

Observations on After-Effect Duration of Kidney-Nourishing and Marrow-Replenishing Therapy on 58 Cases of Mediterranean Anemia

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Objective: To observe the after-effect duration of kidney-nourishing and marrow-replenishing therapy on Mediterranean anemia. **Methods:** To observe the kidney-nourishing and marrow-replenishing therapy on 58 cases of Mediterranean anemia and the influence of various relative factors on the after-effect duration. **Results:** The after-effect duration on 58 cases varied from 3-6 months, about 4 months on average, and was not influenced by sex, clinical types, genetic types, types of Mediterranean anemia and other factors. **Conclusion:** Kidney-nourishing and marrow-replenishing therapy used to treat Mediterranean anemia can not only produce good therapeutic effect during treatment but also keep after effect lasting for about 4 months, indicating that the therapy used to treat Mediterranean anemia has good clinical after effect.

Key words: kidney-nourishing and marrow-replenishing therapy; Mediterranean anemia; follow-up

Mediterranean anemia is a chronic hemolytic disease caused by imbalance of peptide chain because genetic mutation or defect of one globin or more inhibits the synthesis of its peptide chain. In order to determine the after effect of kidney-nourishing and marrow-replenishing therapy on Mediterranean anemia, the research team observed the after-effect duration of the therapy on 58 cases from 1993 to 2004.

CLINICAL MATERIALS

Criteria for Diagnosis and Inclusion

According to the criteria for diagnosing Mediterranean anemia in "Criteria for Diagnosis and Therapeutic Effect on Hematopathy" edited by ZHANG Zhi-nan,¹ patients with α -Mediterranean anemia hemoglobin H disease (HbH disease) as well as severe or moderate β -Mediterranean anemia with no blood transfusion or in take of anti-anemia drug in recent half a year.

Criteria for Exclusion

1) Patients have immunologic deficiency or other

primary diseases of the liver, kidney and blood system. 2) Patients do not take drugs according to instructions or their data are incomplete, thus influencing the determination of therapeutic effect.

General Data

From October 1993 to June 2004, at No.303 Hospital of PLA used as a clinical research base, among 67 out of 89 patients coming from Nanning and its surrounding area who conformed to the criteria for diagnosis and inclusion and were willing to accept treatment according to research conditions, 62 effective cases (with effective rate at 92.5%) were observed for the after-effect duration. 58 appraisable cases were collected (with the rate of follow-up visits at 86.6%).

Among the 58 patients, 3 cases had HbH disease, 25 cases had severe β -Mediterranean anemia and 30 cases had moderate β -Mediterranean anemia. There were 38 males and 20 females aged 2.3–31, 12.2±6.8 on average; 10 people of Han nationality, 45 people

of Zhuang nationality, 2 people of Yao nationality and 1 person of Miao nationality; 2 people from Guangdong and 56 people from Guangxi.

METHODS

Therapeutic Method

Chinese drugs for nourishing the kidney and replenishing marrow (capsule and granule for replenishing marrow and generating blood) were used in the treatment for 2–3 months. During observation, patients were asked to have no blood transfusion, but keep on taking the drugs.

Capsule and granule for replenishing marrow and generating blood, consisting of Shan Zhu Yu (山茱萸 Fructus Corni), He Shou Wu (何首乌 Radix Polygoni Multiflori), Shu Di Huang (熟地黄 Radix Rehmanniae Preparata), Huang Qi (黄芪 Radix Astragali) and Bie Jia (鳖甲 Carapax Trionycis), are provided by the medicament department of Guang'anmen Hospital affiliated to China Academy of Chinese Medical sciences. Each capsule contains 0.4 g powder (1 g powder contains 4.25 g crude drug) with batch number 970318. A pack of granules contains 10 g powder (1 g powder contains 2.368 g crude drug) with batch numbers 990920 and 010811. 4 capsules or a pack of granules is taken each time, 3 times a day, with the dosage reduced for children.

Index and Method of Observation

1) Observations on the after-effect duration: After treatment, the effective cases were asked to come back to hospital at a fixed time every month for reexamination of their blood parameters: hemoglobin concentration (Hb), red cell count (RBC) and reticulocyte count (Ret). The time from the day of withdraw to the day when hemoglobin concentration reduces to the level before treatment is defined as the time of maintaining therapeutic effect. If Hb is equal to or less than the level before treatment, the previous time of reexamination is regarded as valid date calculated by months. 2) Influence of relevant factors on the after-effect duration: Observations were

carried out on the influence of sex, clinical type, genetic type and Mediterranean anemia type on the duration of lasting effect for Mediterranean anemia patients.

