EFFICACY OF PARENTERAL IRON AS COMPARED TO ORAL IRON IN THE TREATMENT OF IRON DEFICIENCY ANEMIA IN CHILDREN

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ABSTRACT

Objective: To compare the efficacy of parenteral iron as compared to oral iron in the treatment of iron deficiency anemia in children presenting at CMH Murree.

Study design: Randomized control trail (RCT)

Setting and Duration: Departments of Paediatrics and Pathology CMH Murree from August 2009 to March 2010.

Materials and Methods: Forty one children diagnosed with iron deficiency anemia on the basis of hemoglobin, red cell indices and morphology and serum iron levels were included. Patients were randomized into two groups with group I of 18 receiving oral ferrous sulphate and group II of 23 receiving parenteral iron sorbitol therapy. Response was assessed by reticulocyte count at 1 week, change in hemoglobin, MCV and serum iron levels at 4 weeks post treatment.

Results: The reticulocyte response at 1 week time was significantly more with intramuscular iron as compared to oral iron. Mean hemoglobin change and serum iron level increase were also significantly more with intramuscular iron therapy. Mean MCV level change was insignificant between the two modalities.

Conclusion: Parenteral intramuscular iron sorbitol treatment with better compliance shows early improved responses in children with iron deficiency anemia as compared to oral ferrous sulphate therapy and should be used as a preferred modality for treatment.

Keywords: Intramuscular, Iron deficiency anemia, pica, reticulocyte count.

INTRODUCTION

Iron deficiency anemia (IDA) is the most common type of anemia and is usually diagnosed clinically in the outpatient setting and confirmed with laboratory tests[1]. Low hemoglobin (Hb) in the setting of a reduced mean corpuscular volume (MCV) is usually the initial finding on a routine complete blood count. Iron deficiency initially manifests as a falling MCV accompanied by a rising RDW. Additional laboratory findings in IDA include low serum ferritin, low serum iron, elevated total iron-binding capacity (TIBC) and low transferrin saturation level. When the diagnosis remains ambiguous after laboratory results are analyzed, a bone marrow biopsy should be considered in order to make a definitive diagnosis. The absence of stainable iron is the 'gold standard' for diagnosis of IDA[2,3].

Treatment of iron deficiency should begin with dietary replacement like fortified cereals and breads, red meat, beans, green leafy vegetables, but when diet alone is inadequate to restore iron stores and Hb to normal levels, or when anemia is severe, treatment with exogenous iron supplements should be implemented. As the first-line treatment for IDA, oral iron is safe, cost-effective, and convenient. Ferrous sulfate and ferrous gluconate are the two preferred oral preparations of iron, given the low cost and good bioavailability of elemental iron. Common adverse effects of oral iron supplements include nausea, epigastric discomfort, and constipation, all of which are dose-related. Adverse effects can occur in up to 20% of patients, impairing compliance. When the patient fails oral iron therapy, parenteral iron therapy is indicated. Indications for parenteral iron therapy include: (1) high iron requirements due to chronic uncorrectable bleeding or chronic hemodialysis; (2) iron malabsorption secondary to a GI condition i.e., chronic diarrhea and malabsorption (celiac disease, atrophic gastritis) (3) severe anemia with patients unwillingness to receive transfusions; (4) intolerance or

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noncompliance with oral therapy; (5) need for rapid restitution of iron stores (e.g., pre-operative). Parenteral intravenous iron preparations are available as ferric gluconate, iron sucrose, iron dextran, and ferric carboxymaltose. Adverse effects include anaphylactic reactions, hypotension, myalgia, arthralgia, nausea, vomiting, and fever[4].

Parenteral intramuscular iron therapy in the form of iron sorbitol is also an excellent option. Recommended single daily dose is 1.5 mg/kg body weight. It has the advantage of being able to be administered even on outpatient basis. Adverse effects include local discomfort and discoloration, transient metallic taste, nausea, vomiting, dizziness, flushing and palpitations[5,6]. This study was carried out to compare the efficacy of parenteral intramuscular iron sorbitol as compared to oral ferrous sulphate in the treatment of iron deficiency anemia in children presenting at CMH Murree.

PATIENTS AND METHODS

This randomized control trail (RCT) was carried out at the department of Paediatrics and Pathology CMH Murree from Aug 2009 to Mar 2010. Forty one children diagnosed with iron deficiency anemia on the basis of hemoglobin, red cell count, red cell indices including MCV, MCH, MCHC and RDW, red cell morphology and serum iron levels were included. Mentzer index was applied to exclude thalassemia trait. A value of more than 14 was taken as evidence of IDA. Further support was taken with the use of RDW with values of >15% taken as evidence of IDA. Final confirmation was done with red cell morphology especially the presence of pencil cells and low serum iron levels.

Patients were randomized into two groups with group I of 18 children receiving oral ferrous sulphate at a dose of 5 mg/ kg of elemental iron per day and the group II of 23 children receiving parenteral intramuscular iron sorbitol at a dose of 1.5 mg/ kg per day therapy. Response was assessed by reticulocyte count at 1 week and change in hemoglobin, MCV and serum iron levels and clinical improvement at 4 weeks post treatment data was analyzed using SPSS version 15 descriptive statistic were used to describe the data. Independent samples t-test was used to compare change in study variables between the two groups. Paired sample t-test was used to compare pre and post treatment levels. *p*-value < 0.05 was considered as significant.

RESULTS

Mean age of children in the oral therapy group was 1 ½ years. There was significant increase in the reticulocyte count, hemoglobin, MCV and the serum iron levels in both the groups (Table-1). Clinically pallor improved and activity level increased.

