Research Article

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Hemaros Tablets: Nutritional Support for Iron Deficiency in Pregnant women

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ABSTRACT

Anemia in pregnancy is defined by the World Health Organization as hemoglobin levels of ≤ 11 g/dl. Globally, a prevalence rate of 38% was estimated by the World Health Organization for pregnant women. To assess the safety, efficacy, tolerability of oral ferrous bis-glycinate in pregnant women in the treatment of iron deficiency anemia (IDA)[16]. Ferrous bisglycinate is an iron amino acid chelate. It is formed by reaction of ferrous iron with two molecules of the amino acid glycine by a covalent bound in a process called chelation. Ferrous bisglycinate is claimed to have better patient compliance because of fewer gastrointestinal tract side effects[1]. During pregnancy, more iron is needed primarily to supply the growing fetus and placenta and to increase the maternal red cell mass. Hemaros™ is containing of ferrous bisglycinate which very effective for iron supplementation for iron deficiency anemia IDA[2]. Pregnant women with second trimester IDA could be supplied with ferrous *bis*-glycinate which is more efficient in increasing HB level. Moreover, it has tolerable adverse effects and high compliance than ferrous glycine sulfate.

Keywords: Anemia, iron deficiency, pregnancy, maternal mortality, birth weight, preterm delivery, infants.

INTRODUCTION

Anemia in pregnancy is defined by the World Health Organization as hemoglobin levels of ≤ 11 g/dl. Globally, a prevalence rate of 38% was estimated by the World Health Organization for pregnant women. Treatment of iron deficiency anemia during pregnancy remains a main public health issue. Oral iron salts have been recommended for treatment of iron deficiency anemia e.g. ferrous fumarate[3]. Increasing the dose of ferrous fumarate will subsequently increase the bioavailability of iron preparation, however it also increases the frequency of gastrointestinal tract side effects e.g. nausea, constipation, diarrhea, flatulence, and black stained stools. Besides, the increased bioavailable ferrous fumarate may decrease by many foods and / or chelating drugs in the gastrointestinal tract which interfere with its absorption leading to variability in the hemoglobin correction during the treatment. Ferrous bisglycinate is an iron amino acid chelate. It is formed by reaction of ferrous iron with two molecules of the amino acid glycine by a covalent bound in a process called chelation. Ferrous bisglycinate is claimed to have better patient compliance because of fewer gastrointestinal tract side effects[4]. It is also claimed that ferrous bisglycinate improves iron absorption, storage and increase hemoglobin level better than the conventionally used iron salts.

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Fig 1
Iron deficiency anemia affects the fetus and the pregnant mother

Iron deficiency anemia affects the fetus and the pregnant mother leading to impairment in oxygen supply to the fetus favoring the development of fetal hypoxia which has been associated with prematurity, low birth weight and neonatal and perinatal death[5]. The increased need of iron during pregnancy, especially after the second trimester, makes iron supplementation mandatory. ferrous sulfate supplementation shows low efficacy for the control of iron deficiency anemia due to poor compliance with the treatment because of its disagreeable[17].

Symptoms of iron deficiency during pregnancy

- Fatigue
- Weakness
- Pale or yellowish skin
- Irregular heartbeats
- Shortness of breath
- Dizziness or lightheadedness
- Chest pain
- Cold hands and feet
- Headache

Types of Anemia During Pregnancy

Several types of anemia can develop during pregnancy. These include

- Iron-deficiency anemia
- Folate-deficiency anemia
- Vitamin B12 deficiency

Here's why these types of anemia may develop

Iron-deficiency anemia

This type of anemia occurs when the body doesn't have enough iron to produce adequate amounts of hemoglobin[6]. That's a protein in red blood cells. It carries oxygen from the lungs to the rest of the body. In iron-deficiency anemia, the blood cannot carry enough oxygen to tissues throughout the body. Iron deficiency is the most common cause of anemia in pregnancy.

Folate-deficiency anemia

Folate is the vitamin found naturally in certain foods like green leafy vegetables A type of B vitamin, the body needs folate to produce new cells, including healthy red blood cells.During pregnancy, women need extra folate. But sometimes they don't get enough from their diet. When that happens, the body can't make enough normal red blood cells to transport oxygen to tissues throughout the body[6]. Man-made supplements of folate are called folic acid.Folate deficiency can directly contribute to certain types of birth defects, such as neural tube abnormalities (spina bifida) and low birth weight.

