Original Research Article

A comparison of Intravenous Iron versus Oral Iron for the Management of Iron Deficiency Anemia: A Changing Paradigm

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Abstract

Background: Iron deficiency is one of the major morbidities worldwide. The standard treatment is the oral iron therapy, however, the concerns of slower response makes it a less feasible option in situations where quicker response is desired. The objective of this study was to compare the response, the quickness of the response and tolerability of intravenous iron with that of oral iron. A prospective, observational cohort study was conducted on 300 patients of iron deficiency anemia in District Hospital Srinagar wherein 110 patients received oral iron and 190 patients received intravenous iron. The mean hemoglobin increase at 3 weeks in oral iron group was 1.71 g/dl and in intravenous group it was 2.75 g/dl. Conclusion: Intravenous iron therapy is more effective than oral iron in terms of rapidity of the response.

Keywords: Hemoglobin, Iron deficiency, Intravenous iron.

Introduction

Iron deficiency anemia is one of the commonest hematological diseases seen worldwide.[1] The approach to iron deficiency anemia is to find the cause and treat the deficiency. The treatment options include oral iron, intravenous iron, intramuscular iron and blood transfusion. The choice depends upon the rapidity of the response needed. Conventionally oral iron has been the standard first line treatment for all iron deficiency anemia patients. The main drawbacks of oral iron are intolerance and probably a slower response. Newer intravenous iron formulations have better tolerability, used in one or two sittings and probably have a quicker response. The studies done on this subject show mixed results. Latest comparisons between the two forms is favoring intravenous iron than oral iron. This study was undertaken to compare the rapidity of the response between the two forms, oral and intravenous iron and also check the tolerability of intravenous iron.

Material and Methods

This study was a prospective observational, analytical cohort study, conducted in the department of Internal Medicine District Hospital Srinagar for a period of two years. Ethical committee approval taken for study .During the study period, all the consecutively diagnosed iron deficiency anemia patients formed the patient group. The Hb cut off for anemia was kept as per WHO guidelines i.e, < 13g/dl for males, <12g/dl for females and <11g/dl for pregnant females. The study was approved by institutional ethics committee. A written consent was taken from all the patients.A total of three hundred patients were selected randomly. These patients included those who visited hematology outpatient department directly and also those who were referred from different OPDs like Obstetrics and Gynecology, gastroenterology, etc. Iron deficiency anemia was diagnosed predominantly on red cell indices, supplemented by clinical setting and iron profile in some cases. CBC was performed on sysmex analyzer at the baseline and at 3 weeks. Patients of anemia due to causes other than iron deficiency were excluded. A detailed history and physical examination was done in each patient. Relevant investigations to find the cause of iron deficiency and exclude other possibilities were undertaken. The patients were divided into two groups based on degree of anemia, tolerability of the drug, co morbid illness and rapidity of the response desired. 110 patients formed group A who received oral iron therapy and 190 patients formed group B who received intravenous iron therapy. The total dose of intravenous iron was calculated as per Ganzoni formula.

Predominant intravenous iron therapy was iron sucrose 200mg twice weekly while as ferric carboxy maltose was used in few patients at a dose of 500mg weekly. The primary endpoint was to demonstrate the performance of oral iron in improving Hb response, compared to intravenous iron at 3 weeks time period. The common indication of intravenous iron therapy was intolerance to oral iron, severe symptomatic anemia, heavy menstrual bleeding, late pregnancy, inflammatory bowel disease and quick preparation for surgery.The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous

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variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

Results

A total of 300 cases of iron deficiency anemia were analyzed. 110 patients formed group A who received oral iron and 190 patients formed group B who received intravenous iron. Their biodata, clinical profile and relevant investigations were recorded at baseline and 3 weeks.The mean age of the patients in group A was 33.4 years, ranging from 13-75 years. The mean age in group B was 33.6 years, ranging from 13-75. The age distribution of both groups is shown in table 1 with age range of 30-39 years as the commonest group in both groups. Table 2 shows the gender distribution of all the patients with approximately 84% in each group constituted by females.The main cause of iron deficiency anemia was menorrhagia (54.7 percent), followed by pregnancy (17.3 percent), lower GI bleed (8%), and upper GI bleed (6.3 percent) (Figure 1). The mean pre treatment hemoglobin in group A was 7.36 and post treatment hemoglobin rose to 9.07. The mean pre treatment hemoglobin in group B was 7.22 and post treatment hemoglobin was 9.97 (p value. <0.001)(Table 3). The mean hemoglobin increment in group A was 1.71g/dl and in group B it was 2.75 g/dl, a statistically significant difference (p value <0.001)(Table 4 and Figure 2). 3% of patients developed mild hypersensitivity reactions and less than1% developed moderate reactions in intravenous group while as there were minor gastrointestinal symptoms and no hypersensitivity reactions with oral iron.

