Effect of triptolide and chemotherapy on carcinoembryonic and carbohydrate antigens levels and first-line treatment of recurrent nasopharyngeal carcinoma

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Abstract: To investigate the first-line treatment of recurrent Nasopharyngeal Carcinoma treprimcab combined with chemotherapy. From January 2019 to January 2020, 48 patients with recurrent nasopharyngeal Carcinoma (RNPC) were treated in our hospital. According to the method of the random number, 24 patients were divided into the combined group and the Control Group. The patients in the combined group were given the Combined Treatment of triptolide and chemotherapy. While the Control Group only received chemotherapy. The therapeutic effects and adverse reactions of the two groups were compared, the levels of Carcinoembryonic Antigen (CEA) and carbohydrate Antigen 19-9 (CA19-9) were measured before and after treatment. The total effective rate of the combined group was 79.17% higher than that of the control group (62.50%). The total effective rate of the two groups was statistically significant (P & Lt; 0.05). The incidence of grade i/ii adverse reaction in the control group was lower than that in the combined group, such as nausea and vomiting, oral mucositis, Leukopenia, liver and kidney function damage, central granulocyte count reduction, anaemia adverse reaction. The incidence of grade iii/iv ADR in the control group was higher than that in the combined group. The incidence of grade i/ii ADR in the thrombocytopenia group was higher than that in the combined group, and the incidence of grade iii/iv ADR in the control group was lower than that in the combined group. The side effects of nausea and vomiting and oral mucositis in the control group and the combined group were statistically significant (P & Lt; 0.05). There was no significant difference between the control group and the combined group in the incidence of Leukopenia, liver and kidney injury, neutrophil, anaemia and Thrombocytopenia (P & GT; 0.05). The level of CD4 + / CD8 + in control group and combined group before treatment was higher than that after treatment (P & Lt; 0.05). The quality of life of the combined group was 91.67% higher than that of the control group (70.83%). The quality of life of the control group was significantly higher than that of the combined group (P & Lt; 0.05). The levels of CEA and CA19-9 in the two groups after treatment were lower than those before treatment, and the levels of CEA and CA19-9 in the combined group were lower than those in the control group (P & Lt; 0.05). The first-line treatment of recurrent nasopharyngeal Carcinoma with treprimmacb combined with chemotherapy has a good clinical effect and has a broad clinical research prospect.

Key words: Toripalimab; Chemotherapy; Recurrent nasopharyngeal carcinoma; Clinical efficacy.

Introduction

Nasopharyngeal carcinoma (nasopharyngeal carcinoma, NPC) is a clinically malignant nasopharyngeal mucosal epithelial tumour, whose incidence is first in the head and neck tumours, most are characterized by undifferentiated or low differentiated squamous cell carcinoma. The main treatment is radiotherapy and chemotherapy treatment (1). Now the improvement of treatment technology has improved the treatment efficacy and prognosis of patients with early nasopharyngeal cancer, but since most patients are diagnosed, characterized by high recurrence rate, high malignancy and high early metastasis rate, the prognosis of their patients is generally poor. The causes are genetic, viral, environmental and lifestyle-related risk factors, and the main virus is EB (Epstein-Barr Virus, EBV), which can be transcribed and produce a variety of stimuli substances prompting the transformation of infected cells into malignant transformation (2). NPC occurs mainly in the south of China and Southeast Asia (3), The rate of failure in treatment is high due to the risk of distant metastasis and local recurrence (4) Well, so the disease needs more effective treatment.

NPC is sensitive to radiation and the lesion is in a typical deep position, so the main treatment of NPC when radiotherapy (Radiation therapy, RT), but the prevention and treatment of distant metastases of advanced nasopharyngeal cancer are not ideal, so the radiotherapy adjuvant method, now clinically induced chemotherapy (Induction chemotherapy, IC) for nasopharyngeal cancer is deeply concerned, usually using yew cisplatin (TP) for IC treatment (5). Triplumab (Toripalimab) is a procedural death receptor class 1 drug that blocks escape while enhancing the body's immune function and kills cancer cells with high specificity and less impact on surrounding healthy tissue cells. It has good tolerance and anti-tumour activity in the treatment of refractory late isolated malignancies (6). In this research, Triplizumab and chemotherapy were used to see the therapeutic effect of recurrent nasopharyngeal cancer.

