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Assessment of Effectiveness and Side Effects of Osveral Chelator Drug in Major Thalassemia Patients with Iron Overload

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ABSTRACT

Major thalassemia is a genetic anemia that requires patients to have frequentblood transfusions. This increased iron deposition in tissues of liver, heart and other organs and it can damage to them. To reduce iron deposition in tissues, several chelator drugs are taken to reduce iron. Osveral, a chelator drug is one of these drugs that in the present study its efficacy and side effects has been studied.In a clinical trial before - after procedure, 80 patients with major thalassemia(38 males and 42 females) aged 3 to 31 years were studied. The duration of trial was one year. The efficacy was determined by comparison of ferritin level before and after treatment and duration of trial. For statistical analysis of data used T- testfor dependent groups (Paired t-test) and repeated analysis of variance (Repeatedmeasure).Serum ferritin changed from first month to last month of trial, which decreased significantly ($t=4.96$, $P<0.05$). Serum ferritin decreased from 2094.4 ± 796.96 significantly decreased to 1578.73 ± 784.6. ($t=4.96$, $P<0.05$). In addition, serum ferritin changes during study. Repeated analysis of variance showed a significant reduction in ferritin levels atduration of study ($F_{1, 79}=22.13$, $P<0.001$).Diagram of changes ofserum ferritin levels showsthat globally Serum ferritin levels decreased but small increase during the third and fourth months was happened.Findings indicate that osveral as a chelator drug decrease serum ferritin levels in majorthalassemia patients.

Keywords: ferritin, major thalassemia, Osveralchelator drug**.**

1. INTRODUCTION

Thalassemia is an inherited autosomal recessive blood disease which is passed from parents to children through genes. A lot of children all over the world suffer this disease especially the ones in regions called 'Thalassemia Belt' with 2.5-15 suffered in thousands. Normal hemoglobin, also called hemoglobin A, has four protein chains—two alpha globin and two beta globin. The two major types of thalassemia, alpha and beta, are named after defects in these protein chains.

Four genes (two from each parent) are needed to make enough alpha globin protein chains. Alpha thalassemia trait occurs if one or two of the four genes are missing. If more than two genes are missing, moderate to severe anemia occurs which leads to the growth problem and also death of red hemoglobin.

One of the major consequences of thalassemia disease and treatment is iron gathering in the body which happen in major thalassemia patients because of blood injection but it happens in intermedia thalassemia patients because of increasing iron suction through bowel. Hemosiderin caused by blood transfusions to patients is the major reason of patients 'morbidity and mortality

So keeping iron level balanced, increases survival of these patients. A study showed that ferritin levels less than 2500 mg / ml increases the chance of living free of heart disease to 91 percent [1]. Considering the existing problems caused by de-Fe injectable medications including problems related to non-compliance resulted by the subcutaneous or intravenous injection nature and short half-life deferoxamine treatment during the past four decades the scientists focused on the discovery of oral de-Fe medications [2].One of these medications is de-Fe osveral (deferasirox)that in this study its efficacy and side effects have been researched. This is an Iranian produced medication which is the same as its similar foreign one and is orally taken.

MATERIALS AND METHODS

This study was performed in clinical trial form and through before and after method. The study population included all patients with major thalassemia, recipient of osveral medication. Inclusion criteria included patients aged 3-31 years that osverall was given as an optional medication- treatment. Exclusion criteria included those who left the test before one year, had kidney disease and did not monthly do the test recommended by researchers.

Thalassemia patients studied were referred to Aboureihan thalassemia center in Bandar Abbas. They were visited in this center in 2008-2009. After obtaining approval from the Ethics Committee and Deputy University Research, the study sample included 103 patients with thalassemia major were selected by random sampling

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method. The patients' age range was 3 to 31 years old with 10.3 mean and a standard deviation of 1.6. It should be noted that 23 of these patients were excluded because of not regularly using the medication and not on time testing. The final analysis was conducted on 80 patients. This study was conducted during a year (2008-2009). The data of 80 patients (38 male: %47.5 and 42 female: %52.5) were collected and analyzed in the study. Other clinical and demographic information of these patients will be presented in Findings part.

Regularly osveral oral medication dose to 20mg per kg body weight was started for participant patients. It is noticeable that due to not decreasing ferritin level in some patients, their medication dose was increased to 40 mg per kg of their body weight and monthly for one year, kidney tests (Bun, CR), liver tests (SGOT, SGPT, Bili) and blood tests (Plt, WBC, PMN) were performed for these participants patients.

The resulted data was analyzed by statistic software SPSS and by computing the mean descriptive measures and standard deviation, paired t-test and repeated measure analyze were used to determine the efficacy of medication taking before and after the study and during test period.

2. RESULTS

As notified in the previous section, 103 patients with thalassemia major started to be treated with the osveral and the data of 80 patients, who completed the study period, was analyzed and studied. Descriptive measures of variables; weight, age and ferritin values in twelve months of the study period are presented in the Table 1.

