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Ferritin in Bone Marrow and Serum in Iron Deficiency and Iron Overload

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Ferritin in Knochenmark und Serum bei Eisenmangel und Eisenüberladung

Zusammenfassung. Das Serumferritin gilt als Parameter des Speichereisens. Wir haben deshalb das Nichthämoglobineisen und das Ferritin im Knochenmark sowie das Serumferritin untersucht. Die Bestimmungen wurden bei Patienten mit Eisenmangelanämie und mit Eisenüberladung durchgeführt. Als Kontrolle dienten Patienten ohne Störung des Eisenhaushaltes.

Es ergab sich eine strenge Korrelation zwischen dem Nichthämoglobineisen und dem Ferritin im Knochenmark bei den Patienten mit und ohne Störung des Eisenhaushaltes. Ebenso fand sich eine Korrelation zwischen dem Ferritin im Knochenmark und dem Serumferritin. Nichthämoglobineisen und Ferritin im Knochenmark sowie das Serumferritin sind erniedrigt bei Patienten mit Eisenmangelanämie. Dieselben Parameter sind erhöht bei Patienten mit Eisenüberladung.

Schlüsselwörter: Ferritin – Nichthämoglobineisen – Eisenmangelanämie – Eisenüberladung.

Summary. Nonheme iron and ferritin in the bone marrow and serum ferritin was investigated in patients with iron deficiency anaemia or iron overload. As controls served patients without any disturbance of the iron metabolism.

There is a precise correlation between the nonheme iron and ferritin in the bone marrow of patients with and without disturbance of iron metabolism. A correlation was also found between the ferritin in the bone marrow and the serum. Nonheme iron and ferritin in the bone marrow and serum ferritin was decreased in patients with iron deficiency anaemia. Conversely, the same parameters were increased in patients with iron overload.

Key words: Ferritin – Nonheme iron – Iron deficiency anaemia – Iron overload.

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In 1972 an immunoradiometric assay was described for the measurement of ferritin in serum [1], which is decreased in patients with iron deficiency anaemia, but increased in patients with iron overload [1,5]. Therefore, the relation between serum ferritin and storage iron was determined. The serum ferritin concentration was correlated with storage iron, as measured by quantitative phlebotomie [12] and iron absorption studies [13]. Serum ferritin is correlated to the amount of stainable iron in the reticuloendothelial cells of the bone marrow in healthy adults [7], in patients with rheumatoid arthritis [2] and in patients with Hodgkin's disease [9]. It is increased in cases of acute leukaemia and in liver disease without increased storage iron [6]. Previous investigationes led to the assumption of a correlation between the storage iron and the ferritin in the iron stores. The storage ferritin does determine the serum ferritin [6]; however, there are no quantitative determinationes of those parameters. Therefore, we estimated the relation between storage iron (nonheme iron) and ferritin in bone marrow and serum ferritin.

Patients and Methods

In 23 patients bone marrow aspirations were performed. Five patients had iron deficiency anaemia as a result of chronic gastrointestinal bleeding or menstruation with increased blood loss. No stainable iron was found in the marrow. Nine patients had refractory anaemia treated with multiple blood transfusions. As expected, a considerable amount of stainable iron was found in the bone marrow. Ten patients had no disturbance of iron metabolism, with normal amounts of stainable iron in the marrow.

The bone marrow tissue particles were retrieved from the aspirates and washed with 9 g/l saline solution [8]. They were weighed and suspended in 5 ml saline solution. A homogenous cell suspension was retained by forcing the tissue through a 26 gauge needle. 4 ml of the cell suspension were homogenised with an "Ultraturrax" (Janke & Kunkel KG, Stauffen). Ferritin was determined in 100 μl of the homogenat with an immunoratiometric assay [1]. Ferritin for standardisation was separated from human liver [15]. The antiserum was raised in rabbits Serum ferritin was measured with the same assay. In our laboratory the range of serum ferritin concentration in control subjects amounts to 40–250 μg/l. Nonheme iron was determined with bathophenantroline in 1 ml of the homogenous cell suspension after extraction with 4,5 n hydrochloric acid and an extraction time of 60 minutes at 90°C [14].

Results

Fig. 1 shows the relation between nonheme iron and ferritin in bone marrow. We found 0.31 ± 0.11 μg nonheme iron/mg wet weight in patients without disturbance of the iron metabolism. The ferritin concentration was 0.31 ± 0.13 μg/mg wet weight bone marrow. Nonheme iron and ferritin in bone marrow were decreased in patients with iron deficiency anaemia and increased in patients with iron overload. Nonheme iron and ferritin in the bone marrow of patients with and without disturbance of iron metabolism are strongly correlated with a linear relationship ($r = 0.989$). The linearity of the curve and the course near to zero demonstrate that a constant part of the nonheme iron is bound to ferritin.