Materials and Methods

General information

Select 48 patients with recurrent nasopharyngeal...
cancer from January 2019 to January 2020, and patients were divided into joint and control groups, with 24 patients each. In the combined group, 13 males, 11 females, aged 26-74 years, average age (41.23±13.25), recurrence time 12-35 months, and average recurrence time (22.56±5.23) months. In the control group, 12 males, 12 females, aged 24-76, average age (43.12±12.85), recurrence time of 10-34 months and average recurrence time (23.01±5.14) months. The general data on gender and age of the two groups showed no significant statistical differences (P> 0.05) and were comparable.

Inclusion of the standards

1. The patient was diagnosed with recurrent nasopharyngeal cancer after MRI or PET/CT in the head and neck scan. 2. The patient's expected survival was longer than 6 months. 3. The patient and his family understood the experiment and signed informed consent.

Elimination criteria

1. Patients have severe liver and kidney function impairment. 2. Patients with multiple tumour diseases, and a history of radiotherapy and chemotherapy. 3. Patients are allergic to experimental drugs. 4. Patients are mentally ill and unable to cooperate with doctors. 5. patients during pregnancy and lactation.

Method

1. The control group was given 25mg/m2Cisplatin (Company: Qilu Pharmaceutical Co., Ltd., Sinopharm: H37021362, Production Batch No.: 20160802), dissolved in 0.9% saline 5000mL intravenous infusion, three times a week, 3 weeks, 2 treatment. 2. the combined group based on the control groupTriplumab (outsourcing, commodity name: Tuoyi, Company name: Shanghai Junshan Biomedical Technology Co., Ltd., 240 mg, Production Batch No.: 201910035) intravenous infusion, every two weeks, one course of 2 weeks, three courses of treatment.

Efficacy evaluation criteria and observation indicators

Conduct a follow-up investigation to record patient efficacy and adverse reactions. 1. Three months after the treatment of both groups, Reviewing both groups of patients, Post-treated nasopharyngeal MRI in both groups were compared with pre-treated MRI, To observe the tumour changes before and after the treatment of the two groups, It is classified into complete remission according to the solid tumour grouping criteria specified by WHO (complete response, CR): The tumour disappears and lasts ≥ 4 weeks; Partial relief (partial remission, PR): Tumor reduces ≥ by 30% and lasts for ≥ 4 weeks, Stability (stable disease, SD): <30% or 20% of tumour; Progress (progressive disease, PD): new lesion or tumour volume increase 20% ≥, Total efficient = (complete + partial mitigation) / total cases × 100%. 2. The adverse reaction assessment is based on the assessment criteria prescribed by the National Cancer Institute, Mild adverse reactions are graded, Moderate adverse reactions are graded, Severe adverse reactions are graded, Life hazards to patients are graded, The patient's adverse reaction symptoms include nausea and vomiting, oral mucositis, decreased number of leukocyte cells, damage to liver and kidney function, loss of central granulocytes, anaemia, and thrombocytopenia. 3. Quality of survival score: quality of survival was scored by Karnofsky (KPS) standard, KPS score increased ≥ 10; decrease to KPS score decreased ≥ 10; stability was between improvement and decrease; (4) immune function: T cell subgroup, including CD4 +, CD8 +, CD4 + / CD8 +; (6) level of embryonic antigen and sugar antigen 19-9 (enzyme-linked immunity) before and after treatment.

Statistical methods

Analysis of the data using SPSS 22.0 software, Use it Normal ± standard difference for count data, using t-test between the two groups; [n(%)] for count data and χ² test between the two groups; χ² for count data and P <0.05 is statistically significant.

Results

Comparison of clinical efficacy in the two groups

After trials, the two groups had a total efficiency of 79.17% higher than the control group (62.50%) and a significant statistical significance (P <0.05), (Table 1).

The incidence of adverse reactions

The data were compared between both groups with nausea, vomiting, oral mucosa, leukocyte number reduction, liver and renal function impairment, central granulocyte count reduction and anaemic adverse reactions less than in the combined group; controls / higher than in the combined group; thrombocytopenia / higher than in the combined group; and controls / lower than in the combined group. The effects of nausea and vomiting and oral mucus inflammation (P <0.05), leukocyte reduction, liver and kidney function injury, neutrophil count, anaemia and thrombocytopenia (P >0.05), shown in Table 2.