Table 1: Age distribution of study patients in two groups

Age (Years)	Group A		Group B		P-value
	No.	%age	No.	%age	
10-19	11	10.0	10	5.3	0.901
20-29	21	19.1	50	26.3	
30-39	48	43.6	82	43.2	
40-49	24	21.8	37	19.5	
≥ 50	6	5.5	11	5.8	
Total	110	100	190	100	
Mean±SD (Range)	33.4±11.36 (13-75)		33.6±10.48 (13-75)		

Table 2: Gender distribution of study patients in two groups

Gender	Group A		Group B		P-value
	No.	%age	No.	%age	
Male	17	15.5	31	16.3	0.845
Female	93	84.5	159	83.7	
Total	110	100	190	100	

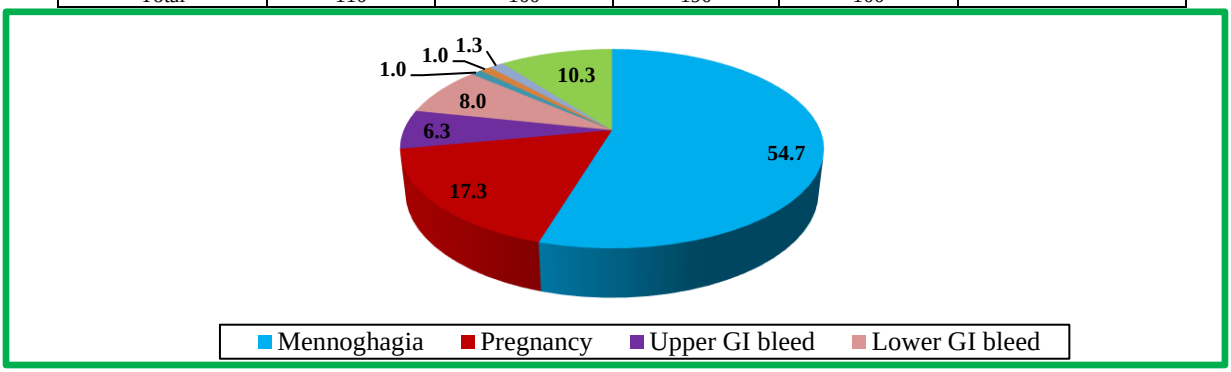

Fig 1:Distribution of study patients as per diagnosis in study group

Table 3: Pre and post treatment hemoglobin (Hb) in two groups

Hb (gm%)	Group A		Group B		P-value
	Mean	SD	Mean	SD	
Pre treatment	7.36	1.064	7.22	1.174	0.304
Post treatment	9.07	1.162	9.97	1.249	<0.001*

Table 4: Comparison based on change in hemoglobin in two group

Group	N	Mean	SD	95% CI	P-value
Group A	110	1.71	0.654	1.58-1.83	<0.001*
Group B	190	2.75	0.861	2.63-2.87	

