EFFECT OF TOTAL DOSE PARENTERAL IRON ON CARDIOVSCULAR FUNCTION IN IRON DEFICIENCY ANEMIA

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ABSTRACT:

Introduction: Iron deficiency is a whole spectrum of clinical manifestation and abnormalities in the physiological functions of the body organs and tissues at rest or during stress, primarily or secondarily to iron deficiency.

Material and Methods: This study was conducted at a tertiary care hospital. A group of thirty five patients of iron deficiency anaemia who had a baseline change in their ECGs were selected. Iron deficiency anaemia was defined as haemoglobin< 10g/dl with a ferritin level of <30µg/L. The patients were then given the required total parenteral iron dose in the form of iron sucrose.

Results: The study noted a significant improvement in electrocardiogram of the patients. Twenty one of the thirty five patients had a normalization of their ECGs with best results seen with juvenile pattern, followed by occasional VPCs and ST-T changes showing the least improvement.

Discussion: An improvement was noted in ejection fractions the patients with a low ejection fraction compared to those with a higher ejection fraction. The study noted a significant improvement in the complaints such as fatigue, leg cramps and menorrhagia.

Conclusion: All these changes were however not associated with a significant increase in haemoglobin levels, thereby showing that iron per se has a significant role in the integrity of the cardiovascular system as well as in the metabolism of the cells in general.

INTRODUCTION

Iron is an essential element for the function of all body cells. It plays a critical role in cell-cycle regulation, electron transport in the respiratory chain, DNA synthesis and other metabolic reactions. Its availability is crucial for the functioning of oxygen binding molecules such as haemoglobin and myoglobin, and many iron containing enzymes including the cytochromes in the mitochondria[1].

Iron deficiency is the most common nutritional deficiency worldwide; it affects nearly 1.6 billion people[2]. Iron deficiency and iron deficiency anaemia are often encountered in the general population, particularly among children and women with abnormal uterine bleeding[3]. Menorrhagia, defined as blood loss of >80ml per menstrual cycle may result from systemic diseases or reproductive tract abnormalities[4]. Among women of reproductive age, the prevalence of abnormal uterine bleeding ranges between10% to 30%[5]. Iron deficiency anaemia is also commonly reported in patients with certain chronic conditions such as chronic kidney disease, inflammatory bowel disease, chemotherapy induced anaemia, chronic heart failure, trauma and as a consequence of certain surgical procedures.

Absolute iron deficiency is characterized by low serum ferritin levels (typically defined as ferritin levels <100 mcg/l) and low transferring saturation values (<20%). It is commonly encountered in patients who experience blood loss during chronic or acute illness or trauma, those with poor intake or decreased gastrointestinal absorption of iron from dietary sources, and those in whom physiological demand for iron is increased, such as pregnancy, infancy and adolescence[6].

Anaemia, defined by the WHO as haemoglobin<11g/dl is frequently seen in the postpartum period and affects 4-48% of women who gave birth. In one study, up to 30% of women in the postpartum period had anaemia and approximately 10% suffered from severe anaemia, with haemoglobin levels less than 9g/dl. Iron deficiency is the most common cause of post partum anaemia, and its prevalence is greatest in women from ethnic minorities and low income families.

While the major portion of iron exists in the body as haemoglobin, iron is also an important constituent of myoglobin in muscles and of various heme and non-heme iron dependent enzymes present in every cell, playing a vital role in cellular respiration and a host of other biochemical reactions. An appreciation of the essential role of iron in the normal

functioning of body tissue as a constitute of energy backbone required for various physiological processes would make one realize how some of the manifestations observed in patients of iron deficiency anaemia could be, and indeed are due to iron deficiency per se independent of the anaemia. These manifestations can occur with haemoglobin within a normal range. In order to emphasize the role of iron in physiological processes and to classify situations where clinically significant effects are seen due to iron deficiency in the absence of or independent to the anaemia, a concept of iron deficiency is essential. Iron deficiency can thus be defined as the whole spectrum of clinical manifestation and abnormalities in physiological functions of body organs and tissues at rest or during stress, primarily or secondarily to iron deficiency.

It has been adequately shown that in iron deficiency states, normal functioning of several body tissues such as myocardium, peripheral nerves, jejunum, brain, liver and kidney is significantly altered and that this is primarily as a result of iron deficiency at the cellular level. These adequately justify the broad concept of iron deficiency syndrome, a term which should replace the conventional but restricted term iron deficiency anaemia.

