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Comparison of quality of life in thalassemia major patients with injectable and oral iron depletion

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Abstract

Background: One of the factors reducing the satisfaction and quality of life in thalassemia is the injection of iron-depleting drugs that always cause complications in these people. But with the advent of oral detoxification drugs, it can be predicted that this problem will be solved to some extent. Given that Sistan province is one of the regions with the highest prevalence of thalassemia in Iran, we aimed to compare the quality of life in major thalassemia patients receiving oral and injectable iron depleting drugs.

Methods: This cross-sectional descriptive-analytic (Prospective) study was performed during a one-year period (2017-2018) in Ali Asghar Hospital of Zahedan University of Medical Sciences. Demographic information of patients was extracted and recorded through history as well as the information in their files. EQ5D questionnaire was used to assess the quality of life. Data were analyzed using SPSS 18 software.

Results: the quality of life score is significantly higher in Patients receiving oral treatment than injecting patients (p= 0.02). The issue is also true in terms of the health degree of the patients in both groups (p=0.03). Furthermore, comparing the quality of life score and health status of patients between the two groups receiving injectable and oral iron deprivation showed that in females, under 15 years of age and the patients with poor acceptance, the degree of health in the group receiving oral decontamination was higher than injectable decontamination.

Conclusion: Quality of life in patients with thalassemia treated with oral iron depletion is higher than patients receiving injectable iron depletion treatment, and in under 15-year-old females and patients with poor acceptance, this difference is significant.

Key Words: Iron depletion, Quality of life, Thalassemia major.

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1- INTRODUCTION

Thalassemia major is today one of the problems of our society and many countries around the world. Due to the disruption in the production of globin chains in the structure of hemoglobin, the red blood cells produced in the bloodstream do not have a normal life and die quickly (1-4).

Thalassemia is found in almost all races, but is most prevalent around the Mediterranean, tropics, and near the equator in Africa and Asia. The thalassemia belt covers the Mediterranean of the Arabian Peninsula and parts of Africa, Turkey, Iran, India, Southeast Asia, especially Thailand, Cambodia and southern China. The prevalence of thalassemia-related genetic disorders in these areas is 2.5 to 15%. (2)

Severe anemia in these patients also impairs the growth, development, and activity of vital organs. Excessive consumption of energy and calories for hematopoiesis leads to weakness and physical analysis and excessive susceptibility to infections. Death due to anemia in the first decade of life is inevitable for the patient if the patient does not start treatment with blood transfusion (5-7).

The most important principle of treatment is regular blood transfusion because anemia causes many complications such as reduced growth, increased bone marrow activity and as a result bone changes, enlarged liver and spleen can cause death. The second principle of treatment of patients is iron therapy. In patients with thalassemia major who do not have adequate iron-depleting treatment, iron accumulation persists, and when about 20 grams of iron is deposited in the body, one can expect severe clinical findings due to increased iron load. The most important side effects of iron overload can be heart disease, liver disease, endocrine diseases, etc. along with the Psychological effects (14).

The quality and longevity of transfusion-dependent thalassemia patients has changed over the last few years, and since the onset of desferrioxamine, thalassemia-related mortality has declined significantly; and so has their quality of life. It easily reaches the third decade and more, which of course is accompanied by a good quality of life, but the complications of this disease are still among the most important issues in these patients. (12-13)

In case of lack of proper treatment and timely blood transfusion, gradually, bone changes due to overactive bone marrow appear in the patient. The size of the head, the bulge of the cheek, the chin, the forehead, the indentation of the nose cause the classic thalassemia face in the patient. Severe growth and developmental disorders, enlarged liver, spleen, heart, severe osteoporosis, and pathological fractures are all complications of inadequate treatment; and if the patient is not treated in time, death occurs in the first decade of life (8-10). The quality and longevity of transfusion-dependent thalassemia patients has changed over the last few years, so that their lifespan easily reaches the third decade or more, which of course is accompanied by a good quality of life, but the complications of this disease are still very important issues in these patients. Therefore, after the treatment of iron depletion, the treatment of various complications has been emphasized and the implementation of the standard and ideal treatment protocol depends on the cooperation of the treating physician and other relevant specialists for the necessary consultations (11).

