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Research Article

Efficiency and Safety of Desferioxamine Chelation Therapy in Paediatric Patients with Transfusion-Dependent Anaemia: Experience of two Centers from Sudan

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ABSTRACT

***Background*:** Repeated blood transfusion is the main therapeutic option for transfusion-dependent anaemias with consequent iron overload and organ damage .Therefore iron chelating agents are important protective measures for these patients. The aim of this study was to investigate the efficiency and safety of Desferroxamine in paediatrics population subjected to iron overload as a consequence of repeated transfusion in a group of Sudanese children

***Subjects & Methods*:** This was a descriptive cross-sectional hospital based study. Conducted in two main paediatric reference hospitals in, Sudan. Within the period between November 2017 and April 2018 (6 months duration). The two centres were JaafarI bn- Oaf hospital and Albulk hospital. The study population included all patients of transfusion dependent anaemia who received desferrioxamine within the study period. Hundred patients were enrolled in the study. The study variables were demographic data, number of blood transfusions , serum ferritin pre and post blood transfusion and treatment of desferrioxamin

***Results*:** Sixty percent (60%) of the studied cases were males and 40% were females ,46% were thalassemic, 46% were sicklers, 5% aplastic anemia and 3% with red cell aplasia .The mean serum ferritin level before starting desferoxamine was 2.14 and after dessferoxamine was 2.48, P –value was highly significant. The most common side effect encountered was skin rash (36%)

***Conclusion*:** This study revealed some features of safety and efficiency of desferoxamine therapy in Sudanese paediatrics population affected by transfusion-dependent anemia. More studies are needed to describe this important health problem.

Introduction

Causes of transfusion dependent Anemias (TDAs) in paediatric population include thalassaemia , sickle cell anemia , aplastic anaemia and pure red cell aplasia (1). These entities pose global childcare challenges ,notably for thalassemia and sickle cell anemias , as both account for 3.4% of children death below the age of 5 years ((2) Repeated RBCs transfusion is the cornerstone for the management of TDAs , with the inevitable consequence of

iron over- load and the pathologic effect of iron deposition in different body organs inducing cardiac, hepatic damage and endocrinoapthies (1) . Therefore iron chelation therapy (ICT) is an essential component in the management of TDAs (2).

Most international guidelines on the management of TDAs indicated initiation of ICT after the transfusion of 10-20 Units of RBCs or when serum ferritin is greater than 1.000ng/ml (1)

Serum ferritin (SF) has been reported as the most important parameter in the diagnosis and follow-up of both iron deficiency and iron-overload disorders (3).

Serum ferritin measurement is well documented as a simple widely used index for assessing body iron status (4).

The overall goal for (ICT) in (TDAs) patients is to decrease the level of serum ferritin in order to protect against iron deposition induced organ damage (3).

The efficiency and safety of ICT in paediatric transfusion- dependent anemias (TDAs) has been well documented (5-9).

The aim of this study was to evaluate the efficiency and safety of desferroxamine therapy in Sudanese paediatric patients with TDAs and to explore the possible complications of iron overload.

Subjects and Methods

This was a descriptive cross-sectional hospital based study Conducted in two main paediatric reference hospitals in Sudan within the period between November 2017 and April 2018. The two centers were JaafarI bn- Oaf hospital and Albulk hospital.

The study population included all patients of transfusion dependent anaemia who received desferrioxamine within the study period and who were under the age 18 years old with complete medical records and whose guardians agreed to participate in the study .

One hundred patients were enrolled in the study using total coverage according to the inclusion criteria. The study variables included demographic data, number of blood transfusions , serum ferritin pre and post blood transfusion .

Statistical analysis was done by SPSS version 22. Descriptive data were displayed in tables . T- test, chi square test were used to compare between variables of the study. The P-value of 0.5 % or less is used to reject the null hypothesis .

Ethical approval was obtained from the ethical Committee board of the faculty of medicine ,Omdurman Islamic university Sudan . Written consent was obtained from the patients guardians.

Results

Twenty-eight 28% of the studied population were of 1-5 years old .42% between 6-10 and 30% between 11-18 years . 60% were males and 40% were females.

