-4 (U/mL)		t	P	Carcinoembryonic antigen (mg/L)		t	P
	Before	After			Before	After			Before	After		
	treatment	treatment			treatment	treatment			treatment	treatment		
Observation group (n = 35)	445.10 ±2.35	188.74 ±3.36	132.100	0.000	30.34 ±1.27	8.97 ±1.13	12.477	0.000	73.10 ±1.10	14.88 ±1.22	50.885	0.000
Control group (n = 35)	445.24 ±2.41	200.10 ±3.50	110.359	0.000	30.40 ±1.30	10.64 ±1.17	9.921	0.000	73.14 ±1.16	17.50 ±1.35	46.397	0.000
t	1.897	33.459	-	-	1.542	11.240	-	-	1.443	15.642	-	-
P	0.155	0.000	-	-	0.210	0.000	-	-	0.278	0.000	-	-

3.3 Comparison of Vascular Endothelial Growth Factor and Inflammatory Cytokines Between the Two Groups

There was no significant difference in vascular endothelial growth factor and inflammatory cytokines between the two groups before treatment ($P > 0.05$). After treatment, these factors were significantly lower than before treatment in this group, and the difference was statistically significant ($P < 0.05$). In the comparison between the groups, the observation group was lower than the control group, and the difference was statistically significant ($P < 0.05$). Table 3 shows the comparison results.

Table 3 Comparison of vascular endothelial growth factor and inflammatory cytokines between the two groups ($\bar{x} \pm s$)

Group	Vascular endothelial growth factor (pg/mL)		<i>t</i>	<i>P</i>	Interleukin-6 (ng/L)		<i>t</i>	<i>P</i>
	Before	After			Before	After		
	treatment	treatment			treatment	treatment		
Observation group (<i>n</i> = 35)	105.40±1.15	55.10±1.24	188.108	0.000	242.88±2.52	164.10±3.10	124.717	0.000
Control group (<i>n</i> = 35)	105.48±1.12	62.33±1.27	159.640	0.000	242.94±2.46	175.50±3.25	111.359	0.000
<i>t</i>	0.315	25.762	-	-	0.108	16.053	-	-
<i>P</i>	0.754	0.000	-	-	0.915	0.000	-	-

Table 3-1 Comparison of vascular endothelial growth factor and inflammatory cytokines between the two groups ($\bar{x} \pm s$)

Group	Interleukin-10 (ng/L)		<i>t</i>	<i>P</i>	Tumor necrosis factor α (μ g/L)		<i>t</i>	<i>P</i>
	Before	After			Before	After		
	treatment	treatment			treatment	treatment		
Observation group (<i>n</i> = 35)	228.74±2.26	104.24±3.26	198.501	0.000	67.59±2.41	36.65±2.35	58.133	0.000
Control group (<i>n</i> = 35)	228.80±2.31	115.11±3.29	169.442	0.000	67.64±2.45	42.10±2.38	42.247	0.000
<i>t</i>	0.117	14.843	-	-	0.092	10.306	-	-
<i>P</i>	0.907	0.000	-	-	0.927	0.000	-	-

3.4 Comparison of Quality of Life Scores Between the Two Groups

There was no significant difference in the quality of life scores between the two groups before treatment ($P > 0.05$). The intra-group comparison after treatment indicated that the quality of life score was higher than that before treatment, and the difference was statistically significant ($P < 0.05$). The quality of life score of the observation group was higher than that of the control group, and the difference was statistically significant ($P < 0.05$). Table 4 shows the comparison results.

Table 4 Comparison of quality of life scores between the two groups ($\bar{x} \pm s$)

Group	Physiological field		<i>t</i>	<i>P</i>	Psychological field		<i>t</i>	<i>P</i>
	Before	After			Before	After		
	treatment	treatment			treatment	treatment		
Observation group (<i>n</i> = 35)	15.50±1.50	24.20±1.20	28.644	0.000	12.88±1.22	20.21±1.02	29.153	0.000
Control group (<i>n</i> = 35)	15.25±1.25	20.00±1.00	18.767	0.000	12.90±1.25	18.85±1.05	23.051	0.000
<i>t</i>	0.810	17.005	-	-	0.072	5.876	-	-
<i>P</i>	0.421	0.000	-	-	0.943	0.000	-	-

