Efficacy of Amino Acid Chelated Iron versus Ferrous Fumarate in Treatment of Iron Deficiency Anemia in Pregnancy: A Randomized Controlled Trial

Thesis

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List of Abbreviations

Abb.	Full term
AOAC	Association of analytical chemists
BMP	Bone morphogenic protein
Dcytb	Duodenal cytochrome-b
DMTI	Diovalent metal transporter-1
EPI	Expanded program of immunization
EPO	Erythropiotien
Fe II	Iron in ferrous form
Fe III	Iron in ferric form
Fe	Iron
Fe-s	Iron sulphur
FPNI	Ferro protein-1
Hb	Haemoglobin
Hbd	Haemoglobin-deficit
HCP1	Haem carrier protein-1
Hct	Haematocrite value
HJV	Hemojuvelin
HO1	Haemoxygenase-1
HP	Hephaestin
ID	Iron defiency
IDA	Iron deficiency anaemia
IRP	Iron regulatory protein
Lf	Lacto ferrin
LIP	Labile iron pool
MCHC	Mean corpuscular haemoglobin concentration
MCV	Mean corpuscular volume
MTf	Melano transferring
PIX	Protoporphyrin IX
Rc	Reticulocytic count
RDA	Recommended daily allowance
sHJV	Soluble Hemojuvelin
SMAD4	Signaling mothers against decapentaplegic homolog4
STAT3	Signal transducer and activator of transcription 3
Tf	Transferrin
TfR	Transferrin receptors
TfRI	Transferrin receptors 1

Abstract

The study was done through giving anaemic pregnant women iron therapy in the form of ferrous fumarate which represents group A arid amino acid chelated iron and it represents Group B.

For each pregnant woman, age, parity and gestational history were taken before treatment. All pregnant women took their allocated treatment regularly for eight weeks after diagnosis of iron deficiency anemia with hemoglobin level and serum ferritin level and followed up after four and eight weeks. Also, epigastric pain, diarrhea, constipation, nausea, vomiting or gastric distress reported to assess tolerability of the drugs.

Key words: Haematocrite value- Hemojuvelin- Iron deficiency anaemia- Hephaestin- Lacto ferrin

INTRODUCTION

The World Health Organization (WHO) defines anemia in pregnancy as a hemoglobin (Hb) concentration of < 11 g/dl. Iron deficiency anemia (IDA) is the most common type of anemia in pregnancy. The iron content of the body is normally kept constant by regulating the amount absorbed to balance the amount lost ***(WHO, 2011)***.

The WHO estimates that 46% of pregnant women in African region, 38% in Eastern Mediterranean region, 25% in European region and 24% in the region of the Americas are anemic mainly because of iron deficiency ***(WHO, 2011)***.

Anemia has a significant impact on the health of the fetus as well as that of the mother. It impairs the oxygen delivery through the placenta to the fetus and interferes with the normal intrauterine growth. Severe anemia can lead to palpitation, tachycardia, breathlessness, and increased cardiac output leading to cardiac stress, which can cause decompensation and cardiac failure ***(Sharma, 2003)***.

Almost all cases of iron deficiency anemia respond readily to treatment with iron supplementation, patients do not always respond adequately to oral iron therapy because of noncompliance due to side effects. Gastrointestinal disturbances characterized by colicky pain, nausea, vomiting, constipation,diarrhea and gastric distress may occur in patients taking iron preparations ***(Kambar et al., 2013)***.

The most widely recommended oral iron forms are ferrous salts such as ferrous sulphate, fumarate and gluconate; however, the use of these salts is limited by low and variable absorption, chelation by food products, and free radical-mediated mucosal luminal damage ***(Sharma, 2001)***.

Oral iron preparations for the correction of iron deficiency anemia also include Iron multi amino acid chelate and ferrous bisglycinate. Iron salts like ferrous fumarate is extensively prescribed for the prevention and treatment of iron deficiency. Results from iron supplementation studies have shown that iron absorption from iron amino acid chelate preparations are superior to that of iron salts preparations ***(Beard, 2000)***.

Amino acid chelated iron (ferrous bisglycinate 27 mg) is attached to two molecules of the amino acid glycine by a covalent bound. This configuration protects the iron from dietary inhibitors and intestinal interactions, which explains its high bioavailability ***(Youssef et al., 2014)***.