Forty –six 46% of the cases were thalassemics , 46% sticklers . Five (5%) were diagnosed with aplastic anaemia and 3% with red cell aplasia . Fifty-three(53%) of the patients were diagnosed before the age of one year ,44% diagnosed between 1-5 years old .3% diagnosed at 6-10 years old . Frequency of blood transfusion was shown in table (1)

Table 1: frequency of Blood transfusion in the population studied

Regular simple blood transfusion	69	69%
Regular exchange blood transfusion	0	0%
Both(regular simple and exchange)	19	19%
Not regular blood transfusion	12	12%
Total	**100**	**100%**

Distribution of patients according to serum ferritin before and after starting desferrioxamine therapy is show in tables (2&3)

Table 2: Serum ferritin levels before desferrioxamine chelation therapy

Sf level (ng/dl	No of cases	Percent
1000-2000	46%	46%
2000-3000	35	35%
3000-4000	6	6%
4000-5000	5	5%
5000- 6000	8	8%
Total	100	%100

Table 3: serum ferritin levels after desferrioxamine chelation therapy:

SF level (ng/dl)	No of cases	Percent
<500	9	9%
500- 1000	63	63%
1000-2000	15	15%
2000-3000	2	8%
3000-4000	8	8%
4000-5000	1	1%
5000-6000	2	2%
Total	100	100%

Fifty –nine (59%) of the cases started desferrioxamine therapy after the transfusion of 11-20 units of blood , 30% after 21-30 units ,10% of the studied cases started chelating therapy after being transfused 30 units ,less than 1% started desferioxamine after transfusion of less than 10 units of blood. Ninety-two(92%) of patients received 5 doses of desferrioxamine and 8% received less than 5doses . Ninety-one (91%) of the studied patients didn't report developing any side effects known to be related to desferioxamine therapy . Only 9% developed side effects shown in table (4).

Table 4:

Pattern of side effect due to desferrioxame chelation		
Skin rash	36	36%
GIT upset	14	14%
Red urine	14	14%
Tremor	22	22%
Injection site reaction	7	7%
Transient blurred vision	7	7%
Total	**100**	**100**

Eighty-six (86%) of the children care- givers reported awareness about the complications of iron overload, while 14% showed no awareness.

The mean difference of serum ferritin level before starting desferoxamine was 2.14 and after dessferoxamine became 2.48, P – value was highly significant, Shown in table (5).

Table 5: The mean difference of serum ferritin before and after starting desferrioxamine therapy

	Test Value = 0					
	t	df	Sig. 2 tailed	Mean differences	Confidence 95% Interval of the Difference	
					Lower	Upper
serum ferritin level before starting desferrioxame	14.289	99	0.000	2.14000	1.8428	2.4372
serum ferritin level after receiving desferrioxame	20.355	99	0.000	2.48000	2.2382	2.7218
P value 0.000 (highly significant)						

The relationship between serum ferritin before starting desferoxamine and age is shown in Table (6), p-value was significant.

Discussion

To the best of our knowledge, this is the first study to be conducted in Sudanese paediatrics population about the efficiency and safety of desferroxamine chelation therapy in patients with transfusion-dependent anemia.

We observed a significant difference of p value of 0.000 and 0.0347 respectively after and before starting chelation therapy.

Furthermore this study showed that only 9%of the studied group developed side effects of desferrioxamine, which were transient (skin rash, tremor, reddish urine color, gastrointestinal upset, and transient blurred vision)

These results were in agreement with Hassan MA et al, who evaluated iron chelation immunotherapy in transfusion-dependent beta-thalassemia major patients: a comparative study of deferasirox and deferoxamine (7&8).

As compared with a study reported by DeBaun et al which evaluated children with sickle cell anemia who receive regular blood transfusions (transfusion group) and standard care (observation group), and this showed the incidence of the primary end point in the transfusion and observation groups to be 2.0 and 4.8 events, respectively , per 100 years at risk, corresponding to an incidence rate ratio of 0.41 (95% confidence interval, 0.12 to 0.99; P=0.04),so regular blood transfusion therapy significantly reduced the incidence of recurrence of cerebral infarct in children with sickle cell anemia (10).

The study showed only 9%of patients developed side effects of desferrioxamine which were transient (skin rash, tremor, reddish urine color, gastrointestinal upset , and transient blurred vision) and most of the patients didn't report any side effects after receiving desferrioxamine, this indicate safety of the treatment, as compared with a study conducted by Sridharan K to compare the efficacy and safety of desferrioxamine (DFO), deferiprone (DFP), deferasirox (DFX) and Silymarin in patients with either thalassemia or sickle cell disorder through network meta-analysis and showed DFX/DFO was associated with better serum ferrintin levels compared to DFO, DFX, DFO/Silymarin and DFP/DFO. (11-12). as limitations to this study, study sample was small and the follow up duration was short.