Table 4-1 Comparison of quality of life scores between the two groups ($\bar{x} \pm s$)

Group	Social relations		<i>t</i>	<i>P</i>	Environmental field		<i>t</i>	<i>P</i>
	Before	After			Before	After		
	treatment	treatment			treatment	treatment		
Observation group (<i>n</i> = 35)	4.10±0.25	10.15±0.25	108.226	0.000	14.77±1.23	28.85±1.15	52.884	0.000
Control group (<i>n</i> = 35)	4.00±0.20	8.90±0.30	85.952	0.000	14.82±1.25	25.10±1.18	37.823	0.000
<i>t</i>	1.975	20.244	-	-	0.180	14.394	-	-
<i>P</i>	0.052	0.000	-	-	0.857	0.000	-	-

3.5 Comparison of Peripheral Lymphocyte Subsets Between the Two Groups

There was no significant difference in peripheral lymphocyte subsets between the two groups before treatment ($P > 0.05$). Intra-group comparison after treatment showed that peripheral lymphocyte subsets decreased compared with pre-treatment, and the difference was statistically significant ($P < 0.05$). The peripheral lymphocyte subsets in the observation group were better than those in the control group, with no significant difference ($P > 0.05$). Table 5 shows the comparison results.

Table 5 Comparison of peripheral lymphocyte subsets between the two groups ($\bar{x} \pm s$)

Group	CD4 ⁺ (%)		<i>t</i>	<i>P</i>	CD4 ⁺ /CD8 ⁺		<i>t</i>	<i>P</i>
	Before treatment	After treatment			Before treatment	After treatment		
Observation group (<i>n</i> = 35)	31.44±1.56	27.85±1.25	11.342	0.000	2.31±0.11	1.55±0.17	7.589	0.000
Control group (<i>n</i> = 35)	31.40±1.59	24.82±1.28	10.897	0.000	2.30±0.10	1.22±0.18	6.874	0.000
<i>t</i>	0.345	5.878	-	-	0.159	4.343	-	-
<i>P</i>	0.771	0.000	-	-	0.821	0.000	-	-

3.6 Comparison of the Incidence of Adverse Reactions Between the Two Groups

There was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$), as shown in Table 6.

Table 6 Comparison of the incidence of adverse reactions between the two groups [*n*(%)]

Group	<i>n</i>	Nausea/vomiting	Anorexia	Leukopenia	Diarrhea	Incidence (%)
Observation group	35	7 (20.00)	4 (11.43)	3 (8.57)	1 (2.86)	42.86
Control group	35	6 (17.14)	4 (11.43)	3 (8.57)	0 (0.00)	37.14
χ^2		-	-	-	-	0.682
<i>P</i>		-	-	-	-	0.409

4. DISCUSSION

Gastric adenocarcinoma tends to occur in middle-aged and elderly population and its incidence is positively correlated with the increase of age. China is one of the countries with a serious aging population in the world, so the incidence of this tumor is bound to show a further increase. The early onset of gastric adenocarcinoma patients generally has no specific symptoms. The symptoms of upper abdominal discomfort and bloating after eating are similar to other diseases of the digestive system, so gastric adenocarcinoma is easily overlooked by patients. With the prolongation of the course of disease, gastric adenocarcinoma patients in the middle and advanced stage generally have metastasis, including supraclavicular lymph node metastasis, liver metastasis, peritoneal lymph node metastasis, peritoneal metastasis, *etc.* Surgical treatment alone cannot achieve the desired results^[6]. Chemotherapy is a treatment that uses chemical drugs to kill cancer cells. Drugs reach most tissues of the human body along with the blood and kill specific tumor cells, but normal cells are also damaged to varying degrees in the process^[7]. The choice of chemotherapy for patients with advanced metastatic gastric adenocarcinoma should be based on its pathological classification, TNM stage and differentiation, as well as age, physical strength and other basic diseases. The principle of individuation should be taken into account while obtaining good evidence basis. At present, the clinical chemotherapy treatment schemes for such patients include FOLFOX scheme, XELOX scheme, and SOX scheme. The above chemotherapy schemes are composed of platinum drugs and FU drugs. In general, SOX protocol is mainly used for patients who can undergo surgical resection, while FOLFOX program and XELOX program are mainly used for patients without surgical resection. However, FOLFOX has a higher requirement on patients' physical condition. However, the patients with metastatic gastric adenocarcinoma in the middle and late stage are in a state of high metabolism for a long time, which causes the rapid loss of nutrients in the body, and the external supplement cannot meet the needs of the poor physical state, malnutrition is relatively obvious, making it difficult for the chemotherapy program to be widely applied. XELOX is a chemotherapy program emerging in recent years, which has achieved relatively ideal efficacy in prolonging patients' life cycle and improving the quality of