Several studies have consistently shown that iron deficiency per se and not anaemia is responsible for the deterioration of cardiac function in patients with iron deficiency anaemia as evidenced by improvements with parenteral iron therapy in such patients of electrocardiogram and 2Decho before significant rise in haemoglobin levels occur[7,8,9]. This study aims to consolidate these findings and to assess the actual role of iron over cardiovascular as well as other systems.Primary aim was to evaluate the improvement in electrocardiogram of patients with iron deficiency anemia, following parenteral iron therapy. Also to look for an improvement in ejection fraction of the left ventricle in patients with iron deficiency anemia, following parenteral iron therapy. We correlated these improvements with an increase in hemoglobin levels. Our secondary aims were to assess the effect of parenteral iron therapy on organs and organ systems other than cardiovascular system.

MATERIALS AND METHODOLOGY

This study was conducted at Sheth VS General Hospital, Ahmedabad, a tertiary care hospital. A group of thirty five patients of iron deficiency anaemia who had a baseline change in their electrocardiogram were selected.

Iron deficiency anaemia was defined as haemoglobin< 10g/dl with a ferritin level of <30µg/L. The patients were explained about the nature of their disease and the study and consent was taken for their participation in the study as well as for receiving intravenous iron sucrose. A baseline 2Decho was done for each patient and the patients were interviewed, examined and evaluated. The patients were then given the required total parenteral iron dose in the form of iron sucrose in divided doses of 200mg 12hrly under strict monitoring for vital signs and development of any adverse reactions.

The dose for the same was calculated using the following formula:

Iron requirement (mg) = [2.4 x body wt (kg) x (15-Hb in g/dl)] + 500 (for stores)

Twenty hours following the last dose of iron the patients were again assessed for symptomatic improvements/ worsening and adverse reactions. A fresh electrocardiogram and a follow up 2D Echo were performed in these patients and any changes therein were noted.

INCLUSION CRITERIA

1. Proven iron deficiency anaemia (as defined above)
2. Baseline electrocardiographic changes (occasional ventricular premature contraction, juvenile pattern, minimal ST-T changes)
3. Age between 25 and 60 years.

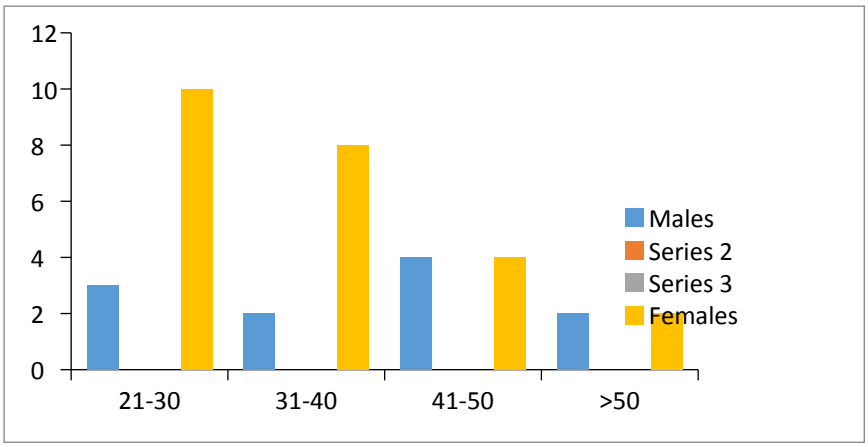
EXCLUSION CRITERIA

1. Anaemia of other causes (chronic disease, genetic defects, B12 deficiency, etc.)
2. Severe anaemia needing Blood transfusion
3. Age < 25 or > 60 years
4. Normal baseline electrocardiogram
5. Ischemic heart disease or serious arrhythmias on baseline electrocardiogram
6. Regional wall motion abnormalities on 2D Echo.
7. Patients who did not give consent for the study/intravenous iron therapy.

OBSERVATIONS AND RESULTS

The study consisted of 35 patients of which 24 were females and 11 were males. The mean age was 37.54 years.