Vitamin B12 deficiency

The body needs vitamin B12 to form healthy red blood cells. When a pregnant woman doesn't get enough vitamin B12 from her diet, her body can't produce enough healthy red blood cells[7]. Women who don't eat meat, poultry, dairy products, and eggs have a greater risk of developing vitamin B12 deficiency, which may contribute to birth defects, such as neural tube abnormalities, and could lead to preterm labor. Blood loss during and after delivery can also cause anemia.During pregnancy, hemoglobinopathies, particularly sickle cell disease, Hb S-C disease, and beta- and alpha-thalassemia, can worsen maternal and perinatal

outcomes. Genetic screening genetic screening for some of these disorders is available.

Risk factors for iron deficiency anemia during pregnancy

- Have two closely spaced pregnancies
- Are pregnant with more than one baby
- Are vomiting frequently due to morning sickness
- Don't consume enough iron
- Have a heavy pre-pregnancy menstrual flow
- Have a history of anemia before your pregnancy

Other Causes for Iron Deficiency:

- Hemoglobinopathies
- Sickle cell disease
- Sickle cell–beta-thalassemia
- Alpha-thalassemia

Hemoglobinopathies

Hemoglobinopathies are genetic disorders affecting the structure or production of the hemoglobin molecule[8]. Hemoglobin molecules consist of polypeptide chains whose chemical structure is genetically controlled.

Sickle cell disease[11]

Particularly if severe, increases risk of the following:

- Maternal infection (most often, pneumonia, urinary tract infections [UTIs], and endometritis)
- Pregnancy-induced hypertension
- Heart failure
- Pulmonary infarction
- Fetal growth restriction
- Preterm delivery
- Low birth weight

Anemia almost always becomes more severe as pregnancy progresses. Sickle cell trait increases the risk of UTIs but is not associated with severe pregnancy-related complications.

Sickle cell–beta-thalassemia: is similar to Hb S-C disease but is less common and more benign.

Alpha-thalassemia: does not cause maternal morbidity, but if the fetus is homozygous, hydrops and fetal death occur during the 2nd or early 3rd trimester[9].

AIMAND OBJECTIVE

Aim:

The aim of this study is to ensure the safety, efficacy, tolerability and absorption of oral ferrous bis-glycinate in pregnant women in the treatment of iron deficiency anemia (IDA).

Objective:

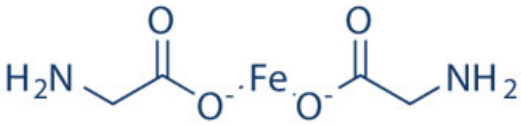
To assess the safety, efficacy, tolerability of oral ferrous bis-glycinate in pregnant women in the treatment of iron deficiency anemia (IDA).

NUTRITIONAL PROFILE

Ferrous bisglycinate

Ferrous bisglycinate is a chelate that is used as a source of dietary iron. Forming a ring structure when reacting with glycine, ferrous bisglycinate acts as both a chelate and a nutritionally functional[9]. It is found in foods for food enrichment or in supplements for the treatment of iron deficiency or iron deficiency anemia.

Structure



Structure of Hemoglobin

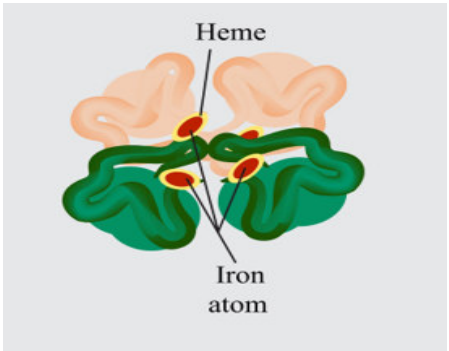


Fig 2
Hemoglobin

Mechanism of Action of Ferrous Bis-Glycinate

With ferrous bisglycinate two molecules of the amino acid glycine are bound covalently to a molecule of iron. This novel type of iron is absorbed like an amino acid by the cells of the small intestine without the usual irritation and constipation of other forms. In addition, there seems to be a mechanism that controls absorption,determined by blood hemoglobin levels.To treat iron-deficiency anemia.