As mentioned earlier, the most important principle of treatment is regular blood transfusion because anemia causes many complications such as reduced growth, increased bone marrow activity resulting in skeletal changes, enlarged liver and

spleen and can even cause death. Repeated examinations, monthly CBC examination, every 1-3-month ferritin, etc. by a hematologist will be very effective in reducing these risks.

The second principle of treatment for patients is iron depletion treatment. In thalassemia major patients who do not receive iron removal treatment, iron accumulation continues continuously and when about 21 grams of iron is deposited in the body, one can expect severe clinical findings due to increased load. Iron occurs one of the most important complications of iron increase is heart disease, liver disease, endocrine diseases, etc. (11).

Quality of life is a dynamic nature, not a static one in the sense that it is a time-dependent process involving internal and external changes. Quality of life is a subjective assessment and patients themselves are the best judges of their quality of life; but sometimes there are situations that make it difficult for the patient to make judgments in which special caregivers, including physicians and nurses, will be able to make this assessment (24, 25).

Children with thalassemia have different feelings from their peers and negative thoughts about their lives, guilt, increased anxiety and low self-esteem. Some psychological findings, such as physical complaints, physical symptoms, and separation anxiety in children with beta-thalassemia, indicate a persistent emotional burden possibly related to fear of future complications (15). There is an interrelationship between disease and quality of life, especially in patients with chronic diseases involved in various issues at all stages of life, and physical disorders; and the presence of physical symptoms has direct effects on all aspects of quality of life. The primary and important goal of treating these patients is to enhance the quality of life by reducing the effects of the disease, and they should not necessarily have a 14% low quality of life (15). Thalassemia children have a lower quality of life than healthy children, which is mainly due to severe problems related to pain and illness (16). Children and adolescents with thalassemia have the most problems in terms of quality of life, especially in the physical and emotional dimensions (17).

One of the reasons that reduce the satisfaction and quality of life in people with thalassemia is the injection of iron-depleting drugs in these patients, which always causes suffering and pain. However, with the advent of iron-depleting oral drugs, this problem is expected to improve to some extent. Therefore, considering that Sistan province is one of the regions with the highest prevalence of thalassemia, this study was performed to compare the quality of life in thalassemia major patients receiving oral and injectable iron chelator.

2- MATERIALS AND METHODS

2-1. Study design and population

This cross-sectional descriptive analytical study (prospective) was performed during a one-year period (2017-2016) in Ali Asghar Hospital of Zahedan University of Medical Sciences. The study population consisted of patients with thalassemia major aged 8 to 18 years.

2-2. Methods

Demographic information of patients was extracted through history and information in their files and recorded in information forms.

2-3. Measuring tools

The EQ5D questionnaire was used to assess the quality of life, the details of this questionnaire are given in full in the appendix.

2-4. Intervention

The questions were asked face-to-face; but if a person wanted to complete the

questionnaire himself, the questionnaire was delivered to him and then collected. To score the questionnaire, in each dimension, the points of the items were added together and converted to a scale from zero (worst condition) to 100 (best condition).

2-5. Ethical consideration

It should be noted that this study has been approved with the code of 1244 in the ethics committee of Zahedan University of Medical Sciences.

2-6. Inclusion and exclusion criteria

The criterion for their exclusion was patients' dissatisfaction with the continuation of the study.

