Aplicación y análisis clínico de Bevacizumab en la terapia antineoplásica

Application and Clinical Analysis of Bevacizumab in Antineoplastic Therapy

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Resumen
Bevacizumab puede unirse al factor de crecimiento endotelial vascular para formar un anticuerpo IgG1 monoclonal humano recombinante. Su aplicación en el tratamiento de tumores malignos con quimioterapia tiene un efecto sobre el efecto clínico y la incidencia de reacciones adversas de los pacientes. Se analizó el valor de la aplicación clínica de bevacizumab. Los resultados mostraron que la tasa de control total del tratamiento clínico en el grupo de observación fue de 96.6% y 73.3% en el grupo de control fue significativamente mayor que en el grupo de control (p <0.05). Las principales reacciones adversas de los dos grupos fueron hemorragia, hipertensión, proteinuria y tromboembolismo venoso. Las reacciones adversas clínicas del grupo de observación fueron significativamente menores que las del grupo de control. En conclusión, bevacizumab puede mejorar significativamente la eficacia clínica y reducir la incidencia de reacciones adversas en pacientes con tumores malignos durante la quimioterapia. La combinación de bevacizumab y fármacos quimioterapéuticos sigue siendo la dirección principal de la aplicación clínica.

Palabras clave: Bevacizumab, Tumores malignos, Fármacos dirigidos moleculares, Programas terapéuticos.

Abstract
Bevacizumab can bind to vascular endothelial growth factor to form a recombinant human monoclonal IgG1 antibody. Its application in the treatment of malignant tumors with chemotherapy has an effect on the clinical effect and the incidence of adverse reactions of patients. The clinical application value of bevacizumab was analyzed. The results showed that the total control rate of clinical treatment in the observation group was 96.6% and 73.3% in the control group was significantly higher than that in the control group (p < 0.05). The main adverse reactions of the two groups were hemorrhage, hypertension, proteinuria and venous thromboembolism. The clinical adverse reactions of the observation group were significantly lower than those of the control group. In conclusion, bevacizumab can significantly improve the clinical efficacy and reduce the incidence of adverse reactions in patients with malignant tumors during chemotherapy. The combination of bevacizumab and chemotherapeutic drugs is still the main direction of clinical application.

Key words: Bevacizumab, Malignant tumors, Molecular targeted drugs, Therapeutic programs

1. Introduction
In recent years, anti-angiogenesis therapy has been questioned clinically. Some studies have shown that bevacizumab alone cannot prolong the overall survival time of patients[1]. Therefore, the combination of chemotherapeutic drugs has become the most important guiding strategy for clinical application of bevacizumab, that is to say, anti-angiogenesis drugs need to rely on other chemotherapeutic drugs to achieve the best effect. Maintaining a long-term angiopoietic state plays a key role in inhibiting the growth of tumors[2-3]. Therefore, the treatment cycle of bevacizumab is also important for patients to benefit from survival. Studies have shown that progression-free survival and overall survival of patients receiving antiangiogenic therapy for more than four cycles are significantly longer than those receiving less than four cycles of treatment[4]. It was also found that bevacizumab was well tolerated in long-term treatment[5]. At present, the combination of bevacizumab and chemotherapy regimens involves almost all the commonly used clinical chemotherapy regimens. However, bevacizumab alone is mostly used as maintenance therapy after combined chemotherapy. However, due to the lack of strong clinical evidence, the dosage of bevacizumab remains to be further clarified[6-7].

Antiangiogenesis is an important strategy in the treatment of malignant tumors. Bevacizumab is a recombinant humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody[8]. It can prevent the latter from binding to the receptor of vascular endothelial growth factor by binding specifically to the
receptor of vascular endothelial growth factor (VEGF), thus playing an anti-angiogenesis role. Therefore, as the first anti-angiogenesis drug, bevacizumab is very active in clinical trials of all kinds of tumors and various schemes[9-10]. The indications of bevacizumab are also expanding, and it has been approved for the treatment of lung cancer, breast cancer and ovarian cancer in the United States, Europe, China and other countries or regions. However, compared with other molecular targeted drugs, the clinical status of anti-angiogenesis therapy is still controversial, including the inability of bevacizumab alone to prolong the overall survival time of patients, unclear beneficiaries, long-term treatment safety and economic doubts[11]. These problems directly lead to the unclear clinical status of bevacizumab in the treatment of some cancers, and the lack of uniform criteria or standards for the relevant indications, treatment regimens, doses and treatment cycles. In this paper, 60 patients with malignant tumors treated in our hospital in 2017 were selected as the research objects. The clinical application value of bevacizumab was analyzed, as follows.

