Original Article

Efficacy of IV in Children

Efficacy of Intravenous Iron Sucrose Infusion in Children with Iron Deficiency Anemia: Experience at Children Hospital & ICH Multan

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ABSTRACT

Objective: To describe the efficacy of intravenous iron sucrose in children with iron deficiency anemia who did not respondto /tolerateoral iron therapy.

Study Design: Quasi experimental interventional study.

Patients and Methods: A prospective study was performed in 100 children, aged between 08 months and 15 years, 66% male and 33% female, diagnosed as iron deficiency anemia with predefined criteriaexcluding other causes. The children who did not respond to /tolerate oral iron therapy were treated with injectable ironin a day care hematology center. Dose of iron sucrose was calculated by a formula. Total dose was divided in three equal aliquots, each one was diluted in 0.9% normal saline and infused over a period of 120 minutes onthree consecutive days. The efficacy of iron sucrose was analyzed by comparing baseline mean hemoglobin at initiation of therapy and mean hemoglobin level two weeks after iron infusion.

Results: Mean age was 4.18±3.68 years.At start of treatment,baseline meanHb was 6.09±1.37 g / dl, mean MCV 51.5±9.03fl and mean ferritin 7.76± 7.6232ng/ml . At day 14, mean Hb was 9.21±1.134 g / dl ($P < 0.05$) , mean MCV 66.5±7.19 fl and mean ferritin 52.47±29.6828ng/ml . Mean hemoglobin rise was 3.12±1.081gm/dl($P < 0.05$). During infusion, only one patient had hypotensionwho was treated.

Conclusion: Iron sucrose infusion is a safe and effective way of raising hemoglobin in iron deficiency anemia in pediatric age group in special set up with minimal side effects.

Keywords: Iron deficiency anemia (IDA), Iron sucrose, Hemoglobin (Hb).

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INTRODUCTION

Iron Deficiency Anemia (IDA) is the most common cause of nutrional anemia.It usually occurs in children between 6-36 months of age.In Pakistan, data revealed that 65-78 % of the children less than five years of age are suffering from IDA, with hemoglobin levels below 11 g/dL.[1,2] Prevalence of IDA among children less than 2 years exhibited 68% and 69 % in semi urban areas of Peshawar[3] and Abbottabad,[3,4] while itwas 61-78.7 % (Hb less than 11 g/dL) in children aged 6-60 months in urban and rural slums of Karachi.[1,5]

Major risk factors for iron deficiency anemia in children include exclusive breast feeding, cow's milk, poor weaning, malabsorption, gastrointestinal blood losses, hook worm infestation and low socioeconomic status[6].

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Treatment consists of nutritional rehabilitation with oral iron therapy and treatment of the underlying cause. [7] Problems encountered along with oral iron therapy are unpleasant taste, intolerance and gastrointestinal discomfort. [8]In such patients, favored treatment is intravenous iron preparation thatleads to an increase in hemoglobin level and restoration of iron stores.[9]Available parenteral iron preparations are Iron dextran and iron sucrose. Iron sucrose has minimum side effect as compare to dextran.[10,11]

The Children hospital and the institute of Child Health, Multan is a tertiary care center catering services to the people of Southern Punjab. Many IDA patients attend Hematology Day Care Center of the Institute. We planned to see the effect of intravenous iron sucrose therapy in IDA children who fail to respond/tolerate to oral iron therapy.

MATERIALS AND METHODS

This prospective interventional study (Quasi-Experimental) was approved by ethical committee of

the Institute. Hundred children, aged between 08 months and 15 years were selected.The study was conductedfrom August 2013 to March 2014 in the outpatient Day Care center of Pediatric Hematology at Children Hospital and institute of Child Health, Multan.The patients with hemoglobin< 9 g/dl,Serum ferritin < 20 ng/ml , failure to response to oral iron therapy or intolerant to oral iron therapywere included in the study. Children with iron deficiency anemia requiring blood transfusion,Hb< 4. 5 g/dlwith cardiac failure, anemia of chronic diseases(chronic kidney disease, liver disease), hemoglobinopathy and known hypersensitivity to iron sucrose were excluded from the study.Non-probability purposive sampling technique was used.

Iron deficiency anemia was defined as Hb< 9 g/dl and serum ferritin < 20 ng/ml .

Failure to response to oral therapy was defined as "a child on oral iron therapy in any form (Polymaltose iron complex, Ferrous gluconate or FerousSulphate)with dosage of 5mg/kg/day elemental iron and increase of hemoglobin is less than 1 gm/dl after 4 weeks of treatment due to any reason like non-compliance, intolerance or malabsorption."

Efficacy was defined as mean Hb rise was more than or up to 1gm/dl after two weeks of iron therapy.

