Original article:

Renal function in Thalassemia major patients who treated by Desferal

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Abstract

Background and purpose: β-thalassemia is the most common inherited hemoglobinopathy in all over the world. Iron over load will be appearing in kidney following blood transfusion. Desferal is one of iron chelator that can be ended renal complication. The aim of this study is evaluation the renal function in β- Thalassemia patients who were treated by Desferal. ***Materials and methods:*** in this descriptive and analytic study 40 thalassemia patients who were treated by Desferal and 40 non Thalassemia subjects enrolled in this study randomly. For evaluation the renal function in these groups, we measured the Cr, BUN, K, Na, Uric acid, β-2 globin, Ca, Mg, P and Urea of blood and Na, K, Cr, protein and volume of urine 24 hours. We compared these variables between two groups. Also descriptive and analytic analyses were used, the significant level in this study was $p \leq 0.05$. ***Results***: comparing the renal function between two groups show that; the level of Na, Ca, K and β-2 Globin in serum and Cr, protein and urine volume in 24 hours had significant difference. ***Conclusion:*** renal dysfunction such as; glomerular and tubular dysfunction and reduced filtration capacity are common in β-thalassemia patients.

Keywords: transfusion dependent Thalassemia major, Desferal, renal function.

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Introduction:

Beta Thalassemia is the most common inherited hemoglobinopathy in all over the world. The endemic areas of this anemia are south of Europe (Italy, Greece, Cyprus), Arabia, Africa, Turkish, Iran, India, Thailand, China. This autosomal recessive disease can ended to reduce or restriction production of β strand of hemoglobin and induce severe anemia in patients with this gene mutation.In 1925, this disease known as a syndrome that include; splenomegaly, bone deformity and severe anemia. Also, it is a serious problem in medicine and society[1-2]. The major treatment of this patients is prolonged blood transfusion[3] .Following blood transfusion, iron can replace in different organs such as; heart, liver, endocrine, and kidney[1]. Iron over load can be ended to this organ dysfunction and mortality[4]. The use of iron chelator in thalassemia patients is necessary and it can be ended to better quality life and survival[5-6-7].

Desferal (DFO) is one of injection iron chelator, that used this 4 decade. Of course oral iron chelator drugs such as; Deferopiron and Deferasirox are common use[6]. In 1965 DFO introduce as an iron chelator and use in thalassemia patient. This drug cannot absorb from GI tract and have short half-life. Immediately after stop the injection of DFO the iron chelator activity will stop. Also, the effectiveness of this drug will accelerate along prolonged injection. DFO should be administrate after 10-20 blood transfusion or in patients with ferritin higher than 1000 mg. The effective dose of DFO is 30-40 mg/kg/day in 5 days a week, the duration of injection is 8-12 hours sub cutaneous via electronic pump. The side effects of this drug are; inflammation of injection site, pulmonary infiltration, night blindness, color blindness, hearing loss[2].

Renal dysfunction in thalassemia patients will be accrue following: 1) side effect of DFO, 2) iron over load in kidney, 3) lipid peroxidation , stress oxidative, release free radicals and thrombosis[8]. In 1975 the

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first case of kidney disability in concentrated urine was reported in thalassemia patients. Since then some studies reported regarding poor performance of proximal portion of kidney, proteinuria, aminoaciduria, low smolarity of urine, acceleration of N-acetyle beta D glucosamidase (NAG) and β micro globin in thalassemia patients who treated with DFO[9].

B_2 micro globin is an unglycosylated polypeptide with 11800 molecular weight, it presented on nucleate cells and neutrophil granules. It metabolized and excretion from kidney. The normal level of it in serum is 2 µg/lit [10]. Measurement of B_2 micro globin can evaluate the injury of proximal tubules of kidney (11). If the level of B_2 micro globin accelerate, it can predict oxidative stress and iron overload in kidney[9], and it is as a sensitive marker for evaluation of the capacity of kidney filtration[12].

It seems that, in thalassemia patients with increasing duration of disease, the side effect of this disease such as kidney complication will increase[4], of course researcher are not agree regarding this theory[4]. So far, many studies were done regarding effect and side effect of DFO, but research regarding kidney side effect is limited and we have limited data regarding kidney complication in thalassemia patients who treated with DFO and the cause of tubular kidney dysfunction is unknown. So this study was done with this purpose; evaluation of kidney function in thalassemia patients who treated by DFO.