Figure-1



The mean ferritin level of the patients was 15.05 and the mean haemoglobin of the study population was 8.41 g/dl at the start of the study which increased to 9.10 g/dl at the end of the study. (p>0.01, not significant)

Table-1

Haemoglobin (gm %)	**No. of patients (pre-study)**	**No. of patients(post-study)**
<8	12	8
8-8.99	13	10
≥9	10	17

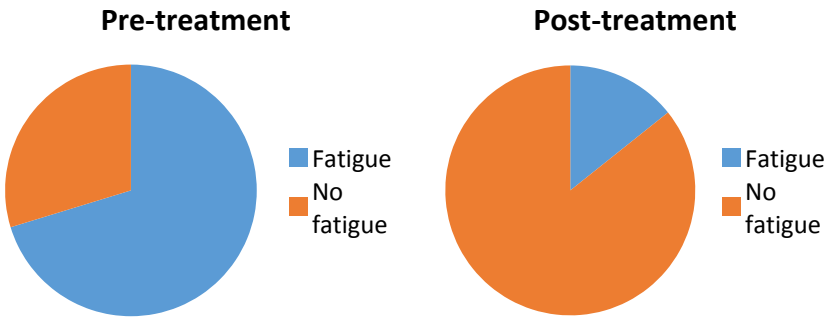
The three ECG changes included in the study included occasional VPCs, minimal ST-T changes and juvenile pattern. 21 of the 35 patients recorded a normalization of their ECGs. (p< 0.05, significant)

Table-2

	Pre-treatment	**Post-treatment**
VPCs	10	4
ST-T changes	10	6
Juvenile pattern	15	4

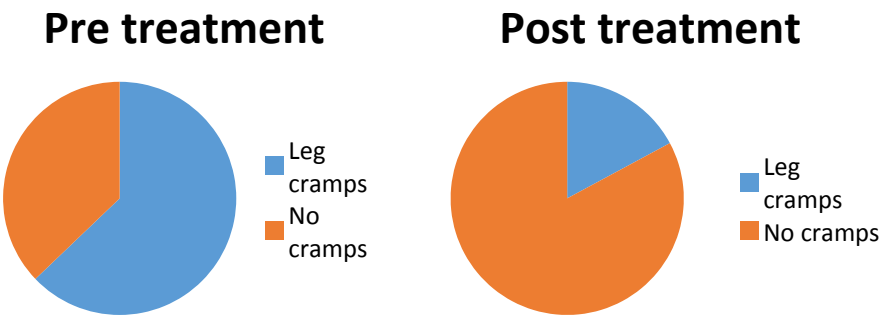
The following chart shows the EF% of the patients before and after IV iron therapy.

Figure-2



Sixteen of the twenty two patients who had leg cramps reported an improvement in their cramps whereas 6 patients noticed no change. ($p<0.01$, significant). Of the 20 patients having joint pain at the start of the study, 5 had an improvement, 9 had no change and 6 noted a worsening of their symptoms. ($p>0.01$, not significant).

Figure-3



All seven patients who had menorrhagia noticed an improvement in their symptom after intravenous iron treatment. ($p<0.01$, significant). Of the four patients with chest pain, two noticed an improvement while two noticed no change in their symptom. Eleven patients had gastrointestinal disturbance at the start of the study in the form of nausea, constipation or dyspepsia. Two patients noted an improvement; seven had the same symptoms, and two noticed worsening of the symptoms whereas eight previously unaffected patients noticed new symptoms.

SUMMARY AND CONCLUSION

35 patients with iron deficiency anaemia with electrocardiogram changes were included in this study to evaluate the cardiovascular effects of total dose parenteral iron therapy. The study noted a significant improvement in electrocardiogram status of the patients. 21 of the 35 patients had a normalization of their electrocardiogram with best results seen with juvenile pattern (11 out of 15), followed by occasional ventricular premature contraction (6 out of 10) and ST-T changes showing the least improvement (4 out of 10). No age or gender association was found for the same with patients of all age groups and both sexes noting equal improvements.

This findings are in correlation with studies conducted by Verghese et al, Pathare et al, Gardner et al, EJ Butchart et al and Mehta et al[10, 11].As far as ejection fractions were concerned an improvement was noted in the patients with a low ejection fraction compared to those with a higher ejection fraction, however the improvement was not found to be statistically significant.

This shows correlation with the findings of Alvares and Mahmood while in contrast to those of Bhadra as well as Sagouri[12,13]. However these studies evaluated an improvement in the ejection fraction of the test subjects 7 days after intravenous iron possibly resulting in the difference of results. The study also noted a significant improvement in the complaints such as fatigue, leg cramps and menorrhagia. No significant associations were noted in complaints like joint pain and chest pain whereas there was a worsening of gastrointestinal symptoms noted in the study population.

All these changes were however not associated with a significant increase in haemoglobin levels, thereby showing that iron per se has a significant role in the integrity of the cardiovascular system as well as in the metabolism of the cells in general.

This has been correlated with several studies including those by Mehra et al, Bhadra et al, Alvarez et al, Hall et al, Gregory et al and Lee et al[12,14,15,16].

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