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Iron Deficiency Anemia: A Review

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ABSTRACT:

Anemia is a group of diseases characterized by a either hemoglobin or the volume of red blood cells, which results in decreased oxygen carrying capacity of the blood. Iron deficiency is the most common nutritional cause of anemia in humans. It can result from inadequate iron intake, malabsorption, blood loss, or an increased requirement, as with pregnancy. When severe, it results in a characteristic microcytic, hypochromic anemia.Iron deficiency can affect metabolism in muscle independent of the effect of anemia on O_2 delivery, possibly due to a reduction in the activity of iron-dependent mitochondrial enzymes.During adulthood, iron stores gradually increase in men; in women, stores start to increase after menopause. Total body iron averages about 3.8 g in men and 2.3 g in women. Iron product which was based on biological background having excellent efficiency were banned due to some regulatory reasons.The iron products that are currently available in the market are totally traditional, based on conventional concepts and do not employ any innovative technology. Artificial iron salts containing formulation are not as efficient as formulation containing biological background (RBC concentrate). Thus there is a wide scope to develop a newer innovative hematinic formulation which can be as efficient as product containing biological background.

KEY WORDS: Iron deficiency anemia, hemoglobin, iron, hematinic.

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INTRODUCTION:

In the earth's crust iron is one of the most abundant elements. Most of the iron is present in the hemoglobin molecule. Hence, anemia is the characteristic feature of iron deficiency[1]. Iron deficiency is the most common form of malnutrition in the world, affecting more than 2 billion people globally. Iron deficiency anemia (inadequate amount of red blood cells caused by lack of iron) is highly prevalent in less-developed countries but also remains a problem in developed countries where other forms of malnutrition have already been virtually eliminated. Iron deficiency is not the only cause of anemia, but where anemia is prevalent, iron deficiency is usually the most common cause. The prevalence of anemia, defined by low hemoglobin or hematocrit, is commonly used to assess the severity of iron deficiency in a population[2].

Iron deficiency is the most common nutritional cause of anemia in humans. It can result from inadequate iron intake, malabsorption, blood loss, or an increased requirement, as with pregnancy. When severe, it results in a characteristic microcytic, hypochromic anemia. Iron is an essential component of myoglobin; heme enzymes such as the cytochromes, catalase, and peroxidase; and the metalloflavoprotein enzymes, including xanthine oxidase and the mitochondrial enzyme *a*-glycerophosphate oxidase. Iron deficiency can affect metabolism in muscle independent of the effect of anemia on O_2 delivery, possibly due to a reduction in the activity of iron-dependent mitochondrial enzymes. Iron deficiency also has been associated with behavioral and learning problems in children, abnormalities in catecholamine metabolism, and impaired heat production[3]**.**Iron deficiency anemia, a reduction in the hemoglobin concentration of oxygen-carrying capacity of blood. Anemia is characterized by loss of appetite, abdominal pains, tiredness, shortness of breath and headaches. Iron deficiency may result from lack of iron in the diet, inadequate absorption from the gut, or losses, usually through bleeding. For example: Iron deficiency anemia affects 10-15 percent of women of menstruating age because the iron they lose in menstrual blood exceeds the iron obtained from food. Therefore, women with high menstrual losses may need higher iron intakes. Too much iron is toxic. An excess can damage the heart, liver, and pancreas, and irritate the gut causing constipation or diarrhea[4].

During adulthood, iron stores gradually increase in men; in women, stores start to increase after menopause. Total body iron averages about 3.8 g in men and 2.3 g in women. The extraordinary capacity of the human body to retain iron (15–40 g) is exhibited in individuals with hemochromatosis. About one third of the total body iron is bound to storage proteins, primarily ferritin or hemosiderin in the liver, spleen, and bone marrow. About two thirds of the total body iron serves metabolic or enzymatic functions[5].

In modern society, the oral iron supplements are clearly needed in the treatment and prevention of iron deficiency in humans.In fact, the diet of most of the world's population is deficient in iron and so iron deficiency has been a worldwide problem. A new oral supplement is needed. Presently available oral supplements are ferrous salts whose side effects can include epigastric pain, diarrhea and constipation, which can often be severe enough to cause the termination of treatment[6].