Table 1. Descriptive measures of variances; weight, age and ferritin in twelve months of the study

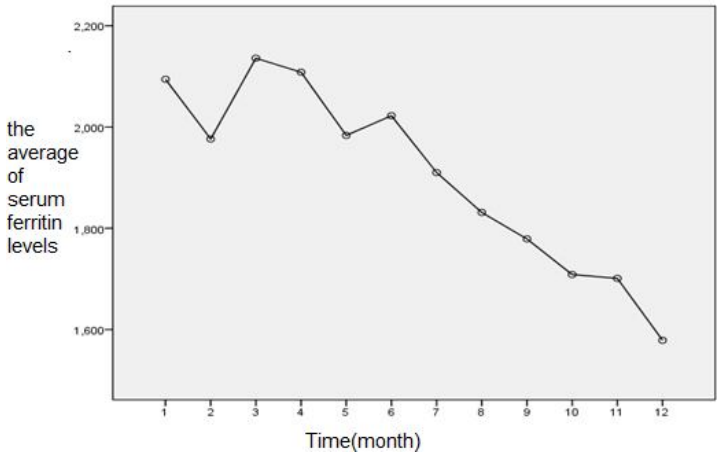
Variables	Minimum	Maximum	Average	Standard Deviation
Age	3	31	10.3	6.1
Weight	5	47	23.92	11.28
First month- Ferritin	897	4200	2094.4	796.96
Second month- Ferritin	864	4000	1976.64	776.98
Third month- Ferritin	820	6000	2136.03	1116.74
Fourth month- Ferritin	639	5400	2108.45	1095.92
Fifth month- Ferritin	700	3950	1983.5	842.87
Sixth month- Ferritin	280	4376	2022.4	917.42
Seventh month- Ferritin	734	4000	1910.13	796.68
Eighth month- Ferritin	560	3823	1831.33	813.89
Ninth month- Ferritin	510	4000	1778.9	781.46
Tenth month- Ferritin	700	3700	1708.58	804.62
Eleventh month- Ferritin	670	3450	1700.98	753.82
Twelfth month- Ferritin	630	4000	1578.73	784.6

To research about efficacy of osveral in reducing serum ferritin levels of studied patients, two statistical analyses were performed. The first analysis compared patients' ferritin mean of the first and twelfth month by paired t-test.

Statistical test results showed that serum ferritin levels from 2094.4 ± 796.96 significantly decreased to 1578.73 ± 784.6. ($t=4.96$, $P<0.05$).

A second analysis using repeated measure examined significant changes in serum ferritin levels during the twelve months test period. The statistical parameters obtained showed a significant ferritin decrease during the period ($F_{1, 79}=22.13$, $P<0.001$). Diagram of changes in serum ferritin (diagram 1), shows a general pattern of continuous decline in ferritin levels. Although a slight increase is observed during the third and fourth months.

Diagram 1. Changes in serum ferritin during the twelve month test period



3.1. Side effects

The other finding of this study indicates the complications arising from the osveral use in some patients. The most common side effects include increased creatinine, elevated liver enzymes, low blood platelets and nausea and vomiting. Frequency and percentage of each of the above effects are presented in table two.

Table 2. Frequency and percentage of side effects in some studied patients taking osveral

Complications	Frequency	percentage
Increased creatinine	4	5
Increased liver enzymes	3	3.75
Low blood platelet	1	1.25
Nausea and vomiting	1	1.25
Total	9	11.25

3. CONCLUSION

The findings of this study showed that in general, medication treatment with de-Fe medication, osveral, led to a significant decrease in serum ferritin levels of studied patients. The efficacy of the mentioned medication and the similar medication in different studies has been reported at an appropriate level [4, 5, and 6]. The results of these studies suggest an appropriate medication tolerated with acceptable safety in child and adult patients. The side effects of this medication have been recorded the same as its foreign similar one [7, 8]. Regarding the studies, the most common side effects of this medication were reported intestinal side effects - including the stomach, diarrhea, vomiting, abdominal pain and nausea [9, 10, 11, 12, 13, and 14]. Regarding the findings of this study and the benefits of medication osveral comparing with its similar foreign one produced in Iran, its use as an effective, available and inexpensive de-Fe medication is recommended.

The findings of this study faced some limitations so we should cautiously generalize its results. The reported side effects of medication should be considered in treatment situations and prevention strategies to avoid complications should be mentioned as well.Some measures including age, environmental and geographical characteristics of the patients are also some other limitations that should be regarded in generalization of the results.

It is suggested that in future studies, medication efficacy and side effects of osveral comparing with existing medications, especially the foreign similar ones to be simultaneously studied on thalassemia major patients. Repeating the study in other clinical situations and medical centers can increase the generalization reliability of the findings obtained in this study.

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