2-7. Data Analysis

All data were entered into SPSS ver. 18 software for analysis. The variables were matched in groups, so that the number of females and males was equal to the average amount of hemoglobin and the average amount of ferritin in both groups. They were in the same Physical conditions (in terms of cardiac complications, splenectomy, liver, etc.). To analyze the data, descriptive statistics (determination of central indices and dispersion, adjustment of frequency distribution tables) and inferential statistics (Pearson correlation test or its non-parametric equivalent at 95% confidence level) were used. To check the existence of relationships between variables and prepare a comprehensive model, the regression test was used. Data were analyzed using SPSS 18 software.

3- RESULTS

In this study, over 200 patients with thalassemia major received oral iron depletion treatment (100 people) and injection (100 people). The mean age of the patients in each group was 13.01 $\pm$ 4.6 years and 16.31$\pm$ 4.5 years, respectively. In terms of sex distribution, in the group receiving oral iron deodorization treatment, 59% were male and 51% were female, and in the injection receiving group, 63% were male and 37% were female, respectively. There was no statistically significant difference (p=0.56) in the mean scores of life quality between the two groups of participants. The participants' total mean score of life quality equaled 0.84 $\pm$0.14 and the total mean score of patient's health was 72.92 $\pm$15.85 (with a score range of zero to 100). As can be seen in **Table 1**, the quality of life scores of patients receiving oral therapy were significantly higher than those of patients receiving injections. This is also true for the degree of health of patients in both groups.

Table-1: Comparison of quality of life and health status between the two groups of patients receiving oral decontamination or injection

Group	Quality of life score (Mean ± SD)	Degree of Health (Mean ± SD)
Oral iron depletion	0.86 ± 0.14	75.25 ± 15.57
Injectable iron removal	0.82 ± 0.15	70.6 ± 15.86
P-Value*	0.02	0.03

*Independent samples t-test

In the age group less than 15 years, the quality of life and the degree of health of the patients receiving oral treatment were significantly higher than those in the injection group. However, in the case of patients in the age group above 15 years, there was no difference between the life quality score and the health degree of the patients in the two treatment groups. No significant

difference was observed in male patients in terms of quality of life and degree of health between the cases receiving oral and those with injectable treatment (P-values were equal to 0.288 and 0.932, respectively). However, the females' quality of life and health degree were significantly higher in patients receiving oral therapy than those with injectable treatment (P-values were equal to 0.011 and 0.001 respectively). Among the under 15-year-old patients, those receiving oral treatment had significantly higher scores in both life quality and health degree (P-values were 0.024 and 0.01, respectively). However, in patients in the age group of more than 15 years, this difference was not significant (P> 0.05).

Among the patients who had thalassemia complications, there was no significant difference in the quality of life and health status among oral and injectable iron depletion treatments (P> 0.05).

This condition was also true in patients who did not suffer from complications and no statistically significant difference was observed between the study groups (P> 0.05). However, among patients with poor acceptance of the disease, the degree of health expressed by the oral treatment group was significantly higher (P=0.007).

The mean hemoglobin level in patients receiving oral treatment was 9.58 ± 0.64 g / dl, which was significantly different with that of patients receiving injectable treatment (9.35±0.65, P=0.013). Patients undergoing oral treatment with hemoglobin above 9 had significant higher scores in life quality than the others. However, at the level of hemoglobin, less than 9, significant differences in quality of life and health were not observed between the study groups.

The mean level of ferritin in patients receiving oral decontamination treatment was equal to 2823.27 ± 1964.19 ng / dl and in patients in the injection group was 5875.8 ± 3051.4, which were significantly different (P<0.001). Patients receiving oral therapy with a ferritin level higher than 3000 ng / ml reported a significantly higher degree of health. However, the life quality mean score of these patients was not significantly higher than the others. There was no significant difference in quality of life and health among patients with ferritin less than 3000 ng / ml.

Table 2 shows the comparison of quality of life score and health status of patients between the two groups receiving injectable and oral iron deprivation according to the study variables.

Table 3 shows the frequency of complications of thalassemia in the studied groups. As can be seen in this table, the incidence of complications such as hypogonadism and heart disease is more in patients receiving high doses through injections.

