Original Article

DOI: 10.21276/APALM.2057

Comparative Improvement of RBC Indices and Hemoglobin After Oral Versus Iron Therapy in Patients of Iron Deficiency Anemia

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ABSTRACT

Background: Iron Deficiency Anemia (IDA) is the single most prevalent nutritional deficiency worldwide. Oral iron therapy is the standard of care, however in some cases parenteral iron therapy is required. This study was undertaken to evaluate the comparative improvement of RBC indices and hemoglobin after treatment with IV Iron sucrose complex and oral iron in iron deficient patients.

Methods: A retrospective study was conducted at Super Speciality Hospital in North India on 50 patients in Department of Pathology and Clinical Hematology who were diagnosed with IDA/state based on complete blood counts (CBC), iron studies and ferritin levels. Patients on chronic proton pump inhibitor therapy or celiac disease were treated with IV iron sucrose complex (IVIS) 100 mg for 10 days and remaining were given oral iron (OI), i.e. Ferrous sulfate 100 mg 2-3 times a day. All patients were given folic acid 5 mg daily in addition to iron therapy. Various hematological parameters were compared at day 12-15 days of therapy. Statistical analysis was done by student t test. Values were considered statistically significant when $p<0.05$.

Result: A total of 50 patients were included, out of which 10 received IVIS and 40 were treated with oral iron therapy. Patient belonged to age group 15-45 years. Although hemoglobin increased in both groups; rise in reticulocyte count, MCV, MCH, MCHC and increase in hemoglobin were higher in IVIS than in OI group at day 12-15 of therapy (25.7% vs 10.8%). IVIS has no major side effects. Compliance was not very good with OI group; 20% patients showed GI side effects and 5 patients left therapy because of the same.

Conclusion: IV iron is convenient, well tolerated and leads to more rapid improvement in hematological parameters. Poor gastrointestinal tolerability and poor compliance are major concerns with oral iron therapy.

Keywords: *Iron Deficiency Anemia, IVIS, OI, Serum Ferritin, Hemoglobin*

Introduction

Iron deficiency anemia (IDA) is the single most prevalent nutritional deficiency worldwide. It accounts for anemia in 70% in children aged 6-59 months, 55% in females aged 15-49 years and 24% in males aged 15-49 years of Indian population. [1] Therefore, the prevention and treatment of IDA is a major public health goal. Regardless of the presence of symptoms, all patients with IDA and most patients without anemia with IDA should be treated. The rationale is that there is risk for further organ damage/ischemia and progression of anemia unless the underlying cause of deficiency is treated and adequate iron stores are replenished. WHO define IDA as hemoglobin < 12gm/dl. [2] The choice between oral and intravenous iron depends on a number of factors including acuity of anemia, cost and availability of different iron replacement products, as well as the ability of patient to tolerate oral iron preparations and factors affecting bioavailability of oral iron. The standard treatment in majority of the institutions is oral iron (OI), with blood transfusion reserved for severe or emergency cases. However, in some cases oral iron cannot meet the requirement and blood transfusion has its own hazards. Current intravenous iron preparations provide a safe and effective treatment alternative to OI or blood transfusion. This study was undertaken to evaluate the usefulness of Intravenous Iron Sucrose (IVIS) for treatment of IDA along with improvement in hematological parameters between IV Iron and Oral ferrous sulfate for the treatment.

Materials and Methods

A retrospective study was conducted in Department of Pathology and Clinical Hematology, at a Super Specialty Hospital, North India. 50 patients were included with hemoglobin less than 12gm/dl, who were diagnosed with IDA/state based on CBC, iron studies and ferritin levels. All the hematological samples were analysed by Advia2120i analyser along with the peripheral blood smear

examination. Serum ferritin analysis was done via direct chemiluminescence immunoassay. Exclusion criteria were causes other than IDA, recent blood transfusions, megaloblastic anemia and hemoglobinopathies. Indications for IVIS were patients on proton pump inhibitor therapy (from gastroenterology department) and celiac disease, both conditions known to cause poor absorption of oral iron therapy. They were treated with IV iron sucrose 100 mg over 30 minutes for 10 days, remaining patients were given oral iron therapy with ferrous sulfate 100 mg twice a day. Various hematological parameters were compared at day 12-15 days of therapy. Statistical analysis was done by student t test via social statistics online. Values were considered statistically significant when $p<0.05$.