Benefits of Chelation

Chelated iron amino acid complex is the bonding of iron to an amino acid, making it easier for the body to absorb and utilize it. No reaction with food ingredients, providing more of the iron potentially for absorption[12]. Preferentially absorption into the intestinal cells in greater quantities.

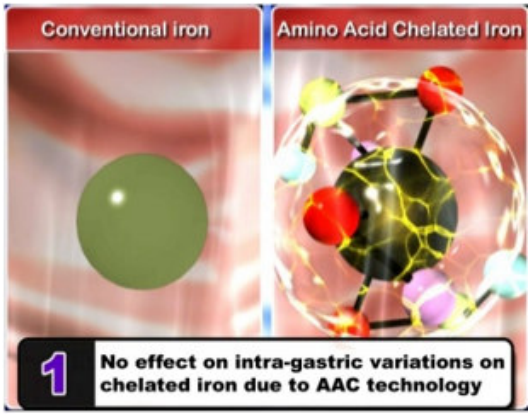


Fig 3

Chelation

Chelation gives protection to the iron by limiting its reactivity with dietary components or gastric acid.

Pharmacology

Iron usually exists in the ferrous (Fe2+) or ferric (Fe3+) state, but since Fe2+ is readily oxidized to Fe3+, which in neutral aqueous solutions rapidly hydrolyzes to insoluble iron (III)-hydroxides, iron is transported and stored bound to proteins. Ferritin is an iron-storage protein that sequesters iron keeping it in a readily available form. About 60% of iron is found in the erythrocytes within hemoglobin, the oxygen transport protein[4]. The remainder is found in myoglobin in the muscles, in a variety of different enzymes ('heme' and 'non-heme'), and in storage form. Most stored iron is in the form of ferritin, found in the liver, bone marrow, spleen and muscles. Serum iron (i.e., iron bound to transferrin) represents only a very small proportion of total body iron (<0.2%). Moreover, the relationship between physiological iron compartments is highly dynamic: Erythrocytes are broken down in the liver and in the spleen, and new red blood cells are produced in the bone marrow.

