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Clinical Effect of Imatinib, Nilotinib, and Dasatinib on Chronic Myeloid Leukemia in Chronic Phase

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Abstract: The study was conducted to explore the effect of imatinib, nilotinib, and dasatinib in the treatment of chronic myeloid leukemia (CML) patients. Around 66 patients with CML in chronic phase were selected, subsequently the patients were subdivided into 3 groups with 22 patients in each group: Group A were treated with imatinib; Group B were treated with nilotinib; and Group C were treated with dasatinib. The study showed that, at 18 months of treatment, compared with group A, the molecular biology remission rates of group B and group C were significantly higher, $p<0.05$; at 6 months and 18 months of treatment, compared with group A, the complete cytogenetic remission rates of group B and group C were significantly higher, $p<0.05$; and compared with group A, the incidences of vomiting, headache and edema in groups B and C were significantly lower, $p<0.05$. However, no significant different $p>0.05$ were observed in the complete hematologic remission rates, and the incidences of neutropenia and thrombocytopenia among the three groups. In summary, nilotinib and dasatinib are effective in the treatment of patients with CML in the chronic phase, which is significantly better than imatinib treatment.

Keywords: Imatinib; Nilotinib; Dasatinib; Chronic myeloid leukemia; Chronic phase; Clinical effect

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1. Introduction

Chronic myeloid leukemia (CML) originates in the hematopoietic stem cells, and the breakpoint clusters are continuously activated to form malignant bone marrow proliferation. Based on clinical research, imatinib is a tyrosine kinase inhibitor. In addition, with the continuous advancement of clinical medical technology [1-3], it is believed that the development of tyrosine kinase inhibitors can improve the clinical treatment effect of patients with CML in the chronic phase. Therefore, in this paper, 66 patients were selected to study the effect of imatinib, nilotinib, and dasatinib in the treatment of CML patients.

2. Materials and methods

2.1. Information

The research subjects were randomly selected in the Shaanxi Provincial People's Hospital from August 2019 to July 2020, and a total of 66 patients with CML in the chronic phase was selected for this study. The research subjects were grouped by random number table method.

(1) Group A; Male 12 cases and female 10 cases, with aged 21-68 (38.5±10.2) years old
(2) Group B; Male 11 cases and females 11 cases, with aged 22-67 (38.4±10.1) years old
(3) Group C; Males 10 cases and females 12 cases, with aged 20-69 (38.1±10.6) years old.

There was no significant difference ($p>0.05$) in the general data among the three groups of patients.

2.2. Methods

The 22 patients in group A were treated with imatinib. Initially, the patients were treated with 400 mg per day of imatinib and was treated once a day. After the onset of drug resistance symptoms appear in the patients, the dose was increased to 600-800 mg per day of imatinib, and was given once a day. In addition, if the patients shown a drug resistance symptom after admission of 800 mg imatinib, the patients will be treated with nilotinib or dasatinib with the similar dosage as group B and group C, and the drug is given once a day. All the patients in this group did not carry out drug change therapy.

The 22 patients in group B were treated with nilotinib, 300 mg per day, and was given once a day. Before taking nilotinib, the patient needs to fast for 2 hours, and subsequently after taking the nilotinib, the patient needs to fast for 1 more hour. When the patients showed a drug resistance symptom, the dose of nilotinib is increased to 600 mg per day, and was given once a day.

The 22 patients in group C were treated with dasatinib, 100 mg per day, and was given once a day. If an adverse reaction occurred in the three groups of patients, thereby the use of the drug will be discontinued.

All three groups of patients were treated for 18 months.

2.3. Effect research

Complete cytogenetic remission: Ph (+) cells are not found in the bone marrow after treatment.

Complete hematologic remission: White Blood Cell (WBC) within 10×109/L, PLT within 450×109/L, no immature cells in WBC classification, no signs and symptoms of leukemia.

Molecular biological remission: bone marrow RT-PCR, BCR-ABL/ABL within 5 [4,5].

2.4. Data verification

SPSS 25.0 statistical software was used for analysis. The $\chi 2$ test is used to express count data by the percentage sign (%), and **t** test is used to express the measurement data by [$\bar{x}\pm s$]. A p value less than 0.05 ($p<0.05$), is assumed to have a statistically significant difference.