Result

Demographic Profile: Fifty patients with iron deficiency anemia were analyzed out of which 8 were males and 42 were females (M: F= 6:1). Age group ranges from 15-45 years, median age was 22 years. Out of total 50 patients, 10 were treated with IV iron sucrose complex for 10 days and remaining were given oral iron.

The IVIS group had lower hemoglobin values, red cell indices and lower serum iron profile. The percentage increase in these variables are significantly higher in IVIS group after treatment than OI group.

Although hemoglobin increased in both groups, rise in reticulocyte count, reticulocyte production index, MCV, MCH, MCHC and increase in hemoglobin were higher in IVIS than in OI group at day 12-15 days of therapy. (Table 2 and 3)

In the present study, 80% in IV group attained target hemoglobin levels against 67% in oral group, the difference between the two groups was statistically significant. The target hemoglobin was achieved within 12-15 days of treatment .

IVIS had no major infusion reactions or other side effects. Compliance was not very good with OI, 20% had GI side effects and 5 patients left therapy because of same. GI symptoms encountered were dyspepsia, constipation and nausea.

Cost of treatment was higher in IVIS group as compared to OI group. Cost of iron sucrose injection is Rs 490 per 200 mg ampoule and ferrous sulfate is Rs 1.69 per tablet.

Table 1: Percentage increase in various Laboratory Parameters after treatment in two groups.(All values with their mean and standard error).

Percentage increase (Value %)	Oral Iron (n = 40)	IV Iron (n = 10)	P value
Δ Hb%	10.8 ±1.7	25.7±2	0.0001
Δ PCV%	9.5±1.7	35.2±3.8	0.0001
Δ MCV%	5.6±1.4	14.6±3.4	0.008
Δ MCH%	4.7±0.9	16.07±3.7	0.0001
Δ Ferritin%	161.57±1.7	1332±3.8	0.0001
Δ R/C %	25.6 ± 4.0	61.7±4.3	0.0001
Δ RPI%	27.21±+3.7	65.29±4.0	0.0001

Table 2: Laboratory Parameters before treatment in two groups. (All values with their mean and standard error).

Parameters	Oral Iron (n=40)	IV IRON (n = 10)	P value
Hb (g/dl)	9.44± 0.2	8.83± 0.5	0.2
PCV(%)	30.5± 0.2	26.86±2	0.001
MCV(fl)	77.04±1.3	72.38±3	0.5
MCH (pg)	24.43±0.6	25.35±2	0.5
MCHC (g/dl)	31.36±1.2	32.41±0.4	0.6
RBC count (cells/cumm)	4.13±1.2	3.5±0.3	0.8
R/C%	2.92±0.3	2.37±0.6	0.3
Reticulocyte index	0.9±0.07	0.8±0.1	0.5
Ferritin (ng/dl)	21.7±2.0	12±1.7	0.01

Table 3: Laboratory Parameters after treatment in two groups. (All values with their mean and standard error).