Materials and methods:

This study is descriptive and analytic study. Research community in this study was patients of thalassemia research center of Mazandaran University of Medical Science. The samples were selected within thalassemia major patients who were treated by Desferal. Sampling method was simple random sampling. The sample size was 40 patients according power 80% and CI (confidence interval) 45%. Fourthly thalassemia major patients who were treated by Desferal entered in this study, also 40 healthy person (non-thalassemia major patients) consider as control group. For evaluation the renal function the variables such as : Cr, BUN, K, Na, Ca, Mg, P, Urea, β- globin in serum and protein, Na, K, Cr and volume of urine 24 hours were measured in case and control groups. The data were entered in SPSS version 16, also we used descriptive and analytic for analysis. For comparing quantitative variables in both groups we used independent T test. The significant level in this study was $p \leq 0.05$.

Results:

Among 40 thalassemia major patients 19(53.4%) and 21(46.4%) were female and male respectively. Duration use of Desferal was 9.3±5.06 years, duration of transfusion was 10.7±5.38 years. Table 1 shows the age and level of ferritin in both groups. According this table, this two groups were matched according age (p=0.05), but level of ferritin were different between them (p=0.000).

Table 2 shows blood markers of renal function in samples of study. According this table level of K, Na, Ca and β-2 globin had significant difference in both groups.

Table 3 shows comparing the level of Na, K, Cr, protein and volume of urine 24 hours in both groups. According this table just the levels of Cr, protein and volume urine 24 hours were had significant difference.

Discussion:

A few study was done regarding renal dysfunction in thalassemia major patients who treated by Desferal. This study designed for evaluation renal function in thalassemia major patients following chorionic anemia, iron over load and dose- related toxicity of Desferal. Fourthy thalassemia major patients who were under treated by regular transfusion and Desferal entered in our study. Tubular and glomerular renal function compared in both groups. Determination of proteinuria assayed glomerular renal function; and determination proteinuria in urine 24 hours and serum level of β- 2 globin assayed tubular renal function. Also, the level of β-2 globin show the kidney filtration capacity. Ferritin level of thalassemia major patients was 2392.09±1839.15 and it couldn't predict the rate of renal damage. On the other hand ferritin level is not important factor for diagnose of hemosiderosis in thalassemia major patients, but we can believe that Desferal hadn't effective role in excretion of kidney iron overload. The result of this study show that the serum level of Na, K, Ca and β-2 globin; also Cr, protein and volume urine 24 hours were different in both groups. According this result we can believe that; thalassemia major patients who treated by Desferal have glomerular, tubular renal dysfunction and reduced kidney filtration capacity. A study was done by Ahmad et al (2010), demonstrated that thalassemia major patients who treated by Desferal

had glomerular and tubular renal dysfunction[13]. The result of this study was similar to our results. The result of Jalaly s study demonstrated that renal dysfunction in thalassemia major patients can be increase by acceleration of age, increased frequency of blood transfusion and hypercalciuria[14]. Of course the nephrotoxicity of Desferal is dose related[6]. In our study the level of Cr had not significant difference in both groups. Although the serum level of Cr is not trustworthy marker of renal function, because it is under the influence of factors such as; muscle mass, protein intake, inflammatory disease and liver disorder[6].

The major cause of renal dysfunction in thalassemia major patients is unknown, probably it is malty factorial disorder. Of course some causes such as; chorionic hypoxia following anemia, hemosidrosis and cellular damages following lipid peroxidation are possible causes[6].the limitation of this study was no measure of some markers such as; N acethyl β di glocoseaminidse, hematuria, GFR, C Cystatin and calciuria. We suggest the measurement of these markers in future studies.

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Tables

Table 1. Mean and standard deviation of age and level of ferritin in both groups.

variables	Case group	Control group	P value
Age	27.5±7.08	25.4±5.4	0.05
Ferritin	2392.09±1839.15	80.15±32.58	0.000

Table 2. The level of blood markers of renal function in both groups.

P value	Control group	Case group	variables
0.15	20.9±0.76	20.7±1.74	BUN
1.77	0.77±0.04	0.67±0.03	Cr
0.05	4.99±0.21	5.08±0.27	Uric acide
0.007	4.13±0.09	4.39±0.06	K
0.01	139±0.52	138.99±0.37	Na
0.000	1.8±0.55	2.57±0.21	-2 globinβ
0.4	23.09±1.31	28.59±1.18	Urea
0.3	3.29±0.1	4.14±0.1	P
0.2	2.04±0.05	1.92±0.04	Mg
0.000	4.2±0.16	9.28±0.07	Ca

Table 3. Comparing variables of urine 24 hours in both groups.

P value	**Control group**	**Case group**	**variables**
0.04	1070±59	757.85±54.85	Cr urine 24 hours
0.4	75.78±4.1	53.4±5.1	K urine 24 hours
0.29	139.1±8.5	138.13±8.04	Na urine 24 hours
0.000	81.19±4.14	97.49±11.42	Protein urine 24 hours
0.007	1445.12±70.44	1182.97±53.42	Volume urine 24 hours

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