3. Results

After 18 months of treatment, the molecular biology remission rate of group B and group C was significantly higher, compared with group A, $\chi 2=4.6972, 4.6972$, $p<0.05$; At 6 months and 18 months of treatment, the complete cytogenetic remission rates in groups B and C were significantly higher, compared with group A, $\chi 2=4.6972, 4.6972$ at 6 months, $\chi 2=4.6588, 4.6588$ at 18 months, $p<0.05$; The incidences of vomiting, headache and edema were significantly lower in groups B and C. Compared with group A, the incidence of vomiting was $\chi 2=4.2471, 4.2471$, the headache was $\chi 2=5.5000, 5.5000$, and the edema was $\chi 2=4.6588, 4.6588$, $p<0.05$; the complete hematologic remission rates of the three groups were compared, group A was compared with groups B and C, $\chi 2=0.3929, 0.3929$ at 3 months, $\chi 2=0.4583, 1.0909$ at 6 months, $\chi 2=2.0308, 2.0308$ at 18 months, $p>0.05$; the incidence of neutropenia and thrombocytopenia in the three groups were compared, and the incidence of neutropenia in group A, group B, and group C was compared, $\chi 2=0.4583, 0.1212$, compared with the thrombocytopenia in group A, group B and group C, $\chi 2=0.6111, 0.6111$, $p>0.05$. The results were summarized in **Table 1**, **Table 2**, **Table 3**, and **Table 4**.

Table 1. Comparison of complete cytogenetic remission rates among the three groups (%)

Group	3 months after treatment	6 months after treatment	18 months after treatment
Group A (n=22)	8	10	14
Group B (n=22)	12	17	20
Group C (n=22)	12	17	20

Table 2. Comparison of complete hematologic remission rates among the three groups (%)

Group	3 months after treatment	6 months after treatment	18 months after treatment
Group A (n=22)	13	15	18
Group B (n=22)	15	17	21
Group C (n=22)	15	18	21

Table 3. Comparison of molecular biology remission rates among the three groups (%)

Group	3 months after treatment	6 months after treatment	18 months after treatment
Group A (n=22)	1	2	5
Group B (n=22)	1	4	12
Group C (n=22)	1	2	12

Table 4. Comparison of adverse reactions among the three groups (%)

Group	Vomit	Headache	Thrombocytopenia	Edema	Neutropenia
Group A (n=22)	6	7	3	8	5
Group B (n=22)	1	1	5	2	7
Group C (n=22)	1	1	5	2	6

4. Discussion

CML is a common hematological malignancy in patients with chronic phase, with high incidence, and severe disease. Due to the disease the patient's condition may change drastically, therefore it will have a serious impact on the patient's prognosis [6-8]. As the disease progresses, the patient may suffer from abdominal distension, fatigue, low-grade fever, spleen enlargement, liver enlargement, and others. In the process of treating the patients, the use of imatinib can competitively inhibit the binding of Adenosine triphosphate (ATP) to tyrosine protein, thereby effectively inhibit the phosphorylation of tyrosine kinase. Additionally, it can also prevent and inhibit the proliferation of fusion genes [9-14] once the targeted therapy process is completed, and it has a specific inhibitory effect. Nilotinib can bind to tyrosine kinase, and its binding affinity is 30 times higher than that of imatinib, further it can inhibit the BCR-ABL phosphorylation in various cell lines, as well can be used to treat the drug-resistant cases. The use of dasatinib, compared with imatinib, is different in the term of the molecular structure [15-18], and it can combine the activated and the inactivated conformation in the ABL kinase domain. Clinical practice has confirmed that the treatment of CML patients with nilotinib and dasatinib can play a positive therapeutic role [19,20], with high safety, however has adverse reactions include vomiting, headache, edema, and others. The improvement of the molecular biology remission rate and complete cytogenetic remission rate are obvious, and the clinical application value is high.

This study demonstrated that; At 18 months of treatment, compared with group A, the molecular biology remission rates of group B and group C were significantly higher; and At 6 months and 18 months of treatment, compared with group A, the complete cytogenetic remission rates in groups B and C were significantly higher. In addition, compared with group A, the incidences of vomiting, headache, and edema were significantly lower in groups B and C.

In short, it is concluded that the treatment of patients with CML in the chronic phase with nilotinib and dasatinib has a significant effect, and the effects of these treatments are significantly better than imatinib, with fewer adverse reactions, thereby it is worthy of clinical recommendation.

Disclosure statement

The author declares no conflict of interest.

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