A written consent was taken from parents or guardian after explaining merits and demerit of treatment. Baseline venous blood sample were taken for hemoglobin and Ferritin estimation. Tests were repeated two weeks after iron sucrose therapy.Outcome variable (rise in hemoglobin at the end of 2 weeks after injection)was noted for final analysis. Iron sucrose infusion is available asamber color solution, 5 ml containing 100 mg of iron. (Bisleri-Sami Pharmaceutical).

Dose was calculated by formula:

$$\frac{\text{Normal Hemoglobin for age} - \text{Initial Hemoglobin}}{100} \times \text{Blood volume} \times 3.4 \times 1.5$$ [12]

3.4 –is a constant that convers grams Hb into mg of iron

1.5 –is a constant that gives extra iron to replace the store

Blood volume - 80ml/kg

Total dose was equally divided in three equal aliquots and administered on three consecutive days. Single dose was diluted in 100cc 0.9%normal saline solution. Intravenous infusion was given slowly over a period of 120 minutes. Cardiopulmonary monitoring was done during infusion period. These patients were followed for evaluation at 2 weeks after therapy by laboratory test and clinical assessment. Data was collected on apredesigned proforma.

Statistical Analysis: Data was analyzed by using SPSS(V-20). Mean ± SD and percentages were used to describe the data.P-value 0.05 is set as predetermined level of significant.

RESULTS

In this study,out of hundred cases,66% were male. Mean age was 4.18±3.68 years with range of 8months to 15 years(Table 1).Mean score value of the end outcome hemoglobin was 9.21±1.1340 that was higher than the baseline hemoglobin 6.09± 1.3730(Table 2).Mean hemoglobin difference between the two groups were noted as 3.12±1.081 g/dl and the result was statistically significant.(P < 0.05).Mean rise in hemoglobin in both gender was shown in Table.3.

Table No.1: Age and sex distribution *N=100*

Age(year)	Number	Percentages
<1	9	9%
>1-3	34	34%
>3-7	36	36%
>7-15	21	21%
Sex		
Male	66	66%
Female	34	34%

Table No.2: Mean hemoglobin, MCV and Ferritin values

	Pre- Treatment (Mean & Standard deviation)	Post Treatment (Mean&Standard deviation)
Mean Hb g/dl	6.09±1.3730 (P<0.005)	9.21±1.1340 (P<0.005)
Mean MCV fl	51.50± 9.0334	66.56±7.1997
Mean Ferittinng/ml	7.76± 7.6232	52.47± 29.6828

Table No.3: Mean hemoglobin difference between male and female.

Gender —	Mean Hb1(g/dl) Pre-treatment	MeanHb2(g/dl) Post-treatment
Male	6.616±1.344 (P<0.476)	9.305± 0.945(P<0.284)
Female	5.953± 1.4379(P<0.487)	9.047± 1.4321(P0.348)

DISCUSSION

Iron deficiency anemia is a common problem in pediatric age group and usually treated by oral iron preparations. Treatment is troublesome in certain circumstances where non-compliance and gastrointestinal upset are the major issues. Most of the time, blood transfusionis opted as the alternate treatment option in these situation which has lot of drawbacks like transmission of infection and undue burden over blood banks. Intravenous iron supplementation has given promising result in pediatric age group in various studies[9,10,13,14,15].

Hundred patients were studied using intravenous iron sucrose according to the said protocol. Mean values of hemoglobin in g/dl increased from 6.09± 1.3730 (P<0.005) to 9.21±1.1340(P<0.005), MCV51.50± 9.0334 to 66.56±7.1997fl and ferritin from 7.76± 7.6232ng/ml to 52.47± 29.6828 ng/ml. Overall, mean increased hemoglobin was 3.12 g/dl (P <0.05).

Very few studies on intravenous iron sucrose infusion in children have been published. Rise in hemoglobin of 3.12 g / dl in this study is comparable to other studies in literature showing a rise of Hb 3.9 and 2.2 g/dl[9,10]After 14 days, mean Hb was 9.21 g/ dl (SD 1.19) is also parallel to the report of Pinsk V et al with a mean Hb. of 9.27 g/dl.[12] The result of our study is also similar toCrary SEet al that showed a median hemoglobin rise of 1.9–3.1[13] g/dl. Safety and tolerability of the therapy in our study was assessed by the occurrence of adverse events that was hypotension while in Schroder O et al exhibited two main adverse effects but therapy was continued in spite of these effects.[14]Theusinger OM found a mean hemoglobin rise of 1±0.6 g/dl after two weeks of therapy in pre-operative cases.[15]

Although several factors account for high prevalence of IDA in children but a multi- pronged approach to alleviate this factor including nutritional education, food selection focusing dietary inhibitor and enhancer, hygiene, iron fortification of food, improved socioeconomic status and campaign may limit the magnitude of IDA.