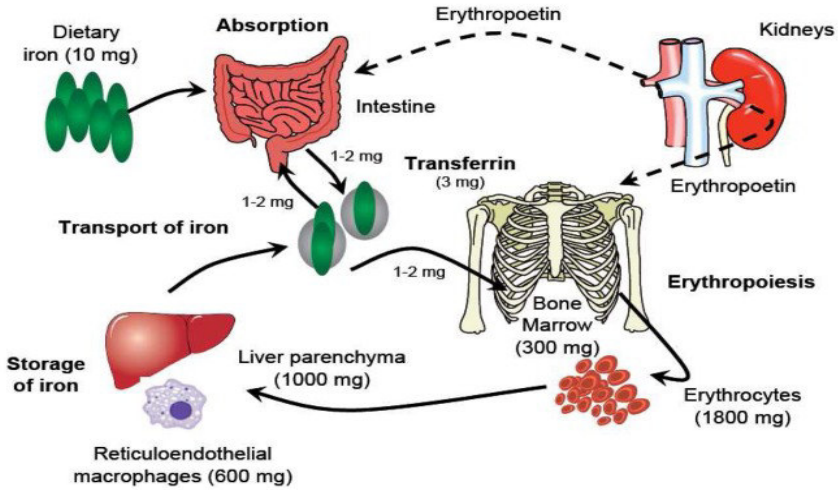


Fig 4

Literature review

The aim of this study is to compare the efficacy and tolerability of oral ferrous bis-glycinate versus ferrous glycine sulfate in the treatment of iron deficiency anemia (IDA) with pregnancy. Methods: A randomized double-blind clinical trial (NCT02590224) conducted at a tertiary University Hospital in the period between 1 January 2016 and 31 July 2017 included pregnant women at 14-18 weeks of gestation with mild to moderate IDA. Patients were randomized into two groups: (Group I) received oral ferrous bis-glycinate tablets once daily for eight consecutive weeks and (Group II) received oral ferrous glycine sulfate capsules in the same dose and duration[7]. The primary outcome of the study was the rate of increase of hemoglobin (HB) level after 8 weeks of iron treatment. Results: The study included 187 women in the final analysis. The mean increase in HB level after 8 weeks of treatment in ferrous bis-glycinate group was 2.48 ± 0.12 g/dL versus 1.32 ± 0.18 g/dL in ferrous glycine sulfate group ($p \leq .0001$). The percentage of women with HB level more than 11 g/dL after 8 weeks of treatment was 89.2% in ferrous bis-glycinate group versus 71.3% in ferrous glycine sulfate group ($p < .0001$). The rate of adverse effects was significantly higher in ferrous glycine sulfate group ($p = .001$). Conclusions: Pregnant women with second trimester IDA could be supplied with ferrous bis-glycinate which is more efficient in increasing HB level. Moreover, it has tolerable adverse effects and high compliance than ferrous glycine sulfate.[1]

Iron deficiency anemia during pregnancy is a significant worldwide health problem, affecting 22% of pregnant women in industrialized countries and 52% in non-industrialized countries. Iron deficiency anemia during pregnancy is associated with increased maternal as well as fetal morbidity, including prematurity, low birth-weight and perinatal and infant loss. Therefore, routine iron supplementation during the second half of pregnancy has been recommended once daily. Others, however, support a selective iron supplementation only for women with iron deficiency anemia, in order to avoid the increased risk of haemo concentration associated with routine iron supplementation. Unfortunately, compliance to either iron-supplementation programs, especially among pregnant women, is poor, due in part to the side effects associated with these preparations. Currently, there are many iron preparations available containing different types of iron salts, including ferrous sulfate, ferrous fumarate, ferrous ascorbate but common adverse drug reactions found with these preparations are mainly gastrointestinal intolerance like nausea, vomiting, constipation, diarrhea, abdominal pain, while ferrous bis-glycinate (fully reacted chelated amino acid form of iron) rarely make complication. Product resulting from the reaction of a metal ion from a soluble salt with amino acids to form coordinate covalent bonds, the resulting molecule is called as chelate and chemical bonding process is called chelation. Ferrous bis-glycinate is highly stable and totally nutritionally functional chelate it is an amino acid fully reacted chelate which is formed by the binding of two molecules of glycine to one $Fe2+$ atom.[2]

This article reviews current knowledge of the effects of maternal anemia and iron deficiency on pregnancy outcome. A considerable amount of information remains to be learned about the benefits of maternal iron supplementation on the health and iron status of the mother and her child during pregnancy and postpartum. Current knowledge indicates that iron deficiency anemia in pregnancy is a risk factor for preterm delivery and subsequent low birth weight, and possibly for inferior neonatal health. Data are inadequate to determine the extent to which maternal anemia might contribute to maternal mortality. Even for women who enter pregnancy with reasonable iron stores, iron supplements improve iron status during pregnancy and for a considerable length of time postpartum, thus providing some protection against iron deficiency in the subsequent pregnancy. Mounting evidence indicates that maternal iron deficiency in pregnancy reduces fetal iron stores, perhaps well into the first year of life. This deserves further exploration because of the tendency of infants to develop iron deficiency anemia and because of the documented adverse consequences of this condition on infant development. The weight of evidence supports the advisability of routine iron supplementation during pregnancy.[3]

RESULTS

Ferrous bisglycinate is an iron amino acid chelate. It is formed by reaction of ferrous iron with two molecules of the

amino acid glycine by a covalent bound in a process called chelation. Ferrous bisglycinate is claimed to have better patient compliance because of fewer gastrointestinal tract side effects. It is also claimed that ferrous bisglycinate improves iron absorption, storage and increase hemoglobin level better than the conventionally used iron salts.Hemaros™ is containing of ferrous bisglycinate which very effective for iron supplementation for iron deficiency anemia IDA. ferrous bisglycinate is Chelated iron amino acid complex is the bonding of iron to an amino acid, making it easier for the body to absorb and utilize it.

CONCLUSIONS

Pregnant women with second trimester IDA could be supplied with ferrous *bis*-glycinate which is more efficient in increasing HB level. Moreover, it has tolerable adverse effects and high compliance than ferrous glycine sulfate.

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