Effect of Granulocyte Colony-Stimulating Factor Combined with Erythropoietin on Chronic Granulocytic Leukemia with Anemia and Its Effect on Nutritional Status

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Objective: To investigate the clinical effect of granulocyte colony-stimulating factor combined with erythropoietin on chronic granulocytic leukemia with anemia and its effect on nutritional status. Methods: 60 patients of chronic granulocytic leukemia of our hospital with anemia induced by maintenance chemotherapy were randomly divided into two groups. Patients in the control group received routine treatment, while patients in the observation group received basal treatment with granulocyte colony-stimulating factor and erythropoietin. The nutritional status before and after treatment as well as the immune function and the incidence of blood transfusion and adverse events were compared between the two groups. Results: There was no significant difference in hemoglobin, hematocrit, nutritional status and immune function between the two groups before treatment (P>0.05). Those after treatment were significantly higher than that before treatment (P<0.05). After treatment, the percentage of CD4* cells in the control group was significantly higher than that before treatment (P<0.05), but the percentage of CD8* cells and CD47/CD8* cells did not change significantly (P>0.05). After treatment, the concentrations of IgA, IgM and IgG in the observation group were significantly higher than those before treatment (P<0.05), but only the concentrations of IgA and IgM in the control group were significantly higher than those in the observation group after treatment (P<0.05). The incidence of adverse reactions in the observation group was significantly lower than that in the control group. Conclusion: Granulocyte colony-stimulating factor combined with erythropoietin can effectively correct anemia, improve nutritional status and improve immune function in patients with chronic myelogenous leukemia.

Key words: Granulocyte colony-stimulating factor; Erythropoietin; Immune function; Nutritional status
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Chronic myelogenous leukemia is prone to secondary myelofibrosis, which severely affects the patient's hematologic function and causes anemia [1]; long-term chemotherapy can also worsen anemia levels in patients with leukemia[2]. G-csf is a stimulating pleurocyte growth factor, innate immune response and adaptive immune response inhibitor [3], which can mobilize strains and exogenous cells to participate in the treatment of MS. EPO is a substance excreted by the liver and kidney. In addition to correcting anemia, it has been shown that granulocyte colony-stimulating factors related to erythropoietin can greatly help patients to improve cardiovascular events. The study also showed that [4] erythropoietin not only corrected anemia, but also significantly improved the nutritional status of patients with chronic granulocytic leukemia, and the serum albumin and transferrin levels of patients were significantly increased, which was consistent with the report of investigators consistent with domestic and foreign standards [5]. At the same time, granulocyte colony-

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stimulating factor also corrects abnormal amino acid metabolism, so the combination of the two can effectively improve the nutritional status of patients with chronic granulocytic leukemia. The report is now as follows:

DATA AND METHODS

General data

Between June 2019 and June 2021, 60 patients with chronic granulocytic leukemia and myelofibrosis were admitted to the hospital, and 20 men and 40 women, aged 22 to 48 years, were divided into two groups and treated with iron, folic acid and other complementary therapies for myelogenous leukemia. The system combines colony-stimulating factors with conventional therapy using conventional treatment methods to treat patients within the observer. The discussion of the implementation is as follows.

Inclusion criteria

① Men and women aged ≥ 18 years; ② Body condition 0-3; ③ Expected survival time ≥ 6 months. Exclusion criteria: ① Uncontrolled hypertension; ② Combined with other types of malignant diseases, serious diseases, hematological diseases, vascular embolism and acute and chronic internal hemorrhage;

Cells and cytokines

CML-BC cells were obtained from the bone marrow of CML patients and their surface markers are shown in Table 1.

Table 1.
CM L-BC cell surface markers

CD3	CD7	CD10	CD13	CD14	CD19	CD33	CD34	CD71	HLA-DR
26.8	63.7	6.4	99.4	1.6	0	99.9	96.9	99.5	89.3

Methods

Treatments

The control group received routine oral iron, folic acid, and other adjuvant therapy. The patients in the observation group received routine treatment and received subcutaneous injection of recombinant human erythropoietin and granulocyte colony-stimulating factor at 4000 U twice a week for 12 weeks [28].