2. Materials and Methods

2.1 General information

60 patients with malignant tumors treated in our hospital in 2017 were selected as the research objects. All patients had pathological diagnosis basis. They were randomly divided into two groups with 30 cases in each group. All patients in this study have informed consent. There was no significant difference in the basic data between the two groups (P > 0.05), which was comparable.

Inclusion criteria: (1) meeting the diagnostic criteria for malignant tumors; (2) complete clinical information and treatment options; (3) age 18-89 years; (4) gender-unlimited; (5) all patients were treated with bevacizumab. Exclusion criteria: those who did not use bevacizumab.

2.2. Treatment

The control group was treated with chemotherapy alone, including paclitaxel, cisplatin, fluorouracil, docetaxel, carboplatin, oxaliplatin, sorafenib and sunitinib. The observation group was treated with bevacizumab (Shanghai Roche Company) on the basis of chemotherapy. The specific application methods were as follows: using normal saline to dilute bevacizumab to the required volume of administration, the concentration was 1.4-16.5mg/ml. The dosage was controlled from 4 mg/kg to 7.5 mg/kg, and the patients were given intravenous drip.

2.3 Observation Indicators

To observe the clinical curative effect of the two groups, the criteria for judging the curative effect are: the clinical symptoms of the patients have been improved completely, for complete remission (CR); the clinical symptoms of the patients have been improved partly, for partial remission (PR); the clinical symptoms of the patients have not improved significantly, but there is no worsening trend, for the condition is stable (SD); the clinical symptoms of the patients have worsening trend, for the progress (PD). The clinical effective rate was the sum of CR and PR, and the total control rate of clinical treatment was the sum of CR, PR and SD. The incidence of adverse reactions in the two groups was analyzed, including hemorrhage, hypertension, proteinuria and venous thromboembolism.

2.4 Statistical Analysis

Statistical software SPSS21.0 was used to process the data. The percentage (%) was used to express the counting data, and the results were parallel and tested. The comparison between the two groups showed that P < 0.05, representing a significant difference.

3. Results

3.1 Clinical Therapeutic Effect

The total control rate of clinical treatment in the observation group was 96.6% (29/30) and 73.3% (22/30) in the control group. The difference was significant (autopsy < 0.05). See Table 1.

3.2 ADRs

The clinical adverse reactions of the two groups were mainly hemorrhage, hypertension, proteinuria, venous thromboembolism, etc. The clinical adverse reactions of the observation group were significantly lower than those of the control group, the difference was significant P < 0.05. No serious adverse events occurred in all patients, as shown in Table 2.
3.3 Treatment plan

In the combined regimen of bevacizumab and chemotherapeutic drugs, there were 59 cases (8.3%) and 5 cases (8.3%). In the combined regimen of bevacizumab and chemotherapeutic drugs, 25 times (41.6%) were combined with antimetabolic drugs such as fluorouracil, 18 times (30%) with taxanes and 12 times (20%) with platinum drugs, as shown in Table 3.

Table 1. Clinical Therapeutic Effect

<table>
<thead>
<tr>
<th>group</th>
<th>cases</th>
<th>CR</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>effective</th>
<th>Total control</th>
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<tr>
<td>observation</td>
<td>30</td>
<td>8</td>
<td>15</td>
<td>4</td>
<td>2</td>
<td>25</td>
<td>29</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(83.3%)</td>
<td>(96.6%)</td>
</tr>
<tr>
<td>control group</td>
<td>30</td>
<td>6</td>
<td>11</td>
<td>5</td>
<td>4</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(56.6%)</td>
<td>(73.3%)</td>
</tr>
</tbody>
</table>

Table 2. Clinical adverse reactions

<table>
<thead>
<tr>
<th>group</th>
<th>cases</th>
<th>hemorrhage</th>
<th>Hypertension</th>
<th>Proteinuria</th>
<th>Venous thrombosis</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>observation</td>
<td>30</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>control group</td>
<td>30</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 3. Treatment plan

<table>
<thead>
<tr>
<th>Treatment plan</th>
<th>programme</th>
<th>Cases</th>
<th>Component ratio, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single use plan</td>
<td>Bevacizumab alone</td>
<td>5</td>
<td>8.3</td>
</tr>
<tr>
<td>Combination scheme</td>
<td>Combined with Platinum Drugs</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Combined with Taxus-containing Drugs</td>
<td>18</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Combined with anthracycline-containing drugs</td>
<td>4</td>
<td>6.6</td>
</tr>
<tr>
<td></td>
<td>Combination with antimetabolic drugs such as fluorouracil</td>
<td>25</td>
<td>41.6%</td>
</tr>
</tbody>
</table>