Criteria for Therapeutic Effect

In reference to “*Criteria for Dagnosis and Therapeutic Effect on Hematopathy*” edited by ZHANG Zhi-nan,¹ increase in red cell count and reticulocyte count (Hb, RBC, Ret) and increase in hemoglobin concentration (Hb) to more than 5 g/L is regarded as effective. Increase in reticulocyte count (Ret) alone is not regarded as an effective case.

Statistical Method

SPSS10.0 software is used. Enumeration data is used for frequency statistics, measurement data is expressed in ($\bar{x} \pm s$). Paired *t* test, grouped *t* test and variance analysis of single factor are applied respectively according to data types.

RESULTS

Observations on The Duration of The After-Effect

Among 58 patients, 23 cases accounting for 39.7% had the therapeutic effect lasted for 3 months, 16 cases accounting for 27.6% for 6 months, 6 cases accounting for 10.3% for 2 months, 6 cases accounting for 10.3% for 4 months, 5 cases accounting for 8.6% for 1 month, 1 case accounting for 1.7% for 5 months and 1 case accounting for 1.7% for 11 months. According to the statistic analysis that 79.3% of the 58 patients had the effect lasted for 3–6 months, 3.8 ± 1.9 months on average.

As shown in Table 1, the level of hemoglobin concentration, red cell count and reticulocyte count of all the 58 patients in the after-effect duration determined by months was higher than the level before treatment ($P < 0.05$ or $P < 0.01$), indicating that the after-effect duration still has a tendency to increase.

Influence of Relevant Factors on The After-Effect Duration

1) Influence of sex on the after-effect duration: As shown in Table 2, there is no statistical difference between males and females in the after-effect duration ($P>0.05$), indicating that after treatment with Chinese drugs for nourishing kidney and replenishing marrow, the duration of after effect is not influenced by sex.

2) Influence of clinical types on the duration of after effect: As shown in Table 3, there is no statistical difference between severe type and moderate type in the after-effect duration ($P>0.05$), indicating that after treatment with Chinese drugs for nourishing kidney and replenishing marrow, the duration of after effect is not influenced by clinical types.

3) Influence of genetic types on the after-effect duration: As shown in Table 4, there is no statistical difference among homozygous type, dual heterozygous type and heterozygous type in the after-effect duration ($P>0.05$), indicating that after treatment with Chinese drugs for nourishing kidney and replenishing marrow, the after-effect duration is not influenced by genetic types.

4) Influence of Mediterranean anemia types on the after-effect duration: As shown in Table 5, there is no statistical difference between β Mediterranean anemia and α -Mediterranean anemia in the after-effect duration ($P>0.05$), indicating that after treatment with Chinese drugs for nourishing kidney and replenishing marrow, the after-effect duration is not influenced by Mediterranean anemia types.

Table 1. Comparison of blood parameters of 58 patients before treatment and the after-effect duration determined by month ($\bar{x} \pm s$)

Time	Hb (g/L)	RBC ($\times 10^{12}/L$)	Ret (%)
Before treatment	66.78 \pm 18.58	3.29 \pm 0.87	0.15 \pm 0.47
After-effect duration determined by month	74.88 \pm 19.62 **	3.66 \pm 0.96 **	0.17 \pm 0.41 *

Notes: * $P<0.05$, ** $P<0.01$ as compared with the datum before treatment.

Table 2 Comparison of after-effect duration and blood parameters of patients with different sex determined month ($\bar{x} \pm s$)

Sex	Cases	Duration of after-effect (month)	Hb (g/L)	RBC ($\times 10^{12}/L$)	Ret (%)
Male	38	3.71 \pm 1.78	74.50 \pm 21.33	3.75 \pm 0.91	0.10 \pm 0.05
Female	20	4.05 \pm 2.11	75.60 \pm 16.36	3.48 \pm 1.05	0.30 \pm 0.69

Table 3 Comparison of time of maintaining therapeutic effect and blood parameters of patients with different clinical types determined by month ($\bar{x} \pm s$)

Clinical types	Cases	Duration of after-effect (month)	Hb (g/L)	RBC ($\times 10^{12}/L$)	Ret (%)
Severe	25	3.76 \pm 1.56	59.04 \pm 15.19	3.20 \pm 0.88	0.12 \pm 0.07
Moderate	33	3.88 \pm 2.13	86.88 \pm 12.97*	4.00 \pm 0.88*	0.21 \pm 0.54

Notes: * $P<0.01$ as compared with the datum in severe type.