Routine blood tests

The patient's venous blood is collected and analyzed and measured using a hematology analyzer to determine the patient's Hb and Hct.

Nutritional status examination

PA and TRF were selected and the concentration of pre-albumin and transferrin was determined by immunomodulatory methods using Hitachi 7180 Biochemistry Analyzer. Perform all operations exactly as directed in the corresponding kit.

Classification of T lymphocytes and detection of immunoglobulins

After the patient's venous blood was drawn and anticoagulated with heparin, the numbers of CD4 *, CD8 *, and CD47CD8 * T cells were determined to determine the cells. The fluorescent antibodies to CD4 * and CD8 * are manufactured by Immunotech, France. Immunoglobulin IgA, IgM, and IgG concentrations were determined by immunoturbidimetry using a Hitachi 7180 automated biochemical analyzer. All operations were performed according to the instructions in the respective kit

Observation indicators

The changes of Hb, the volume of red blood cells in peripheral blood as a percentage of blood volume, nutritional status and immune function were compared between the two groups before and after treatment. To determine the content of Hb and observe the healing effect of granulocyte lines treated with colony-stimulating factor combined with erythropoietin.

Statistical methods

SPSS 17.0 statistical software was used to analyze and compare the two groups using independent t-test, and pairwise t-test was used to compare the intra-group comparison with the ratio of patients in the two groups.

RESULTS

Comparison of Hb and Hct values before and after treatment in the two groups

There was no significant difference in Hb and Hct values before treatment between the two groups

(P>0.05). Hb and Hct values increased after treatment (P<0.05). See Table 2.

Table 2.
Comparison of Hb and Het values before and after treatment in the two groups

Grouping	Number of cases	HB (g/L)		Hct (%)	
		Before treatment	After treatment	Before treatment	After treatment
Treatment group	30	72.6 ± 10.5	102.5 ± 7.9	19.0 ± 6.3	34.3 ± 2.1
Control group	30	70.5 ± 11.1	91.6 ± 7.1	19.6 ± 4.9	25.6 ± 2.4

Comparison of TP and ALB values before and after treatment between the two groups

The levels of PT and ALB in the treatment group were significantly higher than those before treatment, and the difference was statistically significant (P<0.05). See Table 3.

Table 3.
Comparison of TP and ALB values before treatment and after treatment between the two groups

Grouping	Number of cases	TP (g/L)		ALB (g/L)	
		Before treatment	After treatment	Before treatment	After treatment
Treatment group	30	60.3 ± 8.4	71.1 ± 10.2	33.6 ± 6.8	40.1 ± 3.3
Control group	30	61.3 ± 6.9	63.5 ± 4.9	33.6 ± 5.3	36.6 ± 3.5

Comparison of nutritional status before and after treatment between the two groups

After treatment, the PA value of the two groups was significantly higher than that before treatment (P<0.05), and the TRF value of the control group was not significantly different from that before treatment (P>0.05). After TRF treatment, the sum of AP in the observation group was significantly higher than that in the control group (P<0.05). See Table 4.

Table 4.
Comparison of nutritional status before and after treatment in the two groups

Grouping	Number of cases	PA (mg/L)		TRF (g/L)	
		Before treatment	After treatment	Before treatment	After treatment
Treatment group	30	220.36 ± 40.25	276.74 ± 48.34*	1.95 ± 0.26	2.60 ± 0.49*
Control group	30	222.14 ± 42.51	330.69 ± 57.66*#	1.88 ± 0.25	3.24 ± 0.64*#

Note: *, #: Compared with the control group, there was a significant difference, P<0.05.