Mean age of children in the parenteral therapy group was 1 year and 3 months. In this group there was also significant increase in the reticulocyte count and this change was significantly more than that seen in the previous group (*p* value < 0.001). There was also significant increase in the hemoglobin and this change in hemoglobin was also significantly more than that seen in the previous group (*p* value<0.001). MCV also increased significantly however the MCV change between the two groups was insignificant (*p* value=0.270). The serum iron level also increased significantly and the change in serum iron level is also significantly more in group II as compared to group I (*p* value 0.041) (Table-2). No significant side effects were seen with the intramuscular iron therapy. Clinically pallor reversed, activity level increased and scholastic performance improved. Pica symptoms also reversed.

DISCUSSION

Iron deficiency anemia affects approximately 30% of the world's population. Iron deficiency remains extremely common in the adult population and is even more prevalent in children and neonates[7]. In Pakistan IDA is the most common type of anemia with a prevalence of about 65% and is mainly due to nutritional deficiency[8,9]. The prevalence varies greatly according to age and gender and in children is also related to sociodemographic factors including lack of maternal education, poor parenting, low monthly income and the number of siblings[10]. In children, low birth

Table - 1: Description of variables in both groups at pretreatment and post treatment levels.

Variables	Group-I (n = 18) Ferrous sulphate	Group-II (n = 23) Iron sorbitol	*p*-value
Pretreatment retics %	0.95 ± 0.54	1.20 ± 0.74	0.247
Post treatment retics %	3.60 ± 1.24	9.77 ± 2.74	< 0.001
p -value	< 0.001	< 0.001	
Pretreatment Hb g/dl	6.10 ± 1.03	6.20 ± 0.80	0.739
Post treatment Hb g/dl	7.41 ± 0.73	8.33 ± 0.65	< 0.001
p -value	< 0.001	< 0.001	
Pretreatment MCV fl	58.17 ± 6.03	59.87 ± 6.82	0.410
Post treatment MCV fl	66.61 ± 3.87	69.35 ± 5.50	0.081
p -value	< 0.001	< 0.001	
Pretreatment S iron ug/dl	40.22 ± 17.20	34.22 ± 13.91	0.224
Post treatment S iron ug/dl	181.39 ± 47.44	213.22 ± 63.90	0.085
p -value	< 0.001	< 0.001	

Table-2: Comparison of increase in all the variables between both the groups

Variables	Group-I (n = 18) Ferrous sulphate	Group-II (n = 23) Iron sorbitol	*p* -value
Retics %	2.65 ± 0.86	8.57 ± 2.77	< 0.001
Hb g/dl	1.31 ± 0.46	2.13 ± 0.65	< 0.001
MCV fl	8.44 ± 3.33	9.48 ± 2.59	0.270
S iron ug/dl	141.17 ± 52.28	179.00 ± 60.42	0.041

weight, unusual perinatal blood loss including early clamping of the umbilical cord, dietry deficiency with late weaning and prolonged consumption of large amounts of cow's milk, hookworm infestation and lesions of the gastrointestinal tract including milk protein-induced inflammatory colitis, chronic diarrhea, lactose intolerance, Meckel diverticulum, polyp or hemangioma and inflammatory bowel disease account for most IDA diagnoses[11]. Clinical features of IDA include pallor, pagophagia, irritability, anorexia and reduced attention span, alertness and learning[12].

Although a number of local studies show better efficacy of parenteral intravenous iron therapy as compared to oral iron treatment in the adults especially in pregnancy, the efficacy of intramuscular iron therapy remains to be established and only one such study has been carried out on children locally[13,14,15]. In that study by Afzal et al they found intramuscular iron therapy to be more definitive and a rapid alternative mode of treatment of IDA in children with fewer side effects as compared to oral iron preparations which have superior results with prolonged duration of treatment but with which compliance is a limiting factor[16]. Our study also shows that intramuscular iron sorbitol therapy is more efficacious than oral ferrous sulphate therapy. Intramuscular iron therapy given under supervision in the outpatient department reduced the hospital admission burden, improved the compliance rate and also averted the risks associated with intravenous iron therapy. The reticulocyte response at 1 week time was significantly more with intramuscular iron as compared to oral iron. It denotes more effective erythropoiesis with intramuscular iron administration probably because of better compliance and less variation in absorption. Mean hemoglobin change was also significantly more with intramuscular iron because of the same reasons. Mean MCV level change was insignificant with the two modalities. Serum iron levels showed improvement with both modalities of treatment being significantly more with intramuscular iron therapy.

A study by Naz et[17] al shows significantly higher rise in hemoglobin level, more increase in ferritin levels and less adverse effects with intravenous iron sucrose as compared to oral

ferrous sulphate when treating iron deficiency anemia in pregnancy. Similar results have been described by Hassan et al with comparison of intravenous iron sucrose with oral iron hydroxide polymaltose complex[13]. Although more efficacious than intramuscular iron as demonstrated by Hashmi et al and Wali et al, the problem with intravenous iron therapy is need for admission for dose administration and the risk of serious anaphylactic reaction[14,18]. These problems are averted with intramuscular iron while maintaining the efficacy as shown by our stduy and also by Tayab et al according to whom its administration is convenient both for the patient as well as for the doctor. It improves patient compliance and is also cost effective[15].

CONCLUSION

Parenteral intramuscular iron sorbitol treatment with better compliance shows early improved responses in children with iron deficiency anemia as compared to oral ferrous sulphate therapy and should be used as a preferred modality for treatment.

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