Table 4 Comparison of the after-effect duration and blood parameters of patients with different genetic types determined by month ($\bar{x} \pm s$)

Genetic types	Cases	Duration of after-effect (month)	Hb (g/L)	RBC ($\times 10^{12}/L$)	Ret (%)
Homozygous	10	3.70 \pm 1.83	64.50 \pm 28.82	2.99 \pm 1.07	0.13 \pm 0.13
Dual heterozygous	42	3.83 \pm 1.54	75.98 \pm 17.33	3.77 \pm 0.94	0.12 \pm 0.07
Heterozygous	6	4.00 \pm 3.90	84.50 \pm 9.65	3.93 \pm 0.31	0.60 \pm 1.27*

Notes: * $P<0.05$ as compared with the datum in dual heterozygous type.

Table 5 Comparison of after-effect duration and blood parameters of patients with different Mediterranean anemia types determined by month ($\bar{x} \pm s$)

Mediterranean Anemia types	Cases	Duration of after-effect (month)	Hb (g/L)	RBC ($\times 10^{12}/L$)	Ret (%)
β -Mediterranean anemia	55	3.80 \pm 1.59	74.38 \pm 20.02	3.63 \pm 0.98	0.12 \pm 0.08
α -Mediterranean anemia	3	4.33 \pm 5.77	84.00 \pm 3.61	4.04 \pm 0.45	1.13 \pm 1.80

DISCUSSION

Clinical symptoms and signs of patients with Mediterranean anemia are mainly characterized by sallow complexion, pale nails, dizziness, palpitation, short breath, fatigue, lassitude in loin and knees, delayed growth and development. Professor WU Zhi-kui believes that its pathogenesis mainly lies in deficiency of the kidney essence and deficiency of essence and blood. In TCM, it is held that the kidney produces marrow and marrow generates blood, and essence and blood share the same source. According to TCM theory, Mediterranean anemia should be treated with the method for nourishing the kidney and replenishing marrow. Therefore, a representative recipe of Chinese drugs for nourishing the kidney and replenishing marrow (capsule and granule for replenishing marrow and generating blood) has been prescribed. The recipe consisting of Shan Zhu Yu (山茱萸 Fructus Corni), He Shou Wu (何首乌 Radix Polygoni Multiflori), Shu Di Huang (熟地黄 Radix Rehmanniae Preparata) and other ingredients can reinforce the kidney, replenish *qi* and nourish blood with the aim at tonifying kidney-*yin* and marrow to strengthen blood-generating source.² Professor WU Zhi-kui and others used 11 batches of capsules and granules for nourishing the kidney and replenishing marrow to treat 156 cases of β -Mediterranean anemia in an area of Guangxi with high incidence of Mediterranean anemia from 1989 to 2005. The treatment achieved affirmative therapeutic effect which can be repeated with the total effective rate at 92.9%.³

In order to further determine the after effect of kidney-nourishing and marrow-replenishing therapy on Mediterranean anemia, the research team has observed the after-effect duration on some patients treated with kidney-nourishing and marrow-

replenishing therapy. Through statistics, 58 patients generally had the after-effect duration for 3-6 months, about 4 months on average. Further analysis has shown that the after-effect duration is not influenced by sex, clinical types, genetic types and Mediterranean anemia types. Clinical data have shown that the average life-span of mature red cells is 120 days in healthy people and 30-40 days in Mediterranean anemia patients. Owing to greatly shortened life-span of red cells, Mediterranean anemia patients are clinically characterized by hemolysis, anemia and other pathological changes. 4 months after drug withdraw, Mediterranean anemia patients treated with kidney-nourishing and marrow-replenishing therapy can still keep hemoglobin concentration and red cell count higher than the level before treatment, indicating that kidney-nourishing and marrow-replenishing therapy can effectively influence hemolysis and anemia of Mediterranean anemia patients. Yet, concrete pathogenesis and functions remain to be further studied.

In general, the following conclusion can be drawn from the observations during follow-up visits. The treatment of Mediterranean anemia with kidney-nourishing and marrow-replenishing therapy can not only achieve good therapeutic effect during treatment but also let the therapeutic effect last for about 4 months after drug withdraw, indicating that kidney-nourishing and marrow-replenishing therapy has good after effect on Mediterranean anemia.

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