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IMPACT OF HEMATOLOGICAL STATUS FOR ANEMIA OF PREGANCY

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Abstract

Anemia of pregnancy remains highly prevalent in Senegal despite the national iron/folic acid (IFA) supplementation program, which consists of providing prescriptions to purchase IFA to women during prenatal visits. The purpose of this study was to provide a framework for recommendations to improve the effectiveness of the program. We determined the prevalence and risk factors of anemia in a cohort of 480 pregnant women at 6 prenatal health centers in Dakar; we compared compliance after 20 weeks of supplementation between women who received prescriptions at 3 control centers and those who received free IFA at 3 intervention centers; and we assessed the factors that influenced high and low compliance in both groups. Overall, 39% of women were anemic and 71% were iron deficient (ID). Twelve percent were infected with P. falciparum; 21% had intestinal helminthes, and 6.5% had Hb AS. Women consumed foods containing iron absorption inhibitors at high frequency.

Keywords: *Supplementation, Anemia, Pregnancy*

Introduction: Women with high compliance were motivated by 1) the perception of improved health upon taking the tablets, 2) the insistence by midwives that they take them, and 3) the mention that the tablets would improve health. Women with low compliance indicated 1) experiencing side effects that they associated with the tablets, 2) misunderstanding that they needed to continue taking the tablets throughout pregnancy, and 3) forgetfulness.

Our findings indicate that for effective control of anemia in Senegal, iron supplementation is needed in addition to educating women about better food choices. Antimalarial chemoprophylaxis and helminthes screening should be made available to all women. In addition, increasing access to IFA and educating women about the health benefits of the tablets can dramatically increase compliance and therefore improve iron status and decrease the incidence of anemia.

It was in the 1970's that iron deficiency was identified as the leading singlenutrient deficiency worldwide. Today, at the dawn of the 21st century, iron deficiency still affects more than 2 billion people around the world despite the numerous and extensive strategies used to decrease its prevalence (1, 2).

The pathogenesis of iron deficiency can be divided in three stages. The earliest stage involves the loss of iron stores without a decrease in the iron supply to red blood cells (RBC). Continued deficiency leads to iron-deficient erythropoiesis (decline in the iron supply to RBCs), which nevertheless does not affect circulating hemoglobin (Hb) levels. A continued loss of iron or lack of replenishment of iron stores results in the third and final stage, which is termed iron deficiency anemia (3). Anemia can therefore be defined as a state in which the number of RBCs, the quantity of Hb, or the volume of packed red cells (hematocrit) in blood is reduced below normal levels (4).

Even though iron deficiency is the most common cause of nutritional anemia among pregnant women, it is not the only cause, especially in developing countries. These causes include deficiencies in other hematopoeitic nutrients such as folate and vitamin B12 (10-13), deficiencies in vitamin A (14), genetic diseases causing hemolysis (sickle cell and thalassemias) (15), concurrent infections and inflammations (16-18), Malaria (19), and parasitic infections that cause gastrointestinal blood loss: Acylostomaduodenale, Necatoramericanus, Trichuristrichiria, Ascarislumbricoides, and Schistosomes (20). Anemia during pregnancy and specifically iron deficiency anemia during the first and second trimesters of gestation increases the risk of low birth weight (LBW) and preterm delivery, which are the strongest predictors of perinatal mortality.

Research Study

The main objective of this study was to assess the effectiveness of the Senegalese supplementation program and to provide a framework for recommendations for improvement, if necessary. We assessed the prevalence and major risk factors for anemia in a cohort of pregnant women attending health centers for prenatal care in order to evaluate the efficacy of iron/folic acid tablets alone in raising Hb concentration when causes of anemia other than iron deficiency may be prevalent in this population.