life^[8-9]. The chemotherapy regimen consists of oxaliplatin and capecitabine. Oxaliplatin is the third generation of platinum and belongs to diaminocyclohexane - complex. Once it used for the patient, it can cross-link with the cancer cell DNA and form a complex that continues to destroy the cancer cells. Compared with cisplatin, oxaliplatin forms a larger complex with higher hydrophobicity, making the drug more effective. Capecitabine is an antimetabolic flupyrimidine deoxynucleotide carbamate. It can be rapidly converted into 5-fluorouracil in the body of patients, so as to inhibit the proliferation of tumor cells and interfere with RNA and protein synthesis. Because XELOX is relatively mild, it has been recommended by the National Comprehensive Cancer Network (NCCN) as the standard chemotherapy regimen for gastric cancer. However, patients with metastatic gastric adenocarcinoma in the middle and advanced stages are generally more severe. The XELOX solution kills cancer cells while also killing normal cells, resulting in impaired immune function in patients. The quality of life improvement is not very satisfactory. In particular, the overall efficacy and disease control rate of XELOX alone were relatively low.

Xiaoai ping is a traditional Chinese medicine preparation, which is extracted from Oriental Miao nationality medicine, that is, Glaucous fissistigma root, and the effective components of the drug are completely separated by low-temperature extraction technology, biological separation technology and high-tech ion exchange extraction technology. Glaucous fissistigma root contains a variety of anti-tumor components, such as betulinic acid, glaucous fissistigma root glycoside H, glaucous fissistigma root glycoside G, glaucous fissistigma root glycoside I, chlorogenic acid, wild baicalin tetramethyl ether, kaempferol 4'-methyl ether, kaempferol, β -sitosterol, carotene, *etc.* In addition to inhibiting the proliferation and apoptosis of tumor cells, it can also stimulate the immune system to release immune cells and improve the killing effect of immune function. The clinical efficacy of XELOX alone is not sufficient to meet the treatment needs. Immune function plays an important role. Immunosuppression caused by chemotherapeutic drugs greatly reduces the body's ability to resist the invasion of foreign pathogenic microorganisms, leading to multiple complications and shortened survival time of patients. Traditional Chinese medicine and Chinese patent medicine have the advantages of low side effects, balance of viscera functions and improvement of physical condition, which can help to improve the tolerance of patients to chemotherapy drugs and provide a strong guarantee for them to successfully complete a full course of chemotherapy.

Xin Yan *et al.*^[10] pointed out in their study that compared with patients with metastatic gastric adenocarcinoma treated with XELOX alone, patients treated with Xiaoai ping combined with XELOX had higher total effective rate, higher disease control rate, longer median progression-free survival time and longer median total survival time, and lower incidence of adverse reactions. The differences were statistically significant ($P < 0.05$). Based on this, it is concluded that the combined application of Xiaoai ping and XELOX can promote patients with intermediate and advanced metastatic gastric adenocarcinoma to obtain greater benefits. The total effective rate and disease control rate of the two groups of patients with metastatic gastric adenocarcinoma in this study after treatment were 51.42%, 71.43%, 37.14%, and 57.14%, respectively. Compared with the control group treated with oxaliplatin and capecitabine, the observation group treated with Xiaoai ping on the basis of oxaliplatin and capecitabine were all better. The differences were statistically significant ($P < 0.05$). After treatment, the intra-group comparison showed that the tumor markers (CA19-9, CA72-4, carcinoembryonic antigen), vascular endothelial growth factor, and inflammatory cytokines (interleukin-6, interleukin-10, tumor Necrosis factor α) of the patients in the two groups were all decreased compared with those before treatment. Quality of life scores (physical, psychological, social relationship, environmental) and peripheral lymphocyte subsets ($CD4^+$, $CD4^+/CD8^+$) increased significantly compared to before treatment. The differences were statistically significant ($P < 0.05$). The results suggest that both treatment schemes have achieved satisfactory results in clinical treatment. The comparison between groups showed that the tumor markers, vascular endothelial growth factors and inflammatory cytokines in the observation group were lower than those in the control group, and the quality of life score and peripheral lymphocyte subsets in the observation group were higher than those in the control group, with statistically significant differences ($P < 0.05$). The results showed that the use of Xiaoai ping could further improve the clinical efficacy and reduce the damage caused by chemotherapy drugs to patients on the basis of chemotherapy alone, so as to enhance the immune function. In terms of the incidence of adverse reactions, the values of the two groups were similar, with no statistically significant difference ($P > 0.05$), indicating that both treatment regimens had higher safety. Compared with previous research results, there are similarities and differences. The similarity is that Xiaoai ping combined with oxaliplatin and capecitabine (XELOX) can further improve the total effective rate and disease control rate of middle and advanced metastatic