4. Discussion

In this clinical treatment of patients, the total control rate of clinical treatment in the observation group was 96.6%, compared with 73.3% in the control group[12]. There is no doubt about the application value of bevacizumab in the clinical treatment of patients with malignant tumors. Relevant clinical data also point out the advantages of bevacizumab in the treatment of malignant tumors[13-14]. However, the incidence of adverse reactions in the application of bevacizumab has always been a research hotspot. Some studies have pointed out that although bevacizumab has less adverse reactions in the treatment of malignant tumors, it has a serious impact on the clinical quality of life of patients. Observing the clinical adverse reactions of the patients, we can clearly see that the most common ones are hemorrhage, hypertension and proteinuria[15-16]. These adverse reactions have a significant impact on the quality of life of patients. Therefore, it is necessary to strengthen the prevention and treatment of adverse reactions of patients. (1) Hemorrhage. The mechanism of this adverse reaction may be that bevacizumab inhibits the growth of vascular endothelial cells, which leads to endothelial dysfunction in patients, while intravascular hemorrhage is prone to occur. The incidence of hemorrhage in the observation group was 10.0%. Two patients had recurrent epistaxis symptoms, and the patients asked to stop bevacizumab[17]. The other patients were combined with anticoagulant and anti-inflammatory drugs, and routine blood test and blood coagulation function were regularly checked in the clinical treatment of patients. 2. Hypertension, the specific mechanism of action is not obvious at present, possibly and blood vessels. The blockage of endothelial growth factor signaling pathway has a certain correlation. However, attention should be paid to the examination of blood pressure, urinary routine and cardiac function in patients. Once hypertension symptoms are found, antihypertensive drugs can be used as appropriate. 3. Proteinuria, the clinical pathogenesis is that bevacizumab causes a variety of glomerular and tubular lesions in patients, which leads to proteinuria. For patients with mild proteinuria, they can not be treated. If the patient's 24-hour proteinuria is more than 29, and the time is longer, it is necessary to consider the discontinuation of bevacizumab drugs; 4) venous thromboembolism, the occurrence of which is related to the inhibition of bevacizumab on vascular endothelial growth factors, resulting in changes in endothelial cells and cytokine release. If the patient has
thromboembolism, it should be considered. Bevacizumab should be used cautiously and should be discontinued permanently if grade 4 pulmonary embolism occurs.

In recent years, anti-angiogenesis therapy has been questioned clinically. Some studies have shown that bevacizumab alone cannot prolong the overall survival time of patients. Therefore, the combination of chemotherapeutic drugs has become the most important guiding strategy for clinical application of bevacizumab, that is to say, anti-angiogenesis drugs need to rely on other chemotherapeutic drugs to achieve the best effect. Maintaining a long-term angiopoietic state plays a key role in inhibiting the growth of tumors. Therefore, the treatment cycle of bevacizumab is also important for patients to benefit from survival. Studies have shown that progression-free survival and overall survival of patients receiving antiangiogenic therapy for more than four cycles are significantly longer than those receiving less than four cycles of treatment. It was also found that bevacizumab was well tolerated in long-term treatment. At present, the combination of bevacizumab and chemotherapeutic drugs involves almost all the commonly used clinical chemotherapy regimens. However, bevacizumab alone is mostly used as maintenance therapy after combined chemotherapy. However, due to the lack of strong clinical evidence, the dosage of bevacizumab remains to be further clarified.

![Figure 1. Bevacizumab and Angiogenesis inhibitor](image)

Among the treatments containing bevacizumab, 90.84% were combined with chemotherapeutic drugs, mainly with antimetabolic drugs such as fluorouracil, capecitabine, taxol, docetaxel and platinum. In recent years, anti-angiogenesis therapy has been questioned clinically. Some studies have shown that bevacizumab alone cannot prolong the overall survival time of patients. Therefore, the combination of chemotherapeutic drugs has become the most important guiding strategy for clinical application of bevacizumab, that is to say, anti-angiogenesis drugs need to rely on other chemotherapeutic drugs to achieve the best effect. At present, the combination of bevacizumab and chemotherapeutic regimens involves almost all the commonly used clinical chemotherapy regimens. However, bevacizumab alone is mostly used as maintenance therapy after combined chemotherapy. However, due to the lack of strong clinical evidence, the dosage of bevacizumab remains to be further clarified.

5. Conclusion

In summary, bevacizumab, as the first anti-angiogenesis drug on the market, has a certain status in the treatment of clinical malignant tumors (solid tumors), and has become the first line of treatment for colorectal, ovarian and lung cancer. However, due to the limitations of its pharmacological effects, the combination of bevacizumab and chemotherapeutic drugs is still the main direction of clinical application. In conclusion, bevacizumab can significantly improve the clinical effect and reduce the incidence of adverse reactions in patients with malignant tumors during chemotherapy. At the same time, it is necessary to strengthen the monitoring and treatment of adverse reactions in order to improve the quality of life of patients.
References


