

Evaluation of the Therapeutic Significance of Arsenite and Thalidomide in Patients with Myelodysplastic Syndrome

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Abstract: *Objective:* To analyze the therapeutic significance of arsenite and thalidomide in patients with myelodysplastic syndrome. *Methods:* From August 2021 to August 2022, 80 patients with myelodysplastic syndrome were selected and randomly divided into two groups. In the control group, the drug used was thalidomide tablets, whereas in the observation group, the drug used was arsenite and thalidomide. The treatment effect was observed and evaluated. *Results:* Before treatment, there was no statistical significance in the blood and serological indices between the two groups. After treatment, the observation group showed better blood and serological indices than the control group (P < 0.05). The clinical efficacy of the observation group was 77.5%, while that of the control group was 50.0%. The observation group had significantly better treatment effect (P < 0.05). The incidence of adverse effects in the observation group and the control group was 5.0% and 20.0%, respectively. The observation group had significantly fewer adverse effects (P < 0.05). *Conclusion:* In the treatment of patients with myelodysplastic syndrome, the use of arsenite on the basis of thalidomide can effectively improve the treatment effect and optimize the levels of various blood and serological indices, with fewer adverse effects and a relatively high safety profile.

Keywords: Arsenite; Thalidomide; Myelodysplastic syndrome

Online publication: November 25, 2022

1. Introduction

The pathogenesis of myelodysplastic syndrome is due to the abnormal development of human hematopoietic cells, resulting in decreased hematopoietic function and hematopoietic failure in patients. With the development of the disease, frequent bleeding and lethal infection often occur, posing a great threat to the safety of patients. Therefore, it is necessary to use effective treatment methods against this condition to save the lives of patients ^[1]. In recent years, the drug combination method has been applied in the treatment of this condition, wherein arsenite is used on the basis of thalidomide tablets. In order to explore the treatment effect of these two drugs on myelodysplastic syndrome, 80 patients were selected for this study and grouped according to different treatment methods.

2. Materials and methods

2.1. General information

From August 2021 to August 2022, 80 patients with myelodysplastic syndrome were selected and randomly divided into two groups. In the observation group, there were 16 males and 24 females, age ranging from

15 to 67 years, with an average age of 42.2 ± 9.4 years. In the control group, there were 17 males and 23 females, age ranging from 15 to 67 years, with an average age 42.5 ± 9.8 years. The difference in the general data between the two groups was insignificant (*P* > 0.05). All the patients signed the informed consent.

2.2. Methods

The control group received oral thalidomide tablets; the initial dose was 100 mg/d, which was later adjusted according to the patient's drug tolerance; the dose on the second week was 150 mg/d, and on the third week, it was increased to 200 mg/d. After one month, a dose of 300 mg/d was given if deemed appropriate. The observation group was given sodium arsenite injection on the basis of the control group. After mixing 10 mg of arsenous acid in 500 mL of 0.9% sodium chloride, the patients were given intravenous drip once a day. The treatment was over four weeks.

2.3. Observation indicators

(1) Blood indices

White blood cells (WBC), hemoglobin (Hb), and platelets (PLT).

(2) Serological indices

Tumor necrosis factor α (TNF- α), interferon γ (IFN- γ), and vascular endothelial growth factor (VEGF). Before and after treatment, 5 mL of venous blood was drawn from the patient's vein at the cubital fossa on an empty stomach in the morning, and an automatic chemiluminescence immunoassay was used to detect these indices.

(3) Clinical efficacy

Criteria to determine the treatment effect: "complete remission" means that the symptoms related to the disease have disappeared completely, and the blood and serological indices are basically normal; "partial remission" means that the clinical symptoms have basically disappeared, the primitive and promyelocytic cells in the peripheral blood are less than 5%, the primordial and promyelocytic cells in the bone marrow have decreased by more than 50%, and the maintenance time is not less than 3 months; "progress" refers to the improvement of various clinical symptoms compared with the first month of treatment, an increase in Hb not less than 30 g/L, and the primitive and promyelocytic cells in the bone marrow have reduced; "invalid" means that all indicators and symptoms have not improved, or the condition has deteriorated.

(4) Adverse reactions

Abdominal distension, headache, nausea, edema, constipation, etc. The adverse reactions and their incidence were observed.

2.4. Statistical analysis

SPSS 20.0 was used for data comparison and statistical analysis. The measurement data and enumeration data were expressed in $\bar{x} \pm s$ and n/%, respectively. The former was tested by chi-square test, while the latter by t-test. P < 0.05 indicates statistical significance.

3. Results

3.1. Comparison of blood index levels between the two groups

Before treatment, there was no significant difference in the levels of white blood cells, hemoglobin, and platelets between the two groups (P > 0.05). After treatment, the blood index levels of the observation group were significantly better than those of the control group (P < 0.05) (**Table 1**).

Group	Number	Hb (g/L)		WBC (×10 ⁹ /L)	PLT (×10 ⁹ /L)	
	of cases	Before	After	Before	After	Before	After
		intervention	intervention	intervention	intervention	intervention	intervention
Observation	40	45.26 ± 6.06	94.05 ± 8.14	2.14 ± 0.85	4.89 ± 0.92	35.62 ± 3.25	69.64 ± 5.83
Control	40	45.27 ± 6.36	82.07 ± 7.26	2.47 ± 0.69	3.86 ± 0.83	35.37 ± 3.14	59.35 ± 4.77
<i>t</i> -value		0.007	6.947	1.906	5.257	0.350	8.640
<i>P</i> -value		0.994	0.000	0.060	0.000	0.727	0.000

Table 1. Comparison of blood index levels between the two groups $(\bar{x} \pm s)$

3.2. Comparison of serological indices between the two groups

Before treatment, there was no significant difference in TNF- α , IFN- γ , and VEGF levels between the two groups (*P* > 0.05). After treatment, the serological indices of the observation group were significantly better than those of the control group (*P* < 0.05). See **Table 2** for details.