Evaluation of quality of survival scores

After tests, the two data were compared with the quality of survival of 91.67% higher than 70.83% in the control group, significantly (P <0.05) (Table 3).

<table>
<thead>
<tr>
<th>Table 1. Comparison of the clinical efficacy of the two groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>Complete relief</td>
</tr>
<tr>
<td>Some patients</td>
</tr>
<tr>
<td>Stability</td>
</tr>
<tr>
<td>Progress</td>
</tr>
<tr>
<td>Always be efficient</td>
</tr>
</tbody>
</table>
Nasopharyngeal carcinoma treatment with triptolide and chemotherapy.

Table 2. Incidence of adverse reactions in both groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Control group (n=24)</th>
<th>Joint Group (n=24)</th>
<th>Z.Value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea and vomiting Level I/II</td>
<td>15 (62.50%)</td>
<td>19 (79.17%)</td>
<td>2.110</td>
<td>0.041</td>
</tr>
<tr>
<td>Level III/IV</td>
<td>8 (33.33%)</td>
<td>3 (12.50%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral mucositis Level I/II</td>
<td>17 (70.83%)</td>
<td>22 (91.67%)</td>
<td>2.010</td>
<td>0.046</td>
</tr>
<tr>
<td>Level III/IV</td>
<td>6 (25.00%)</td>
<td>2 (8.33%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cell count decreases Level I/II</td>
<td>15 (62.50%)</td>
<td>17 (70.83%)</td>
<td>0.712</td>
<td>0.491</td>
</tr>
<tr>
<td>Level III/IV</td>
<td>5 (20.83%)</td>
<td>3 (12.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver and kidney function damage Level I/II</td>
<td>10 (41.67%)</td>
<td>3 (12.5%)</td>
<td>0.311</td>
<td>0.510</td>
</tr>
<tr>
<td>Level III/IV</td>
<td>8 (33.33%)</td>
<td>1 (4.17%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The of uuyis decreased Level I/II</td>
<td>18 (75.00%)</td>
<td>20 (83.33%)</td>
<td>0.125</td>
<td>0.712</td>
</tr>
<tr>
<td>Level III/IV</td>
<td>4 (16.67%)</td>
<td>2 (8.33%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia Level I/II</td>
<td>20 (83.33%)</td>
<td>22 (91.67%)</td>
<td>0.194</td>
<td>0.645</td>
</tr>
<tr>
<td>Level III/IV</td>
<td>2 (8.33%)</td>
<td>1 (4.16%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plabocytopenia Level I/II</td>
<td>22 (91.67%)</td>
<td>17 (70.83%)</td>
<td>2.145</td>
<td>0.152</td>
</tr>
<tr>
<td>Level III/IV</td>
<td>1 (4.16%)</td>
<td>5 (20.83%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comparison of the immune function

After trial, the two groups of data were compared with the combined group. So that CD4 + / CD8 + was higher than after treatment and CD4 + / CD8 + was higher than the control group (P <0.05), (Figure 1).

Comparison CEA and CA19-9 levels in both groups before and after treatment

After trial, the data obtained were compared to the two groups after treatment CEO and CA19-9 levels were lower than before treatment and CEA and CA19-9 in the control group showed significant statistical significance (P <0.05), (Figure 2).

Discussion

Nasopharyngeal cancer is mainly present in one of the common head and neck tumours in Southeast Asia and North Africa. According to the survey, about 130,000 patients occurred worldwide in 2018, and nearly half of the patients came from China. The standard incidence of southern China was 20 to 50,000/100 and 0.5 per 100,000 whites (7). After examination, nearly 70% of patients were diagnosed with locally advanced nasopharyngeal cancer (8). The main treatment method of patients is radiotherapy and chemotherapy treatment, but the high recurrence rate and high treatment failure rate of the disease are investigated because the disease is prone to distant metastasis (9). The onset of nasopharyngeal cancer is associated with the EB virus, cancer typically an “inflamed tumour” that exhibits dense lymphocyte infiltration and increased expression of procedural death-ligand 1 (pd-l1) (10-11).