Iron is required for a number of vital functions which include: oxidative metabolism, reproduction, cellular growth, wound healing, execution of various metabolic processes. The main role of Iron is to carry oxygen to the tissue where it is needed. It is also essential for the proper functioning of numerous enzymes involve in DNA synthesis, energy me-tabolism, and protection against microbes and free radicals, because free radical produced in the body can promote the development of heart diseases and can damage cholesterol in the blood.There are two forms of dietary iron: heme and non-heme. The heme is derived from hemoglobin, heme iron is found originally in animal food that originally contains hemoglobin such as fish and poultry. Iron in plant foods such as lentils and beans is arranged in a chemical structure called non-hemeiron. This is the form of iron added to iron-enriched and iron-fortified foods. Heme iron is absorbed better than non-heme iron, but most dietary iron is non-heme iron[4].

BLOOD:

Blood is a connective tissue. It provides one of the means of communication between the cells of different parts of the body and the external environment, e.g. it carries:

- Oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs for excretion
- Nutrients from the alimentary tract to the tissues and cell wastes to the excretory organs, principally the kidneys
- Hormones secreted by endocrine glands to their target glands and tissues
- Heat produced in active tissues to other less active tissues
- Protective substances, e.g. antibodies, to areas of infection
- Clotting factors that coagulate blood, minimizing its loss from ruptured blood vessels.

Blood makes up about 7% of body weight (about 5.6 litres in a 70 kg man). This proportion is less in women and considerably greater in children, gradually decreasing until the adult level is reached.Blood in the blood vessels is always in motion. The continual flow maintains a fairly constant environment for the body cells.Blood volume and the concentration of its many constituents are kept within narrow limits by homeostatic mechanisms[7].

GENERAL COMPOSITION OF THE BLOOD:

Blood is composed of a straw-coloured transparent fluid, *plasma*, in which different types of cells are suspended. Plasma constitutes about 55% and cells about 45% of blood volume.

Plasma

The constituents of plasma are water (90 to 92%) and dissolved substances, including:

- Plasma proteins: albumins, globulins (including *antibodies)*, fibrinogen, clotting factors
- Inorganic salts (mineral salts): sodium chloride, sodium bicarbonate, potassium, magnesium, phosphate, iron, calcium, copper, iodine, cobalt
- Nutrients, principally from digested foods, e.g. monosaccharides (mainly glucose), amino acids, fatty acids, glycerol and vitamins
- Organic waste materials, e.g. urea, uric acid, creatinine
- Hormones
- Enzymes, e.g. certain clotting factors
- Gases, e.g. oxygen, carbon dioxide, nitrogen.

Plasma proteins

Plasma proteins, which make up about 7% of plasma, are normally retained within the blood, because they are too big to escape through the capillary pores into the tissues. They are largely responsible for creating the osmotic pressure of blood (normally 25 mmHg), which keeps plasma fluid within the circulation. If plasma protein levels fall, because of either reduced production or loss from the blood vessels, osmotic pressure is also reduced, and fluid moves into the tissues (oedema) and body cavities.

Albumins

These are formed in the liver. They are the most abundant plasma proteins and their main function is to maintain a normal plasma osmotic pressure. Albumins also act as carrier molecules for lipids and steroid hormones.

Globulins

Most are formed in the liver and the remainder in lymphoid tissue. Their main functions are:

- as antibodies (immunoglobulins), which are complex proteins produced by lymphocytes that play an important part in immunity. They bind to, and neutralise, foreign materials (antigens) such as micro-organisms.
- transportation of some hormones and mineral salts; e.g. thyroglobulin carries the hormone thyroxine and transferrin carries the mineral iron

Clotting factors

These are substances essential for coagulation of blood. Serumis plasma from which clotting factors have been removed.

Fibrinogen

This is synthesised in the liver and is essential for blood coagulation. Plasma viscosity (thickness) is due to plasma proteins, mainly albumin and fibrinogen. Viscosity is used as a measure of the body's response to some diseases.