4- DISCUSSION

The present study aimed to compare the quality of life in patients with thalassemia major under treatments of oral and intravenous iron depletion. 200 patients in two groups of 100 people were included in either oral or injectable iron chelator groups. Results showed that the mean hemoglobin levels in patients receiving oral treatment is significantly higher than injection therapy (P-value=0.013) but ferritin level was significantly higher in IV group of patients receiving oral therapy (p<0.001). Quality of life score was significantly higher in the patients receiving the IV treatment, which was also true for the health degree of the patients in the two groups (P-value equal to 0.02 and 0.03, respectively). 24 Patients in the oral treatment group and 70 patients (70%) in the injection group had complications, which was a significant difference (p <0.001).

Table-2: Comparison of quality of life and health between two groups of patients receiving oral decontamination or injection

Variable	Variable mode	Group	Quality of life score (Mean ± SD)	Degree of Health (Mean ± SD)
Age	Age<15	Oral iron depletion	0.87 ± 0.13	75.34 ± 15.14
		Injectable iron removal	0.81 ± 0.14	68.33 ± 14.67
		P-Value	0.032	0.013
	Age>15	Oral iron depletion	0.85 ± 0.15	75.00 ± 16.98
		Injectable iron removal	0.82 ± 0.15	72.69 ± 16.75
		P-Value	0.387	0.565
Gender	Male	Oral iron depletion	0.87 ± 0.14	72.37 ± 16.30
		Injectable iron removal	0.85 ± 0.13	72.61 ± 15.42
		P-Value	0.288	0.932
	Female	Oral iron depletion	0.85 ± 0.13	79.39 ± 13.61
		Injectable iron removal	0.76 ± 0.16	67.16 ± 16.22
		P-Value	0.011	0.001
Duration of Disease	Year<15	Oral iron depletion	0.87 ± 0.13	75.25 ± 15.72
		Injectable iron removal	0.81 ± 0.14	68.18 ± 14.82
		P-Value	0.024	0.01
	Year>15	Oral iron depletion	0.85 ± 0.15	75.21 ± 15.40
		Injectable iron removal	0.82 ± 0.16	73.55 ± 16.74
		P-Value	0.452	0.692
Complication	Yes	Oral iron depletion	0.88 ± 0.15	71.66 ± 17.79
		Injectable iron removal	0.81 ± 0.16	70.42 ± 17.52
		P-Value	0.068	0.76
	No	Oral iron depletion	0.86 ± 0.13	76.38 ± 14.75
		Injectable iron removal	0.84 ± 0.12	71.00 ± 11.32
		P-Value	0.43	0.07
Acceptance of treatment	Good	Oral iron depletion	0.87 ± 0.13	75.30 ± 15.80
		Injectable iron removal	0.84 ± 0.15	75.00 ± 15.72
		P-Value	0.184	0.915
	Bad	Oral iron depletion	0.85 ± 0.15	75.14 ± 16.71
		Injectable iron removal	0.79 ± 0.14	65.43 ± 14.56
		P-Value	0.096	0.007
Hb Level	<9 g/dl	Oral iron depletion	0.83 ± 0.15	75.38 ± 19.02
		Injectable iron removal	0.81 ± 0.17	68.71 ± 16.59
		P-Value	0.512	0.15
	>9 g/dl	Oral iron depletion	0.87 ± 0.13	75.20 ± 14.32
		Injectable iron removal	0.82 ± 0.13	71.61 ± 15.48
		P-Value	0.022	0.158
Ferritin Level	<3000Ng/ml	Oral iron depletion	0.87 ± 0.13	75.22 ± 15.38
		Injectable iron removal	0.91 ±0.11	78.33 ± 16.08
		P-Value	0.265	0.453
	>3000Ng/ml	Oral iron depletion	0.85 ± 0.14	75.30 ± 16.90
		Injectable iron removal	0.79 ±0.15	68.90 ± 15.39
		P-Value	0.085	0.049