Comparison of immune function between the two groups before and after treatment

After treatment, the proportion of CD4 +, IgA and IgM cells in the control group increased significantly (P<0.05), while the proportion of CD4 + / CD8 + cells and IgA, IgM and IgG cells in the observation group increased significantly (P<0.05). A comparison of immune function between the two groups before and after treatment is shown in Tables 5 and 6

Table 5.
Comparison of immune function between the two groups before and after treatment

Grouping	Number of cases	CD4+ (%)		CD8+ (%)		CD4+/CD8+ (%) Ig	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment group	30	38.14 ± 6.54	40.23 ± 7.17*	36.38 ± 5.99	36.02 ± 4.67	1.045 ± 0.126	1.072 ± 0.121
Control group	30	38.24 ± 6.51	45.01 ± 8.22*#	36.90 ± 5.88	30.47 ± 4.23*#	1.053 ± 0.132	1.696 ± 0.131*#

Table 6.
Comparison of three classes of immunoglobulins (IgA, IgM and IgG) before and after treatment in the two groups

Grouping	Number of cases	IgA(g/L)		IgM(g/L)		IgG(g/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Treatment group	30	1.176 ± 0.255	1.322 ± 0.2311*	1.596 ± 0.284	1.69 ± 00.3.1*	10.56 ± 2.14	11.07 ± 2.21
Control group	30	1.183 ± 0.237	1.617 ± 0.457*#	1.577 ± 0.293	1.974 ± 0.341*#	10.51 ± 2.10	16.45 ± 3.47*#

Note: *, #: Compared with the control group, there was a significant difference, P<0.05.

Comparison of the incidence of adverse reactions

Table 7.
Comparison of the incidence of adverse reactions between the two groups

Grouping	Number of	Ostalgia	Fever	Leukocytosis	Injection site	Skin rash	Incidence of adverse reactions	P
Observation group	30	1 (3.33)	1 (3.33)	0 (0.00)	0 (0.00)	1 (3.33)	3 (10.00)	
							x2 23.177	0.000
Control group	30	10 (33.33)	6 (20.00)	5 (16.67)	3 (10.00)	1 (3.33)	27 (90.00)	

DISCUSSION

Myelofibrosis is an excessive increase in fibrous tissue and a decrease in the hematopoiesis of RBC, resulting in anemia [7-10]. In addition, infusion of exogenous proteins can result in decreased immune function, which is a major cause of fatal infection in these patients [11-13]. Anemia occurs in patients with secondary myelofibrosis in chronic myelogenous leukemia [14-15]. Also, patients with leukemia are approximately 70% to 90% likely to develop anemia during chemotherapy due to long-term chemotherapy [16]. Therefore, anemia should be actively prevented. In the opinion of Chinese experts, erythropoietin is indicated in patients with mild to moderate anemia or iron allergy caused by radiotherapy and chemotherapy [17]. Based on the degree of risk and serum erythropoietin concentration, it was decided whether combined granulocyte colony-stimulating factor and erythropoietin could be used to treat patients with chronic granulocytic leukemia with anemia [18-20].

The results showed that erythropoietin further increased hemoglobin and hematocrit during chemotherapy in patients with chronic granulocytic leukemia compared with conventional therapy, suggesting that erythropoietin has good efficacy in patients with chronic granulocytic leukemia and anemia [21-22]. In addition to correcting anemia, studies have shown that granulocyte colony-stimulating factors associated with erythropoietin can greatly help patients improve cardiovascular events [23]. The study also showed that erythropoietin not only corrected anemia, but also significantly improved the nutritional status of patients with chronic granulocytic leukemia, and the serum albumin and transferrin levels of patients were significantly increased, which was consistent with the report of investigators consistent with domestic and foreign standards [24-25]. At the same time, granulocyte colony-stimulating factor also corrects abnormal amino acid metabolism, so the combination of the two can effectively improve the nutritional status of patients with chronic granulocytic leukemia. Our study demonstrates that erythropoietin effectively increases the proportion of CD4 + cells to CD4 +/ CD8 + cells in patients and increases the concentration of multiple immunoglobulins, indicating that rhuEPO exerts its effects. Therefore, it is necessary to strengthen the monitoring of symptoms and related indicators in patients with chronic granulocytic leukemia [26-27].

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