Parameters	Oral Iron (n=40)	IV IRON (n = 10)	P value
Hb (g/dl)	10.6±0.2	11.6±0.01	0.01
PCV(%)	32.27±0.5	34.98±1.4	0.001
MCV(fl)	78.18±0.2	81.4±0.2	0.001
MCH (pg)	25±0.6	28.34±1.8	0.03
MCHC (g/dl)	31.4±0.2	32.42±0.3±	0.02
RBC count (cells/cumm)	4.43±0.09	3.98±0.2	0.01
R/C%	2.1±0.2	3.6±1.1	0.02
RPI	0.9+0.1	1.77+0.5	0.008
Ferritin(ng/dl)	56.5+1.9	164.7+3.8	0.0001

Discussion

Iron deficiency anemia remains the most common medical disorder in developing world. Highest sensitivity and specificity for diagnosing lies in measurement of serum ferritin levels (< 10-15 micrograms/l). Ferritin is a protein that stores iron and releases iron as per need. It is basically body's natural regulator against iron deficiency. By the time a patient is anemic, his iron stores are already depleted as evidenced by decrease levels of serum ferritin. However, ferritin can be falsely elevated due to secondary inflammatory response.

Currently the standard treatment for anemia is Oral iron supplementation. However, major concerns with oral therapy are poor patient compliance and various GI symptoms such as nausea, vomiting and diarrhea.[3] Absorption of oral iron is influenced by dosage, patient iron storage and proximity of taking the medicine relative to mealtime. Ideally, the supplement should be taken on an empty stomach as food hinders with its absorption.[4] Alternatives includes IV Iron therapy and blood transfusion. Blood transfusions are costly and associated with potential infectious complications. [5]

Intravenous iron can be a good substitute to oral iron therapy being safe, feasible, corrects anemia in a short duration and replenishes iron stores better than oral iron with high patient compliance. [6] Iron sucrose consist of poly-nuclear complex analogous to ferritin with apo-ferritin component replaced by sucrose, well tolerated and least antigenic hence an advantage over other parenteral iron therapies and oral Iron. It is available for erythropoiesis within 5 minutes of infusion and has 68-95% utilization rate after 2-4 weeks since it is stored in reticuloendothelial cells. Organ toxicity is less likely even with iron sucrose overload. [7] Its half-life is 6 hours. [8] Hematologic parameters like hemoglobin and ferritin show rapid increment with IV Iron along with positive effect on body's iron storage which is measured by ferritin levels. IV iron administered with iron sucrose has been available from several years and routinely used. It has an excellent safety record, unlike older IV formulations such as ferrous dextran which has increased risk of anaphylactoid reaction. [9]

In the present study, 80% in IV group attained target hemoglobin levels against 67% in oral group, the difference between the two groups was statistically significant. The results are comparable to Wali et al., (2002) and Abdullah et al., (2014). In the study, Wali et al.,2002 target hemoglobin levels were achieved by 70-80% in intravenous groups. Abdullah et al., (2011) also reported a significant a significant rise in hemoglobin levels in intravenous group. [10]

It also showed statistically significant increase in other red cell indices (MCV, MCH and MCHC) and reticulocyte count between IVIS and OI group however these results not comparable to other studies. [11]

There is a significant increase in reticulocyte production index between IVIS and OI group.

There is a significant increase in ferritin levels after treatment between the two groups, which has also been observed by Bayoumeu et al, Neeru et al 2012. [12]

Gastrointestinal side effects were noticed in 20% of OI group while no serious adverse drug reactions and no episodes of anaphylaxsis were observed in IVIS group. The results are similar to other studies Neeru et al 2012, Al momen et al.,1996. Other studies by Bayoumeu et al.,2002 and Al momen et al.,1996 reported unpleasant taste and fever which were not observed in the present study. [13]

Once the anemia is corrected with OI, absorption slows down. This is responsible for iron stores not replenished with OI, unlike intravenous iron.

Iron sucrose is costlier than oral iron and require hospital setting for administration whereas OI cheaper and easy to take.

Conclusion

Present study illustrates that although OI increases hemoglobin comparably with IVIS but does not replenish iron stores as much as IVIS. IV iron is more effective, convenient, well tolerated with no serious side effects. So current guidelines for management of iron deficiency anemia should incorporate intravenous iron sucrose as effective and safe treatment.

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Financial or other Competing Interests: None.