Efficacy Observation of Pre-Excitation Regimen in the Treatment of Refractory Relapsed Acute Non-Lymphocytic Leukemia

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Abstract: *Objective:* To explore the clinical effect of applying the pre-excitation regimen in the treatment of patients with refractory relapsed acute non-lymphocytic leukemia (ANLL). *Methods:* This research work was carried out in our hospital (Shaanxi Provincial People's Hospital) from September 2021 to September 2022. A total of 50 cases were selected for this study, and all were given a pre-excitation treatment plan, mainly low-dose cytarabine, aclarithromycin, etoposide, granulocyte colony-stimulating factor, and more were implemented. The clinical intervention effect was then analyzed. *Results:* Among the 50 patients in this study, the results showed that the treatment was very effective for 22 cases, accounting for 44.00%; effective for 14 cases, accounting for 28.00%; and ineffective for 14 cases, accounting for 28.00%. The total rate of effectiveness was 72.00%. The hematopoietic system adverse reactions of the patients were mainly bone marrow suppression. All 50 patients had different degrees of blood count decline, among which some patients' neutrophils were less than 0.5×10^9 /L. The median time was 7 days. Among them, 25 patients had infection problems, the incidence rate was 50.00%, the patient's platelet count PLT < 20 × 109/L, and the median time was 10 days. At the same time, among the 50 patients in this study, 34 (68.00%) patients had symptoms such as loss of appetite, nausea, vomiting, and fatigue, 17 (34.00%) patients showed hair loss, mildly elevated transaminases were observed in 8 (16.00%) patients, and 11 (22.00%) patients had muscle soreness. *Conclusion:* In the treatment of patients with refractory complex acute non-lymphocytic leukemia, the application of pre-excitation regimen has a significant effect, which can improve the adverse symptoms of patients, reduce the incidence of adverse reactions, and promote the recovery of patients.

Keywords: Pre-excitation regimen; Refractory; Complexity; Acute non-lymphocytic leukemia

1. Introduction

From the perspective of clinical development, the incidence of patients with refractory and complex non-lymphocytic leukemia is on the rise, posing a serious threat to the life and health of patients [1]. In the treatment of patients, conventional chemotherapy methods such as MA, DA and HA are used. The drug resistance of patients is high, resulting in insignificant curative effect. Moreover, some patients are affected by factors such as age and organ function. The implementation of an equal-dose chemotherapy regimen lacks tolerability [2]. Judging from the current clinical development, there are many methods in the application of the pre-excitation program for the treatment of patients with refractory and complex acute non-lymphocytic leukemia (ANLL) [3] such as GAG program, using granulocyte colony-stimulating factor, low-dose cytarabine and aclarithromycin, and so on [4]. The HAG regimen included granulocyte colony-

stimulating factor, low-dose cytarabine, and homoharringtonine. The clinical application effects of various treatment methods are relatively significant, and it is necessary to make a reasonable choice in combination with the actual situation [5]. This study mainly provides the basis of the GAG program, in which etoposide was added, and patients with complex and refractory ANLL in our hospital were selected as subjects, and the research effect is analyzed as follows.

2. Materials and methods

2.1. Data analysis

This experimental study was carried out in our hospital from September 2021 to September 2022. 50 subjects were selected, all of whom were patients with complex and refractory acute non-lymphocytic leukemia. Among the patients, there were 30 males and 20 females. The oldest patient was 66 years old and the youngest was 22 years old. The mean age of the patients was (46.56 ± 3.23) years old. When using French–American–British (FAB) classification systems as the classification standard, there were 3 M1 patients, 16 M2 patients, 10 M4 patients, 17 M5 patients, and 4 M6 patients.

Inclusion criteria: Patients who received standard mitoxantrone and cytarabine (MA), homoharringtonine and cytarabine (HA), or daunorubicin and cytarabine (DA) induction chemotherapy, but no obvious effect was obtained, or patients who relapsed after half a year of cure; patients who were resistant to the use of this pre-excitation regimen; patients who were informed and voluntarily participated in the experiment and cooperated; this study was in line with the standard of the hospital's experiment.

Exclusion criteria: patients who had a history of mental illness or had mental abnormalities; patients who did not comply with the treatment, and dropped out of the study halfway; patients with incomplete data.

2.2. Research methods

All patients were treated with a pre-excitation regimen, and 10 mg of cytarabine was administered from the 1st day to the 14th day via subcutaneous injection every 12 hours. 20 mg/d of aclarithromycin was administered from 1st day to the 4th day via intravenous infusion. For etoposide, it needs to be administered from the 1st day to the 14th day, with a dosage of 50 mg/d via intravenous drip. The dosage of granulocyte colony-stimulating factor was $100 ug/m^2$-$200 ug/m^2$ and was administered subcutaneously from the 1st day to the 14th day.

2.3. Observation indicators

The observation indicators of the patient's drug treatment effect include "very effective," "effective," and "ineffective.": Very effective means that the patient's symptoms were significantly relieved; effective means that the patient's symptoms were relieved to some extent; ineffective means that the patient's symptoms were not relieved after the treatment. The total efficiency was calculated by excluding inefficiencies.

To observe and compare the adverse reactions of the patients during the treatment, routine electrocardiogram, liver and kidney function of the patients were monitored before chemotherapy; after chemotherapy, the blood test results, liver and kidney function, and gastrointestinal adverse reactions of the patients were observed. Further observations and analysis were conducted to determine the effect of chemotherapy regimens on adverse reactions of patients.

