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DETERMINATION OF THE SERUM FERRITIN AND ITS INTERFERENCES

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Abstract

The iron from the body differs depending on the age and sex. The newborn on term have 75 mg Fe/kgc coming mainly from the mother during the third semester of pregnancy. During the period of growth, the deposits of iron decrease. After the adolescence the need of iron decreases, the men presenting a gradual increase of the iron deposits during their lives having a minimum of 50mg Fe/kgc. In exchange the women present a continuous decrease of the iron until the menopause, approximately 35mg Fe/kgc, so that, after the menopause the women accumulate iron, in a laniary way, reaching to a level similar to the men. Most part of the iron from the body is found in hem compounds, especially hemoglobin and myoglobin, the form of Fe^{3+} connected to the transport protein.

Keywords: ferritin, iron deposit, hemic

INTRODUCTION

A very small quantity is contained in the enzymes that use the iron in exchange of electrons: peroxidases, catalases and ribonuclotide reductases. The most part of the non-hemic iron is stored under the form of ferritin or hemosiderin in macrophage and hepatocytes. Only a very small fraction circulates in the plasma under the form of Fe^{3+} connected to a transport protein - transferin.

The iron is absorbed from the proximal small intestine under the form of hemic iron and ferrous iron (Fe^{2+}), its absorption being influenced by the gastric acidity (it decreases in aclorhidia or gastrectomy), enhancers and inhibitors food factors. The absorption is achieved by means of transport proteins and using enzymes ferrireductase that converts Fe^{3+} from food into Fe^{2+} transfer in cells lining the gut, and ferrioxidase (hefaestina), which converts Fe^{2+} and Fe^{3+} on the membrane basolateral to transfer plasma[1].

Ferroportin is the basolateral transporter by which the iron leaves the enterocyte and the place of action of the hepcidin, peptidic hormone recently discovered, formed of 25 aminoacides, synthetized on the hepatic level, that interacts with ferroportin, inducing its internalization and degradation.

Because the human body doesn't poses a physiological mechanism of elimination of excess of iron, its absorption is very well controlled, the key elements being hepcidin with regulating role negative on the plasmatic iron, having as effect the decrease of the iron emission from enterocyte and from the cells of the reticuloendothelial system. The synthesis of hepcidin is stimulated by the inflammation or when the iron deposits of the body are saturated. The hypoxia as the increase of the need of iron for the erythropoiesis inhibits the hepatic synthesis of the hepcidin. The affecting of the regulating mechanism of hepcidin – respectively of the signal molecules that intervene in the stimulation or inhibiting of its synthesis - has a role in the pathogenesis of some affections owed to the disorders of the metabolism of iron (iron deficiency anemia, hereditary hemochromatosis, loading with iron from the inefficient erythropoiesis, the anemia associated with infections and inflammations, the anemia from chronic diseases).

The excretion of iron takes place by the cellular losses on the gastrointestinal cutaneous, urinary level, and the menstrual losses in women. The greatest part of the functional iron from the body comes from the reutilization of the iron already existent coming from the senescent erythrocytes destroyed on the reticuloendothelial system, mainly from spleen.

MATERIAL AND METHODS

The method by which is determined the hemogram, serum iron is spectrophotometric.

The hemogram is harvested à jeun (before meal) or postprandial (it still needs to be avoided the meals rich in lipids that can interfere with certain parameters of hemogram).

The sex, the age of the patient, and certain conditions as would be: the shock condition, incoercible vomit, massive administration of liquids i.v. etc. that can lead to dehydration, respectively the hyper hydration of the patient, and certain treatments followed by the patient, have to be communicated to the laboratory.

It is preferable the avoiding as much as possible of the stress in the moment of harvesting.

In case of regulate monitoring (daily or every two days) of certain parameters, the test of blood for the performing of the hemogram has to be obtained in the same moment of day (because of the circadian physiological fluctuations of some parameters).

Harvested specimen, recipient and harvested quantity – venous blood harvested on anticoagulant: EDTA tripotassium/dipotasium/disodium

(vacutainer with purple/pink lid – K3 EDTA); for small children it can be harvested capillary blood from the finger/heel on heparin (microtainer).

It is mixed the content by light inversion of the tube approximately 10 times.

The tube has to be filled at least three quarters in order for the report blood/anticoagulant to be optimum (the recommended concentration of EDTA is of 1.2 – 2.0 mg/mL of blood).

The data is processed a jeun in the morning when the values of the serum iron are the largest, before the administration of iron products/blood transfusions; if the patient was transfused, the determination of the serum iron is made after 4 days. Also it has to be avoided the deprivation of sleep, the extreme stress that decrease the serum iron or the iron sequestrants deferoxamine.

Causes of rejection of the sample – hemolysis specimen.

Stability of the sample – separated serum is stable: 7 days at 15-25°C; 3 weeks at 2-8°C; a few years at (-15)-(-25)°C[6].