Conclusion

This study revealed some features of safety and efficiency of desferoxamine therapy in Sudanese paediatrics population affected by transfusion-dependent anemias. Importantly, more studies including bigger sample reflecting the diversity of Sudanese population and investigating other aspects of the disease (e,g imaging, tissue biopsy and detailed blood indices) is needed to give a more detailed prospect about transfusion –dependent anaemia in Sudanese paediatrics patients.

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Conflicts of interests

The authors declare that there are no conflicts of interest.

References

[1] Saliba AN, Harb AR, Taher AT. Iron chelation therapy in transfusion-dependent thalassemia patients: current strategies and future directions. J Blood Med. 2015 Jun 17;6:197-209.

[2] Botzenhardt S, Li N, Chan EW, Sing CW, Wong IC, Neubert A. Safety profiles of iron chelators in young patients with haemoglobinopathies. Eur J Haematol. 2017 Mar;98(3):198-217.

[3] Nielsen P, Günther U, Dürken M, Fischer R, Düllmann J. Serum ferritin iron in iron overload and liver damage: correlation to body iron stores and diagnostic relevance. J Lab Clin Med. 2000 May;135(5):413-8.

[4] Garcia-Casal MN, Peña-Rosas JP, Pasricha SR. Rethinking ferritin cutoffs for iron deficiency and overload. Lancet Haematol. 2014 Dec;1(3):e92-4.

[5] Botzenhardt S, Li N, Chan EW, Sing CW, Wong IC, Neubert A. Safety profiles of iron chelators in young patients with haemoglobinopathies. Eur J Haematol. 2017 Mar;98(3):198-217.

[6] Perifanis V, Christoforidis A, Vlachaki E, Tsatra I, Spanos G, Athanassiou-Metaxa M. comparison of effects of different long-term iron-chelation regimens on myocardial and hepatic iron concentrations assessed with T2* magnetic resonance imaging in patients with beta-thalassemia major. Int J Hematol. 2007 Dec;86(5):385-9.

[7] Meloni A, Pistoia L, Renne S, Restaino G, A. Vallone, A. Olivi, A. Barone, M. Allo', D. Maddaloni D, De Bari, C, Positano V, Pepe A.4094 MRI prospective survey on heart and liver iron and cardiac function in thalassemia major patients treated with Deferasirox versus Deferiprone and Desferrioxamine in monotherapy, European Heart Journal, Volume 38, Issue suppl_1, August 2017, ehx504.4094

[8] Hassan MA, Tolba OA. Iron chelation monotherapy in transfusion-dependent beta-thalassemia major patients: a comparative study of deferasirox and deferoxamine. Electron Physician. 2016 May 25;8(5):2425-31.

[9] Meloni, A., Neri, M.G., Resta, M.C. et al. MRI prospective survey on cardiac and hepatic iron in transfusion-dependent

thalassemia intermedia patients treated with desferrioxamine, deferiprone and deferasirox. J Cardiovasc Magn Reson 17, P357 (2015

[10] Gomber S, Jain P, Sharma S, Narang M. Comparative Efficacy and Safety of Oral Iron Chelators and their Novel Combination in Children with Thalassemia. Indian Pediatr. 2016 Mar;53(3):207-10.

[11] DeBaun MR, Gordon M, McKinstry RC, Noetzel MJ, White DA, Sarnaik SA, Meier ER, Howard TH, Majumdar S, Inusa BP, Telfer PT, Kirby-Allen M, McCavit TL, Kamdem A, Airewele G, Woods GM, Berman B, Panepinto JA, Fuh BR, Kwiatkowski JL, King AA, Fixler JM, Rhodes MM, Thompson AA, Heiny ME, Redding-Lallinger RC, Kirkham FJ, Dixon N, Gonzalez CE, Kalinyak KA, Quinn CT, Strouse JJ, Miller JP, Lehmann H, Kraut MA, Ball WS Jr, Hirtz D, Casella JF. Controlled trial of transfusions for silent cerebral infarcts in sickle cell anemia. N Engl J Med. 2014 Aug 21;371(8):699-710.

[12] Sridharan K, Sivaramakrishnan G. Efficacy and safety of iron chelators in thalassemia and sickle cell disease: a multiple treatment comparison network meta-analysis and trial sequential analysis. Expert Rev Clin Pharmacol. 2018 Jun;11(6):641-650. doi: 10.1080/17512433.2018.1473760. Epub 2018 May 18. PMID: 29727586.

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