Triplimumab is an anti-PD-1 humanized IgG 4 monoclonal antibody, one of the first anti-PD-1 monoclonal antibodies approved by the China Food and Drug Administration (China food and drug administration, CFDA) for clinical trials (12). It is shown that mab showed better safety and good anti-tumour activity in patients with advanced melanoma, urinary tract epithelial carcinoma, renal cell carcinoma and advanced gastric cancer (13-14). Wang et al (15) Among the results of the study, the drug achieved good clinical efficacy and safety in patients with NPC and reduced the number of EB viruses in their plasma. Chemotherapy is one of the common means used to treat cancer. According to research, chemotherapy drugs can seasonal apoptosis of immunogenic cells, change the microenvironment of tumour cells, the body produces new antigens to activate the tumour immune system, and achieve the synergistic effect of cytotoxic therapy and immune checkpoint inhibitors (16). Activated cytotoxic therapy can also sti-
mulate the immune response of T cells, enhancing the effect of chemotherapy on disease (17). Chemotherapy can cause severe adverse reactions to patients and can have symptoms of severe discomfort.

The results of this study show that Combined group efficiency is 79.17% higher than the control group (62.50%), the effect of drug combined chemotherapy drugs for nasopharyngeal cancer is higher than individual chemotherapy, triplizumab activates the human tumour-immune system, produce new antibodies against the tumour, control the genes of cancer cells, chemotherapy drugs can act on cancer cells, cancer cells apoptosis, thus control the proliferation of cancer cells, prevent cancer cell metastasis to other tissues. Data from the two groups were compared and the rates of nausea and vomiting, oral mucosa, decreased leukocyte count, liver and renal functional impairment, decreased granulocyte count, and anaemia was lower in the combination group; in the control group/level was higher than in the combined group; thrombocytopenia was higher than in the combined group, and in the control group/level than in the joint group. No significant adverse reactions occurred except malignant vomiting and oral mucosal inflammation. Most of the adverse reactions of patients are moderate and mild adverse reactions, a small part of them are severe and life-threatening adverse reactions, because the patient is basically moderate, so the two drugs jointly treat NPC patients is very good, the cause of serious adverse reactions may be the patient has serious intolerance to the drug, may not adapt to the dosage. Moreover, fewer combined patients than control groups may also suggest that Triplizumab can reduce the toxic side reaction of cisplatin in humans. Pre-treatment in the control and combined groupCD4+ / CD8+ was higher than after treatment, and CD4+ / CD8+ was higher than after control, and the immune function was improved, which was associated with the immune function of Triplizumab and increased the own removal of tumour cells. The quality of survival was 91.67% higher than 70.83%, the combination group had better efficacy, and the quality of survival improved. Two groups after the treatmentCEA and CA19-9 levels were lower than before treatment, and CEA and CA19-9 were lower than the control group, the results showed that the CEA and CA19-9 levels in the patient decreased significantly after treatment, the number of cancer cells in the patient was greatly reduced, and the combination had a significant effect on the patient.

In recent years, in Xu et al (18), experiment the use of Triplizumab for nasopharyngeal cancer patients, most patients, but mainly level adverse reactions, only 14.5% of patients with grade adverse reactions, a small part of no adverse reactions, the clinical treatment effect is also good, showed good clinical activity in the experiment, and the safety can be controlled. In Ma et al (19) experiment chemotherapy drugs and other drugs were combined to treat recurrent nasopharyngeal cancer, and the treatment results showed that this regimen was more effective for tumour treatment, but fewer studies needed further research (20). A human study of indophol alkaloids and chemotherapy drugs cisplatin, investigate the proliferation and migration of nasopharyngeal cancer cells, the combination has a good inhibition of NPC cells, patients, indophol alkaloids also slowed the rela-
ted pain of cancer patients, experimental results show that the two have a good effect on the value increase and migration of NPC cells. There is now much research on drugs for nasopharyngeal cancer patients (21). The compatibility of Pabosib (palbociclib) with cisplatin for primary and recurrent nasopharyngeal cancer showed that the combination has significant inhibition of tumour and promotes apoptosis in vivo and in vitro, this combination can further inhibit tumour growth by inducing autophagy-related cell death, when simultaneous palbociclib therapy reduces the cytotoxicity of cisplatin in vitro and reduce adverse reactions in patients. For further study, it is necessary to do more studies on more genes as well as to study a wide range of gene networks (22-27).

To sum up, the clinical effect of Triplizumab and frontline chemotherapy in the treatment of recurrent nasopharyngeal cancer is good. In clinical practice, many researchers need to study recurrent nasopharyngeal cancer with anti-cancer drugs and chemotherapy drugs.

Acknowledgements
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References