RESULTS AND DISCUSSIONS

Table 1

The values of reference of ferritin reported to the age

Age (years)		***Values (ng/mL)***
<1 year		12-327
1-3 years		6-67
4-6 years		4-67
7-12 years	Girls	7-84
	Boys	14-124
13-17 years	Girls	13-68
	Boys	14-152
Adults <60 years	Women	13-150
	Men	30-400

The intracellular iron is deposited in two compounds, ferritin and hemosiderin. Apoferritin (ferritin without iron) has a GM of 440 kD, the form of an empty sphere, with the diameter of 13 nm, with a central cavity with the diameter of 6 nm, where the iron is deposited, that communicates with the exterior by 6 channels (by which enters and comes out the iron) and a protean layer formed of 24 molecules, represented by two distinct subunits: H (heavy) and L (light), with GM of 21, respectively 19 kD and coded on chromosomes 11 (H), respectively 19 (L). A single molecule of apoferritin can keep ~4500 iron atoms, GM crossing in this case 800 kD, but, usually are found ferritin molecules with mostly 2000 iron atoms. The

iron enters in the molecule under the form of Fe2+ and is oxidized under the catalytic action of apoferritin (the H chains have a ferroxidase center) and is kept as trivalent polymer of iron phosphate hydroxide, the protean layer protecting the cell of the toxic effects of iron ions. The synthesis of the apoferritin is stimulated by the exposure to iron. There are at least 20 distinct proteins of isoferritin, with variable proportions of chains H and L, that differ by the surface load: acid isoferritin contains an increased proportion of H chains and prevails in the cardiac, kidney tissue, placenta, lymphocytes, monocytes, erythroid precursors but also in the tumoral tissues; the basic isoferritin is rich in L chains, is more stable and is found in the liver, spleen, and also in the serum. The ferritin is found in the plasma in small quantities and its concentration is correlated to the iron deposits. The serum ferritin is glycosylated (suggesting the secretion by the cells of the phagocytic system) and relatively poor in iron. In the iron deficit, the ferritin decreases before the appearance of the anemia /other hematologic modifications.

The overload with iron, a normal serum ferritin suggests that an overload with iron clinically significant is less probable.

In hereditary hemochromatosis the serum iron and the saturation of the transferrin increase before the ferritin (even in the presence of increase content of iron on the hepatic level). The increase of ferritin is an indication of hepatic biopsy.

In the overload syndromes secondary with iron the ferritin is always increased.

Although it doesn't always manifest a linear relation with the iron deposits, the ferritin is the best serum parameter to measure the iron deposits. In the noncomplicated iron deficiency anemia, the ferritin is <12µg/L. When it is present together with an infectious/inflammatory disease, the serum ferritin is greater, but generally <50-60 µg/L[1]. The decreased serum ferritin signifies always iron deficit (dormant/clinical manifest) but the sensitivity of the test is decreased, because a normal value doesn't exclude the iron deficit[1].

In order to differentiate the iron deficiency anemia from the chronic diseases it is necessary sometimes the performing of additional tests (the soluble receptors of transferrin – TfR, the TfR index/ferritin or the examination of the iron deposits from the bone marrow, especially when both forms of anemia are present).

The harvesting with the patient in sleeping position determines the decrease of the number of erythrocytes (and of the hematocrit) with 5-10% (by redistribution of the liquid from the interstitial space to circulation due to the modification of the hydrostatic pressure on the level of the inferior

limbs). The stress can determine the increase of the number of erythrocytes. The prolonged venous stasis >2 minutes during the venopuction determines the increase of the number of erythrocytes with ~10% (and the significant increase of the hematocrit). Also, the harvesting after an *intense* physical effort determines the increase of the number of erythrocytes with up to 10% (as the increase of the hemoglobin concentration). All these are owed to the hemoconcentration. The dehydration with consecutive hemoconcentration (shock, severe burns, intestine obstruction, persistent vomit/diarrhea, abuse of diuretics) can mask the presence of the anemia. Also, the hyper hydration of the patient (the massive administration of liquids i.v.) can determine false decreased levels of the number of erythrocytes. The presence of agglutinins at cold in large title determined, if the blood is kept at the room temperature, false decreased levels of the number of erythrocytes and a VEM false decreased; as a consequence the hematocrit is false decreased, and HEM and CHEM are increased. The presence of cryoglobulins in large concentration can interfere with the determination of the number of erythrocytes. *The large* thrombocytes / macro thrombocytes (ex.: from the essential thrombocythemia) can numbered as erythrocytes. The numerous medicine can determine the increase or decrease of the number of erythrocytes:

1. Can decrease the number of erythrocytes almost all the classes of medicine;
2. Can determine the increases of the number of erythrocytes: the corticotrophin, glucocorticoids, danazol, erythropoietin, antitiroidinas, hydrochlorothiazide, pilocarpine, mycophenolate.

CONCLUSIONS

After approximately 120 days the senescent erythrocytes are intercepted by the macrophages of the reticulo-endothelial system on their level the iron is set free from the hemoglobin. Most part of the iron thus set free is recirculated connected to the transferrin, being used especially on the level of the bone marrow for the synthesis of the hemoglobin, but also in other tissues for the formation of the enzymes that contain the hem group. Physiologic variations with larger levels can be met more in men than women, and the differences disappear after the menopause. Also larger levels can be met in those with rich diet of red meat compared to the vegetarians.

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