2.4. Statistical methods

SPSS20.0 statistical software was used for data comparison and statistics in this study. The data statistics process involves two indicators, namely measurement data and count data. The expressions of the two are

(x ± s) and (n, %), the former needs to be guaranteed to meet the normal distribution, and the data needs to be verified after the calculation is completed to verify that there is a standard value, which is based on 0.05, which is greater than the standard value, indicating that the comparison of this research is meaningless. On the contrary, it shows that this comparison is meaningful, and the corresponding verification expressions are χ^2 value and t value [6].

3. Results

3.1. Therapeutic effect

Among the 50 patients in this study, 22 cases showed significant results, accounting for 44.00%, 14 cases showed some effect, accounting for 28.00%, and 14 cases showed no effect, accounting for 28.00%, the total rate of effectiveness of the treatment was 72.00%. The hematopoietic system adverse reactions of the patients were mainly bone marrow suppression. All 50 patients had different degrees of blood count decline with a median time of 7 days, among which the neutrophils of some patients were less than 0.5×10^9/L. Among them, 25 patients had infection problems, and the incidence rate was 50.00%. The infection sites included oral mucosa, periodontal, lung, upper respiratory tract, etc., and antibiotics were the main treatment option. After 5-10 days of treatment, the symptoms of the patients were relieved. At the same time, the patients' platelet count was less than 20×109/L, and the median time was 10 days. The patients' symptoms were mainly bleeding gums and skin and mucous membranes. Platelet transfusion therapy was given, and the patients improved after treatment.

3.2. Incidence of adverse reactions

Among the 50 patients in this study, 34 (68.00%) patients had symptoms such as loss of appetite, nausea, vomiting, and fatigue, 17 (34.00%) patients showed hair loss, and 8 (16.00%) patients showed mildly elevated transaminases, and improved symptoms after hepatoprotective intervention was given. At the same time, 11 patients (22.00%) developed muscle soreness.

4. Discussion

Refractory complex ANLL is a difficult problem in clinical treatment, because the disease is more complex, which makes its treatment difficult and the clinical treatment effect is poor [7]. From the perspective of clinical development, the incidence of patients with refractory and complex non-lymphocytic leukemia is on the rise, posing a serious threat to the life and health of patients. Such patients usually have undergone chemotherapy intervention for many years, resulting in declination if the patients' physique, and a decrease in their immune function. The effect of the treatment plan is not significant; therefore, the clinical treatment of patients is difficult [8]. Judging from the actual development situation, domestic and foreign research results on the therapeutic efficacy of patients with refractory complex ANLL are different, and the cure rate is usually below 30%-40% [9].

The use of G-CSF in pre-excitation regimen can enhance the apoptosis-inducing effect of low-dose Ara-C on myeloid leukemia cells, and in the specific implementation process, it can have an effect on quiescent ANLL, make it enter the cell cycle, intervene with thin and cycle-specific chemotherapeutic drugs, maximize their killing effect, and inhibit the self-renewal of leukemia cells, affect the metabolism of chemotherapeutic drugs in leukemia cells, and help chemotherapeutic drugs induce programmed cell death in leukemia cells [10]. The earliest clinical research on this drug was in 1995, which showed that the G-CSF pre-stimulation chemotherapy regimen has a significant effect on patients with refractory and relapsed ANLL, and a satisfactory result was obtained [11]. The CAG program was applied in another research, with 12 patients with refractory and complex ANLL as the research subjects; the results showed that 42% of the patients were significantly treated, and the total rate of effectiveness was 75% [12].

VP-16 is an inhibitor of DNA topoisomerase II, which is a porcine mastiff factor that causes DNA strand breakage, which affects DNA repair and inhibits tumor cell proliferation [13]. This drug is a time-dependent drug, and VP-16 is a reliable apoptosis inducer, which not only has the effect of inhibiting the proliferation of tumor cells, but also can promote cell apoptosis to achieve dual anti-tumor effects. Aclacinomycin can be embedded in the DNA double helix structure, thereby affecting the template function of DNA and affecting the DNA polymerase. Both of them will be combined with Ara-C to fight against leukemia [14]. According to relevant research data, 36 patients with ANLL were treated with the conventional dose of cytarabine, aclacinomycin and etoposide (AAE) regimen, and the results showed that the rate of effectiveness was 80.6% [15]. Because most of the patients with refractory and complex non-leukocytic leukemia are elderly, have poor organ functions, poor economic conditions, and other problems, when treating patients in this study, the pre-excitation program was applied combined with the characteristics of the two aforementioned treatment programs. The results showed that among the 50 patients in this study, the results showed that there were 22 cases, accounting for 44.00%, the results showed that there were 14 cases that were not effective, accounting for 28.00%, and 14 cases were ineffective, accounting for 28.00%, and the total effective rate was 72.00%. At the same time, among the 50 patients in this study, 34 (68.00%) patients had symptoms such as loss of appetite, nausea, vomiting and fatigue, 17 (34.00%) patients showed hair loss, and 8 (16.00%) patients Mildly elevated transaminases were observed, and 11 (22.00%) patients had muscle soreness. The results show that the application of pre-excitation regimen therapy in the treatment of patients with refractory and complex non-lymphocytic leukemia has a significant effect, can promote the recovery of patients, and reduce the incidence of adverse reactions in patients.

5. Conclusion

In conclusion, the application of the pre-excitation regimen has a significant effect on the treatment of patients with refractory complex acute non-lymphocytic leukemia, in which it improves the adverse symptoms of patients, reduce the incidence of adverse reactions of patients, and promote the development of patients. Hence, it has high clinical application value and should be popularized and implemented.

Disclosure statement

The author declares no conflict of interest.

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