Treatment of IDA should be aimed specifically at the underlying cause.Oral iron therapy should be initiated as first –line therapy. Whena patient is refractory to oral treatment due to any reason, parenteral therapy may be considered. Currently, preferred choice is iron sucrose due to favorable pharmacological properties combined with low rates of adverse drug events. Economic considerations are also a factor in selecting this treatment.Intravenous treatment is more costly than oral.However,treatment may result in reducing overall burden of parents and physicians. It is also helpful tool in avoiding blood transfusion in treatable disease. Reluctance in prescribing this effective treatment could be explained by considering serious side effects.Data is showing low rate of occurrence of serious side effects induced by intravenous iron sucrose in treatment of IDA. It may be reasonable to re-evaluate intravenous iron sucrose indications and uses in special circumstances and even in primary care clinic.

Data suggests effectiveness and tolerability for iron sucrose but larger multicenter trials may be needed to prove a possible advantage of iron sucrose in short-term efficacy. An immediate subjective change like mood elevation & eating habit after iron infusion was noted. A long term follow up may be needed in order to see the cognitive function in later ages as there is evidence that iron deficiency without anemia affects cognition in adolescent girl[16].

Single quasi experimental study is the limitation of study. Multicenter study, randomized control trial and larger sample size would give better result for suggesting iron sucrose infusion in children.

CONCLUSION

Parenteral iron sucrose is a safe and effective way to treat iron deficiency in children who are refractory to oral iron due to intolerance, poor compliance, or iron malabsorption.

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REFERENCES

1. Molla A, Khurshid M, Molla AM. Prevalence of ID anemia in children of the urban slums of Karachi. J Pak Med Assoc 1992;42:118-21.
2. Jhaveir JH, Baig L. Anaemia in Children Part I – Can simple observation by primary care provider help in diagnosis?. J Pak Med Assoc 1994;44: 282-4.
3. Paracha PI, Hameed A, Simon J, Jamil A, Nawab G. Prevalence of anaemia in semi-urban areas of Peshawar, Pakistan: A challenge for health professionals and policy makers. J Pak Med Assoc 1997;47:49-53.
4. Idris M, Rehman AU. ID anaemia in moderate to severely anemic patients. J Ayub Med Coll Abbottabad 2005;17:45-7.
5. Rahbar MH, Hozhabri S, Wang J. Prevalence of anaemia among children living in five communities in and near Karachi, Pakistan. Toxicol Environ Chem 2007;89:337-46.
6. Mills A. Surveillance for anaemia: risk factors in patterns of milk intake. Archives of disease in childhood 1990;65(4):428-31.
7. Worwood M, Hoffbrand AV. Iron metabolism, iron deficiency and disorders of haemsynthesis. In: Hoffbrand AV, Catovsky D, Tuddenham, Edward GD, editors. Postgraduate Haematology, 5th ed. Massachusetts: Blackwell Publishing;2005.p. 26-43.
8. Norma B, Richard S. Iron deficiency Anemia. In: Kliegman RM, Stanton BF, Schor NS, Joseph WS,

Behrman RE, editors. Nelson text book of Pediatrics. 19th ed. Philadelphia:NB Sauders; 2011.p 1655-58.

9. Iqbal MM, Malik BA. Parental Iron Therapy in Malnourished Children. Pakistan Arm Forces Med J 2006;;1-5.
10. Shimada A. Adverse reaction to total-dose infusion of iron dextran. Clin Pharm 1982; 1(3): 248 -9.
11. Al-Momen A-K, Al-Meshari A, Al-Nuaim L, Saddique A, Abotalib Z, Khashogji T, et al. Intravenous iron sucrose complex in the treatment of iron deficiency anemia during pregnancy. Europ J of Obs & Gynae and Reprod Biol 1996;69(2): 121-4.
12. Vezed P, Jacov L,Asher M,Baruch Y, Joseph K. Efficacy and safety of intravenous iron sucrose Therapy in a group of children with iron deficiency anemia. Israil Med Assoc J 2008;10:335 -38.
13. Crary SE, Hall K, Buchanan GR. Intravenous iron sucrose for children with iron deficiency failing to respond to oral iron therapy. Pediatric blood & cancer 2011;56(4):615-9.
14. Schröder O, Schrott M, Blumenstein I, Jahnel J, Dignass A, Stein J. A study for the evaluation of safety and tolerability of intravenous high-dose iron sucrose in patients with iron deficiency anemia due to gastrointestinal bleeding. Zeitschriftfür Gastroenterologie 2004;42(08):663-7.
15. Theusinger OM, Schanz U, Spahn DR. Efficacy of intravenous iron sucrose administration for correcting preoperative anemia in patients scheduled for major orthopedic surgery. Anesthesiol 2008;109(1):152.
16. Algarin C, Peirano P, Garrido M, Pizarro F, Lozoff B. Iron deficiency anemia in infancy:long lasting effects on auditory and visual system functioning. Pediatr Res 2003;53:217-23.