Inorganic salts (mineral salts)

These are involved in a wide variety of activities, including cell formation, contraction of muscles, transmission of nerve impulses, formation of secretions and maintenance of the balance between acids and alkalis. In health the blood is slightly alkaline. Alkalinity and acidity are expressed in terms of pH, which is a measure of hydrogen ion concentration, or $[H+]$.

The pH of blood is maintained between 7.35 and 7.45 by an ongoing complicated series of chemical activities, involving buffering systems.[7]

Nutrients

Food is digested in the alimentary tract and the resultant nutrients are absorbed, e.g. monosaccharides, amino acids, fatty acids, glycerol and vitamins. Together with mineral salts they are required by all body cells to provide energy, heat, materials for repair and replacement, and for the synthesis of other blood components and body secretions.

Organic waste products

Urea, creatinine and uric acid are the waste products of protein metabolism. They are formed in the liver and conveyed in blood to the kidneys for excretion. Carbon dioxide, released by all cells, is conveyed to the lungs for excretion.

Hormones

These are chemical compounds synthesised by endocrine glands. Hormones pass directly from the cells of the glands into the blood which transports them to their target tissues and organs elsewhere in the body, where they influence cellular activity.

Gases

Oxygen, carbon dioxide and nitrogen are transported round the body in solution in plasma. Oxygen and carbon dioxide are also transported in combination with haemoglobin in red blood cells. Most oxygen is carried in combination with haemoglobin and most carbon dioxide as bicarbonate ions dissolved in plasma. Atmospheric nitrogen enters the body in the same way as other gases and is present in plasma but it has no physiological function.[7]

Blood consists of a faintly yellow fluid, the plasma or liquor sanguinis,in which are suspended numerous minute particles, the blood corpuscles,the majority of whichare colored and give to the blood its red tint. If a drop of blood be placed in a thin layer on a glass slide andexamined under the microscope, a number of these corpuscles will be seen floating in the plasma.

The blood corpusclesare of three kinds:

1. Colored corpuscles or erythrocytes;
2. Colorlesscorpuscles or leucocytes;
3. Blood platelets.[8]

HEMATINIC FORMULATION:

Hematinics broadly refer to iron containing that critically enhances the hemoglobin content of the blood, which is usually employed to treat or prevent the ensuring iron deficiency anemia[9]. The brand, Dexorange and others, with biological background (RBC concentrate) was a very popular iron-tonic but it was to be substituted by the artificial iron source because of some regulatory reasons. The product was top-selling and unquestioning for its super-efficacy. Now, in its new version with artificially added iron-source, is unlikely to produce the same impact due to loss of very important biological components and henceforth patient is at loss.

In the light of above problems, it is worth looking for the alternative after identification of the real problem, to help restore the glorious performance of biological-iron-product such as Dexorange. Fortunately, there has been a substantial progress in the field of formulation development with the emergence of newer technologies. The right delivery of the molecules and synergism with other components has revolutionalised the field of pharmaceutics. Our experience over the period of years gives us a feeling to venture into this product to help regain its unambiguous status. First is the identification of the problem related to the absence of biological components, which are responsible in the augmentation of iron-metabolism and transport and thereafter working on relevant formulation strategies. Therefore, we put forward a developmental proposal to bring transformation of iron-tonics trying to mimic the biological one, of course by means of non-biological approach in compliance with the regulatory bodies.

CURRENT RESEARCH SCENARIO AND THE NEED:

The iron products that are currently available in the market are totally traditional, based on conventional concepts and do not employ any innovative technology. The efforts so far rests upon the inclusion of vitamins like Vit.C to improve the absorption of iron. No attention is paid on the delivery aspects, such as using novel excipients and the transport facilitation across the bio-membranes and into compartments.

Following iron salts could be considered for developing hematinic product:

1. Ferric ammonium citrate
2. Ferrous sulphate
3. Ferrous fumarate
4. Ferrous succinate
5. Ferrous glycine sulphate

CONCLUSION:

There is a need to develop a hematinic formulation which can match up the quality of the hematinic formulation containing biological background by using different techniques and different novel excipients. Thus, there is wide scope for development of a research based hematinic product with improved properties that would help the mass sufferers of iron deficiency.

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