gastric adenocarcinoma. The difference is that patients were followed up and the median progression-free survival time and the median total survival time were collected. This study did not involve this aspect, but discussed the clinical efficacy from tumor markers, vascular endothelial growth factor, inflammatory cytokines, quality of life score, peripheral lymphocyte subsets and other aspects. The index system is more diverse and the results are more convincing. Therefore, this study is highly innovative. Notably, studies have shown that the incidence of adverse reactions caused by the combination of XELOX and Xiaoaiping with XELOX is not the same. The incidence of the latter was lower and the difference was statistically significant ($P < 0.05$). This was not confirmed in this study, and the incidence of adverse events after treatment was similar in both groups. The reasons for this difference may be related to the physical condition of the enrolled patients and their tolerance to the treatment drugs. Due to different levels of economic development, different dietary preferences and different dietary habits in different regions, there are some differences in the physical conditions of patients. In addition, this study further concluded that both groups showed immunosuppression after treatment. Peripheral lymphocyte subsets were all significantly lower than before treatment. The reason is that chemotherapy couldn't differentiate between normal cells and cancer cells. Normal cells will be damaged by the use of chemotherapy drugs, and even abnormal apoptosis will occur. However, the value of each index in the observation group with Xiaoaiping was higher than that in the control group. This indicated that the immunosuppression was relatively mild in this group after treatment. The reason is that Xiaoaiping is a traditional Chinese medicine preparation formed after the preparation of the active ingredient of glaucescent fissistigma root. The herbal medicine has the functions of removing wind and dampness, activating blood circulation and stopping bleeding. The body of patients with metastatic gastric adenocarcinoma in the middle and late stage is in an unbalanced state, resulting in the excess or decline of Yin and Yang. However, Xiaoaiping can activate the biological activity of mononuclear macrophages in the body, promote the activation of T lymphocytes, and play the immune function of the body to fight the proliferation of tumor cells. The results of the final clinical study showed that Xiaoaiping combined with XELOX could alleviate the immunosuppressive state of the body. It lays a solid foundation for strengthening the body's immune resistance and improving its physical condition. Combined application can give full play to the advantages of each treatment and further improve the clinical efficacy by synergistic effect, but it will not aggravate the immunosuppression and increase the incidence of adverse reactions in patients with advanced metastatic gastric adenocarcinoma. It has high safety and effectiveness, and is worth popularizing in the future clinical treatment. However, there are limitations in this study. First, due to the limited study time, this study did not conduct statistics on the long-term efficacy of the two groups of patients, but only analyzed the short-term efficacy. Second, the number of samples is small, and the reliability of the results needs to be supported by future large sample and multi-randomized controlled center clinical trials.

In conclusion, Xiaoaiping combined with oxaliplatin and capecitabine has a definite effect on the treatment of advanced metastatic gastric adenocarcinoma, which can further improve the total effective rate and disease control rate of patients on the basis of chemotherapy alone. The incidence of adverse reactions is similar to it, which has a high safety. At the same time, because the immunosuppression caused by chemotherapy is less severe, it provides a strong guarantee for patients to successfully complete the full course of treatment, which is of great significance for improving the quality of life of patients and worth promoting.

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