*Independent samples t-test

Table-3: Frequency of thalassemia complications in the studied groups (Chi-square test)

Complication		Group		Sum	P-Value
		Oral iron depletion	Injectable iron removal		
Hypogonadism	Yes	14 (35.0%)	26 (65%)	40 (100%)	0.034*
	No	86 (53.8%)	74 (46.3%)	160 (100%)	
Cardiac	Yes	13 (20.6%)	50 (79.4%)	63 (100%)	<0.001*
	No	87 (63.5%)	50 (36.5%)	137 (100%)	
Diabetes	Yes	0 (0%)	12 (100%)	12 (100%)	**
	No	100 (53.2%)	88 (46.8%)	188 (100%)	
Thyroid dis.	Yes	1 (16.7%)	5 (83.35%)	6 (100%)	**
	No	99 (51%)	95 (49%)	194 (100%)	
Liver dis.	Yes	0 (0%)	7 (100%)	7 (100%)	**
	No	100 (51.8%)	93 (48.2%)	93 (100%)	
Splenectomy	Yes	1 (50%)	1 (50%)	2 (100%)	**
	No	99 (50%)	99 (50%)	198 (100%)	

* Chi-square test

** P-Value cannot be calculated due to lack of values

In a study by Shyargar et al. evaluating the quality of care and life quality of patients with thalassemia who had referred to thalassemia Bu Ali center in 2013, it was shown that the average age at diagnosis was 7.5 months. No significant relationship was found between age (P=0.246), gender (P-value= 0.259), place of residence (P-value = 0.753), type of treatment received (P-value = 0.733), and the patients' quality of life (18). The results of this study are not consistent with those of ours, because our findings indicate a higher quality of life in patients under the age of 15 receiving oral decontamination treatment. In this regard, it can be stated that by the increase in age, and in disease complications, the life quality of patients is affected for a long time. At the same time, the development of neurological disorders such as depression in patients with chronic diseases is not unexpected, which in turn will affect their quality of life.

In a study conducted by Najafi et al. to evaluate the quality of life of school-age children referred to the Center for Special Diseases in Kerman in 2010, it was found that the type of treatment in patients has no effect on patients' quality of life (19). This conclusion is not in line with the findings of the present study. The present study reports a higher quality of life and health in patients treated with oral iron deprivation.

In 2008, Negin et al. studied the health-related quality of life in patients with thalassemia major. In this study, it was found that the type of treatment did not have a significant effect on the quality of life score (20). Another study by Porter et al., in 2012 found that taking oral iron-depleting drugs in people with thalassemia increased their quality of life (21). An article by Ellis, based on a 2006 study in Boston, England, found that oral iron-depleting drugs had few side effects. About 15% of the patients had gastrointestinal symptoms and 11% of patients had skin rashes (22). In 2009, a study by Cappellini and Tahir Ali in Milan, Italy, found that oral iron-depleting drugs were effective in increasing iron load in adults and young children (23).

Clinical research has confirmed the effectiveness and therapeutic efficacy of oral iron-depleting drugs over a period of 4.5 years in patients with various levels of anemia, including thalassemia,

myelodysplastic syndrome, sickle cell disease, aplastic anemia, and other rare anemias. In addition to reducing key indicators of total body iron levels (serum ferritin, liver iron concentration and toxic plasma unstable iron), oral iron-depleting drugs are able to remove the accumulated iron in the heart and prevent the re-accumulation of iron in heart. Findings show that oral iron depletion drugs are a suitable treatment choice for patients with chronic conditions who need iron depletion treatment; and improve their quality of life (23).

5- LIMITATIONS OF THE STUDY

Patients' dissatisfaction with participating in the study.

6- CONCLUSION

Quality of life in patients with thalassemia treated with oral iron depletion is higher than patients receiving injectable iron depletion treatment.

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