We then determined compliance with supplementation and compared it with that of women who received iron/folic acid tablets free of charge during the prenatal visit. We hypothesized that giving women iron/folic acid tablets during the prenatal visit rather than merely prescribing the tablets for purchase would eliminate some of the known barriers to program success. The net effect would be an increase in compliance and therefore improved iron status, and decreased incidence and prevalence of anemia among pregnant women. Lastly, we

determined the factors that influence compliance in this population because understanding these factors can be the basis of recommendations to improve patient care and counseling.

The role of iron in the human body

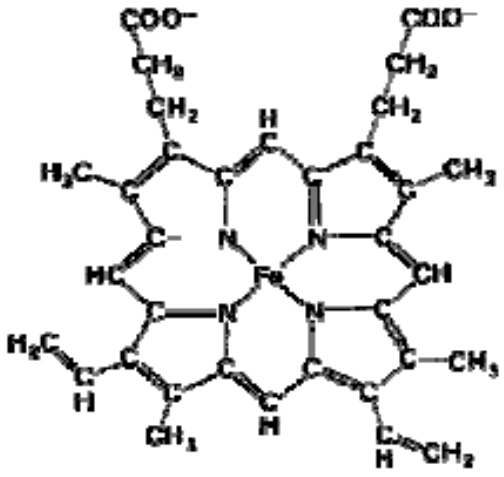
Iron is an essential mineral in the metabolism of all living organisms. The most important iron-containing compounds in the body are the heme proteins hemoglobin (Hb), myoglobin (Mb), and cytochromes, which have an iron-protoporphyrin prosthetic group. Iron is bound at the center of the heme group (Figure 1), which is the site of oxygen uptake by Hb and Mb. In turn, Hb plays an important role in transferring oxygen from the lungs to tissues, while the primary function of myoglobin is to transport and store oxygen within muscles. Cytochromes are critical to respiration and energy metabolism through their role in mitochondrial electron transport. Thus, iron plays central roles in energy metabolism and electron transfer.

Total body iron averages 4.0 g for men and 2.5 g for women. Seventy five percent of this iron is in the functional form mostly as Hb in circulating RBCs and 15% as Mb. The remaining 10% of body iron is in storage form in the liver, the reticuloendothelial cells, and bone marrow; storage iron exists in the form of two proteins, ferritin and hemosiderin.

Iron digestion and absorption

Iron bioavailability from foods varies widely. It is greatest from mammalian meat, less from poultry or fish, and least from liver, eggs, milk, and foods of plant origin such as legumes. This difference in absorbability of iron is related to the difference between heme and non-heme iron, which form different iron pools in the body. Nonheme iron consists mostly of iron salts; it is found mainly in plants, dairy products, and iron-fortified foods. More than 85% of the human diet consists of this form of iron. Heme iron is mostly found in Hb in meat, poultry, and fish. Although heme iron is less 7 frequent in our diet than non-heme iron, the former is 2 to 3 times better absorbed than the latter (34).

Figure 1: The chemical structure of heme



In meats of mammalian origin, iron in the ferric form (Fe 3+) is complexed with the heme groups of Hb and Mb. Prior to absorption, the heme group is hydrolyzed from the globin portion of Hb and/or Mb by proteases in the stomach. The acidity in the stomach reduces Fe 3+ to the ferrous form (Fe 2+), which dissociates from ligands more readily than Fe 3+ . In the small intestine, further hydrolysis of the heme complex by proteases occurs and because of the alkaline environment, heme is readily absorbed in the duodenum and upper jejunum.

Within the mucosal cell, hemeoxygenase liberates iron from the protoporphyrin ring of heme. Iron is then transferred successively to the cytosolic proteins mobilferrin and paraferritin. It is then transported to the serosal surface of the cell and enters circulation via the basolateral transporter known as ferroportin. As it enters the blood, iron is oxidized by ceruloplasmin to Fe 3+ and then binds to transferrin.