***Statistically significant difference (P-value<0.05)**

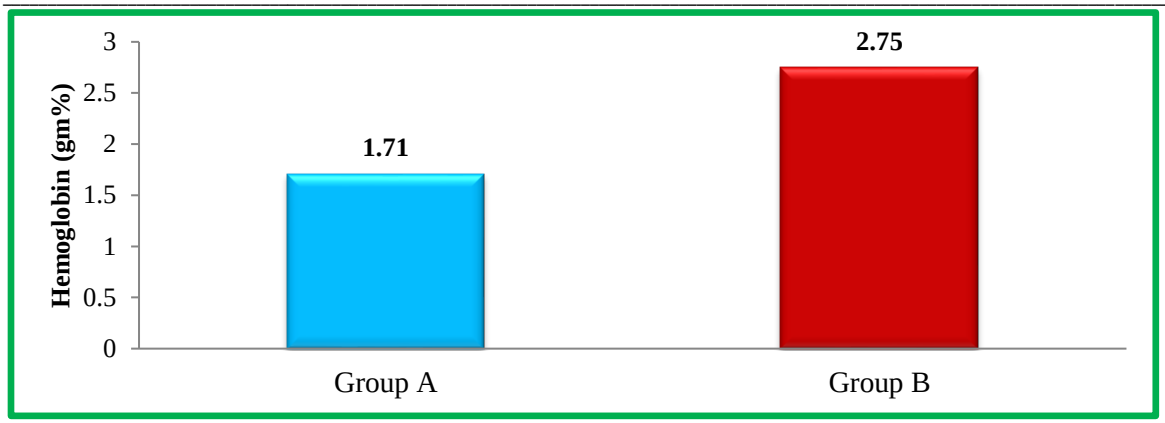

Fig 2:Comparison based on change in hemoglobin in two groups

Discussion

The treatment options in iron deficiency anemia include oral iron , intravenous iron, intramuscular iron and blood transfusion. Lately intramuscular iron has gone into disrepute because of its side effects like pain, variable absorption, similar risk of anaphylaxis as that of intravenous iron and gluteal sarcomas.[1] Blood transfusion is required at the time of hemodynamic instability, congestive cardiac failure and when very little time is left for surgery or intervention.[2]. The conventional therapy for iron deficiency has been oral iron. The issues with oral iron are longer duration of intake (few months), GI intolerance and slower response.[3] The intravenous iron drugs have been traditionally linked to higher hypersensitivity reactions but with the introduction of newer iv iron formulations this risk is very minimal.[4] Another advantage of intravenous iron is shorter duration of treatment i.e, one or two sittings. In situations where rapid response is needed, intravenous iron might score over oral iron. Only few studies have shown this benefit with intravenous iron.[5] This study was taken to compare the efficacy of the two forms of iron at 3 weeks.This study of 300 cases of iron deficiency anemia revealed a female preponderance with age group of 30-39 years as commonly affected group. Etiologically menorrhagia proved out to be the most prevalent cause followed by pregnancy and GI losses.Gozzard D showed that menorrhagia is one of the common causes of iron deficiency anemia and iv iron is better suited for these patients as oral iron will not suffice for heavy iron losses.[6]Our study also showed the similar results. Mishra V et al, studied 90 females with iron deficiency anemia secondary to menorrhagia and found very good response at 3 weeks with intravenous ferric carboxy maltose.[7]In their study the mean Hb improved from 8.33g/dl to 10.89g/dl with a jump of 2.56g/dl. Our study revealed similar results in iv iron group with mean Hb increase from 7.22g/dl to 9.97g/dl with 2.75g/dl as absolute increment. Bhavi SB et al, in their randomized controlled trial of iv iron sucrose vs oral iron in pregnancy showed better efficacy and lesser toxicity with intravenous iron in pregnancy.[8]Froessler B et al in their randomized study for Intravenous iron sucrose versus oral iron ferrous sulfate for antenatal and postpartum iron deficiency anemia showed a faster rise of ferritin but equal rise in Hb in both iv and oral groups.[9] A meta analysis by Sultan P et al in 2019 for oral vs intravenous iron therapy for postpartum anemia concluded that iv iron produces faster response in Hb with less toxicity than oral iron and considered it a viable option for post partum anemia.[10] Abhyankar A et al in their meta analysis for iron replacement in patients with inflammatory bowel disease showed no significant difference in iv iron and oral iron regarding the increment in Hb.[5] StefanosB et al in their systematic review for intravenous Versus Oral Iron for the Treatment of Anemia in Inflammatory Bowel Disease showed better response with iv iron.[11,]In our study the mean difference between intravenous iron and oral iron Hb response at 3 weeks was 1.04g/dl. The tolerability of intravenous iron was excellent. Oral iron had significant GI side effects due to which many patients had to be shifted to intravenous iron. The oral iron group was the one who tolerated oral iron well. With a mean jump of 2.75g/dl at 3 weeks with intravenous iron , it is definitively a better option when a quicker response is desired.

Conclusion

Intravenous iron is safe and effective in the treatment of iron deficiency anemia . Intravenous iron sucrose is a most promising iron preparation for use because it is safe, effective and easy to administer. Prevents, unnecessary use of blood in iron deficiency anemia. Thus preventing transfusion related infection risk and morbidity.

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