Table 2. Comparison of serological indices between the two groups $(\bar{x} \pm s)$

Group	Number	TNF-α (ng/mL)		IFN-γ (pg/mL)	VEGF (g/mL)	
	of cases	Before	After	Before	After	Before	After
		intervention	intervention	intervention	intervention	intervention	intervention
Observation	40	$1,\!306.03\pm$	$915.11 \pm$	11.14 ± 1.65	4.89 ± 1.92	$247.62 \pm$	$140.24~\pm$
		206.06	156.30			32.25	5.95
Control	40	1,285.27 \pm	1,002.07 \pm	11.52 ± 1.71	7.88 ± 1.80	$248.58 \pm$	$159.16 \pm$
		219.21	150.15			33.05	4.86
<i>t</i> -value		0.436	2.538	1.011	7.186	0.132	15.576
<i>P</i> -value		0.664	0.013	0.315	0.000	0.896	0.000

3.3. Comparison of clinical efficacy between the two groups

The effective rate of treatment in the observation group was 77.5%, while that in the control group was 50.0%. The treatment effect in the observation group was significantly better (P < 0.05), as shown in **Table 3**.

Table 3. Comparison of clinical efficacy between the two groups (n/%)

Group	Number of cases	Complete remission	Partial remission	Progress	Invalid	Efficacy
Observation	40	20	11	7	2	31 (77.5)
Control	40	9	11	14	6	20 (50.0)
χ2						6.5450
P-value						0.011

3.4. Comparison of incidence of adverse reactions between the two groups

The incidence of adverse reactions in the observation group was 5%, while that in the control group was 20%. The observation group had significantly lesser adverse reactions (P < 0.05). See **Table 4** for details.

Group	Number	Abdominal distention	Edema	Headache	Nausea	Constipation	Incidence
	of cases						
Observation	40	1	0	1	0	0	2 (5.0)
Control	40	3	1	2	1	1	8 (20.0)
χ^2							4.114
P-value							0.048

Table 4. Comparison of incidence of adverse reactions between the two groups (n/%)

4. Discussion

In clinical practice, myelodysplastic syndrome is a relatively common condition. It is a clonal disorder of hematopoietic stem cells. Its etiology is associated with abnormal hematopoietic function, which may threaten the patient's life. The pathogenesis of this disease is relatively complex. Abnormal clones can be found in the early stage of the disease, and there is increased hematopoietic proliferation and apoptosis in the bone marrow. In the late stage of the disease, in addition to abnormal clonal proliferation and increased hematopoietic proliferation in the bone marrow, there is low apoptosis in the bone marrow. Many patients die due to complications caused by low levels of functional blood cells ^[2-4]. At this stage, there is a lack of specific drugs for the treatment of this disease. Several studies have pointed out that bone marrow monocytes can synthesize and secrete TNF and VEGF^[5,6]. TNF plays an important role in regulating apoptosis. With the advancements in medical technology, there is a growing number of research in China, especially on various drugs for the treatment of this disease. Among them, arsenous acid is a commonly used drug, and its active ingredient, arsenic trioxide, can directly act on the EVI gene, control its expression, and affect red blood cells. Inhibition of differentiation causes erythrocytopenia, which has a significant effect on the control of disease progression. Moreover, the inhibition of VEGF secretion helps to promote the apoptosis of vascular endothelial cells ^[7-9]. Thalidomide is a glutamic acid derivative with poor water solubility. It can inhibit the synthesis of TNF by blocking angiogenesis regulators, transforming growth factors, and endothelial growth factors. It has an anti-angiogenic effect. The use of thalidomide in the treatment of MDS allows the inhibition and reduction of TNFs, controls the apoptosis of bone marrow cells, and has a positive effect on maintaining hematopoietic function ^[10-12]. Not only that, the use of this drug can counteract the decline of VEGF, control angiogenesis, inhibit abnormal clones, and prevent the condition from progressing into leukemia. The combined use of the two drugs further promotes the effect of inhibiting angiogenesis and anti-VEGF, significantly improves the related blood and serological indices, and effectively reduces the incidence of adverse effects, along with the mortality rate ^[13-15].

In this study, after treatment, the blood index levels and serological indices of the observation group were better than those of the control group (P < 0.05). The clinical efficacy of the observation group was 77.5%, while that of the control group 50.0%. The observation group had significantly better treatment effect than the control group (P < 0.05). The incidence of adverse effects in the observation group and the control group was 5.0% and 20.0%, respectively, indicating that the observation group had fewer adverse effects (P < 0.05).

In conclusion, satisfactory therapeutic effects can be achieved with the use of thalidomide in combination with arsenite in the treatment of myelodysplastic syndrome. In addition to an improving effect, blood and serological indices can be effectively improved, and patients have less adverse effects. This traditional Chinese medicine has high safety profile and a positive impact on the recovery of patients with MDS. Therefore, this combination of drug is worth promoting in clinical practice for the treatment of MDS.

Disclosure statement

The authors declare no conflict of interest.

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