The digestion and absorption of non-heme iron differs from that of heme iron, which accounts for the difference in bioavailability. Stomach secretions and hydrochloric acid that release non-heme iron from food components are thought to delay or prevent its reduction to the ferrous state; this means that iron dissociates less readily from its ligands and is therefore less readily absorbed. Non-heme iron is taken up by one or more proteins of the luminal surface of the mucosal epithelium of the duodenum, including a transporter protein called divalent metal transporter 1 (DMT1) which facilitates transfer of iron across the intestinal epithelial cells.

Once inside the cell, Fe 3+ is reduced to Fe 2+ and absorption continues as described above. Non-heme iron absorption can be 8 enhanced or hindered by food components ingested in the same meal. Some chelators that increase absorption are ascorbic acid and other undefined factors contained in meat, fish, and poultry. Non-heme iron absorption from a meal containing meat, fish, or poultry is about 4 times greater than that from a meal containing equivalent portions of milk, cheese, or eggs.

Some chelators that decrease absorption are tannins (contained in tea), phosvitin (contained in egg yolk), calcium and phosphate salts, and phytates in cereals. Diets poor in heme iron and rich in iron absorption inhibitors have been documented all over sub-Saharan Africa. The staples in Senegal are white rice and millet, which are high in phytates. The Senegalese diet also includes a high consumption of green and black tea.

Iron transport and metabolism

Regardless of which form of iron is ingested, once absorbed, iron either remains in the mucosal cells for intestinal use or is bound by the glycoprotein transferrin for transport through the bloodstream to other body tissues (under normal conditions, transferrin binding sites are about 20 to 45% saturated with iron). Most of the absorbed iron is transported to the bone marrow where Hb is formed in RBCs and later released into circulating blood.

RBCs have a life span of 120 days; to replace each 1/120 of erythrocytes, the daily iron turnover for an adult is about 20 mg. Most of the iron from hemolysis is recaptured for the synthesis of Hb. A smaller portion of iron enters iron stores as ferritin and hemosiderin in many organs, as myoglobin in the muscle cells, and as iron in cytochromes and cytochrome oxidase. An even smaller portion of iron remains bound to transferrin.

The pathogenesis of iron deficiency

When dietary iron intake is inadequate or when the diet is high in non-heme iron and iron absorption inhibitors over a significant period of time, the process of iron deficiency begins with depletion of iron stores and impaired iron supply to various tissues. During this phase of deficiency, the continuous supply of iron for erythropoiesis is adequate but no iron reserves exist to cover short-term needs. Generally, no clinical symptoms are noted at this point. If iron deficiency persists, the second stage of physiological iron deficiency ensues. This stage is characterized by an impairment of erythropoiesis with little if any effect on circulating red blood cells.

Some clinical symptoms may be seen in this stage. The third and last stage of iron deficiency, when left untreated, is anemia where the impairment of erythropoiesis is so severe that the number of RBCs is reduced, Hb concentration, and hematocrit concentration fall below normal levels.

Assessment of iron status

Iron status can be measured using hematological and biochemical indices. Each iron status index reflects changes in different body iron compartments and is affected at different levels of iron depletion. Serum ferritin (SF) is directly proportional to body iron stores in normal individuals. Quantitative phlebotomy studies indicate that 1 µg/L SF is equivalent to 8-10 mg of stored iron for an average-sized adult. SF is considered the most specific test for iron deficiency because very low levels of the protein are almost always indicative of low iron stores.

Enzyme-linked immunosorbent assay (ELISA) with colorimetric fluorescent or chemoluminescent end points is widely used to measure SF. The SF cutoff commonly used to identify low iron stores is 20 µg/L even in the presence of advanced iron deficiency. The acute phase response is a short-term metabolic change characterized by increased plasma concentrations of certain proteins, such as C-reactive protein (CRP) [CRP >190 nmol/L is considered elevated] and haptoglobin, and decreased concentrations of other proteins, such as albumin and retinol binding protein. The 11 inflammatory response may last for several days or several weeks and months, in which case it is termed "chronic inflammation".

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