Ferrous bisglycinate 27 mg is marketed and claimed to have low gastrointestinal intolerance and therefore better patient compliance. Few of these newer preparations are also claimed to increase Hb level faster as well as improve iron storage better than conventionally used ferrous fumarate ***(Youssef et al., 2014)***.

AIM OF THE WORK

This study aimed to compare between the efficacy of amino acid chelated iron and ferrous fumarate in treatment of iron deficiency anemia during pregnancy.

Chapter One

IRON AND PREGNANCY

Iron Metabolism

Iron (Fe) is essential for life. It is essential for DNA synthesis, respiration and key metabolic reactions. The levels of iron in the cell must be delicately balanced, as iron loading leads to free radical damage by reacting with oxygen to generate hydroxyl radicals ***(Fleming et al., 2012).***

The understanding of iron metabolism was built around its absorption in the duodenum followed by its delivery to tissues through the plasma iron transport protein transferrin (Tf). Transferrin binds to transferrin receptor-l (TfRl) on the cell membrane and is internalized by receptor- mediated endocytosis. Iron is then used for cellular processes, and excess iron is stored within the protein ferritin ***(Hentze et al., 2004)***.Cellular iron levels are post-transcriptionally controlled by iron regulatory protein IRP-1 and IRP-2 ***(Smith et al., 2006)***.

When cells are iron-deficient, IRP-l and IRP-2 bind to iron responsive elements in certain regions of mRNA transcripts of molecules such as the TfR 1or ferritin, stabilizing them against degradation or inhibiting translation, respectively ***(Romney et al., 2011)***.

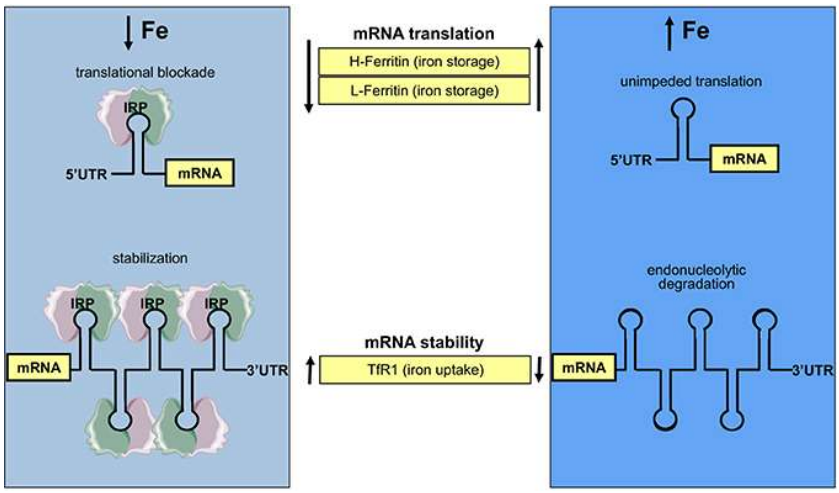

Figure (1): Coordinate iron-dependent regulation of ferritin and TfR1 mRNA expression by IRE/IRP interactions. Iron deficiency promotes the binding of IRPs to cognate IREs in the untranslated regions of ferritin and TfR1 mRNAs. These inhibit ferritin mRNA translation and stabilize TfR1 mRNA against endonucleolytic degradation. In iron-replete cells, IRPs do not bind to IREs, allowing ferritin mRNA translation and TfR1 mRNA degradation ***(Rouault, 2006).***

This results in increased cellular iron uptake through the TfRl and decreased intracellular iron storage within ferritin, leading to elevated levels of intracellular iron. This straight forward version of events has been renewed in the last decade by the discovery of many new proteins that mediate iron transport and its metabolism. The proteins ferroportin-l (FPNl) ***(Donovan et al., 2005)***, hepcidin ***(Lesbordes-Brion et al., 2006)***, hemojuvelin (HJV) ***(Huang et al., 2005)***, transferrin receptor-2 (TfR2) ***(Wallce et al., 2005)*** and hemochromatosis gene product, have led to a large shift in our perception of iron homeostasis. Animal models have been crucial in discovering the roles of these molecules in iron homeostasis and disease, whereas