Fig. 2 shows the relation between ferritin in bone marrow and serum. There is a strong correlation in patients with and without disturbance of iron metabolism ($r = 0.937$). It appears that the serum ferritin is a constant part of the bone marrow ferritin. Both investigations demonstrate that storage iron and ferritin in bone marrow and serum ferritin are strongly correlated.

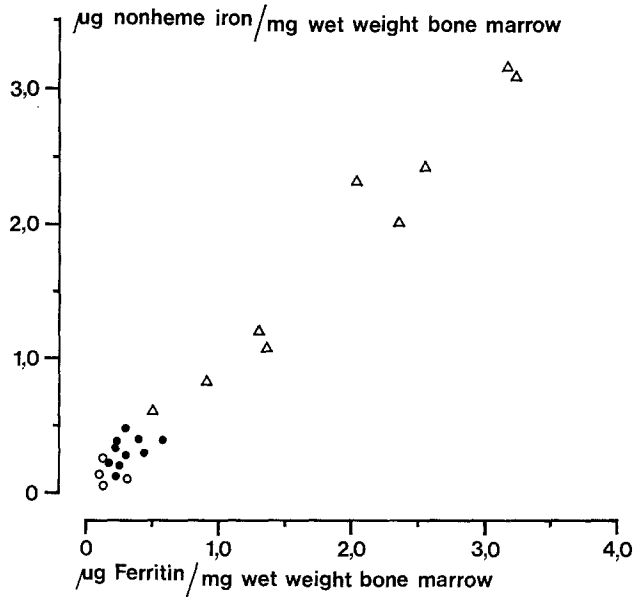

Fig. 1. The relationship between nonheme iron and ferritin in bone marrow (○ = iron deficiency anaemia; ● = without disturbance of iron metabolism; △ = iron overload)

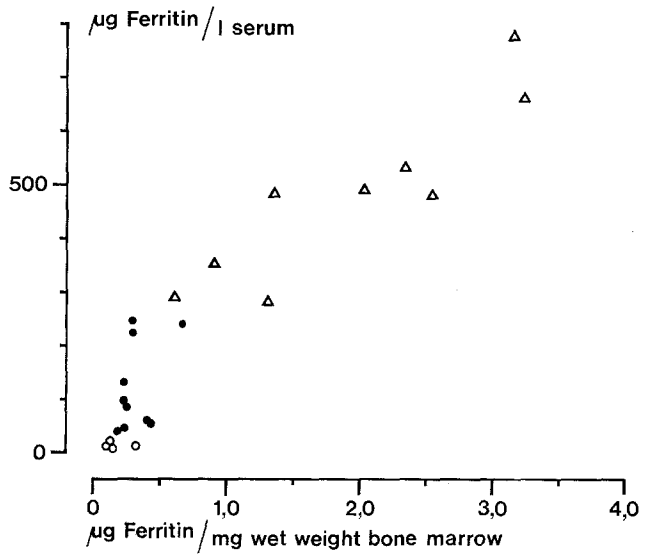

Fig. 2. The relationship between ferritin in bone marrow and serum

Discussion

We found 0.31 ± 0.11 µg nonheme iron/mg wet weight bone marrow in patients without disturbance of iron metabolism. These values are somewhat higher as found by other investigators [4, 10, 11]. The selection of control persons might account for the difference.

In the liver and the bone marrow approximately 60% of the nonheme iron is bound to ferritin. This value is nonvariable in pathological situations. The iron bound to ferritin was separated in this investigation by its solubility at 75° C [14]. Our results agree in part with this date. We also found a constant relation between nonheme iron and ferritin in bone marrow in patients with and without disturbance of iron metabolism. We did not measure the iron bound to ferritin. However, it is reported that the ferritin contains 20–25% iron. Our results suggest, that 20–25% of the nonheme iron is bound to ferritin. These values are lower than those reported by other investigators [14]. There are several possible reasons for this discrepancy: 1. Insufficient extraction of ferritin by our method. 2. Overestimation of the iron bound to ferritin with separation at 75° C [14]. However, the relation between these parameters in normal and pathological situations is more important than the absolute concentrations.

Hepatic ferritin represents 70% of the nonheme iron in the liver in growing female rats. Splenic ferritin represents only 25% of the nonheme iron in these animals [3]. This is in aggreement with our results on human bone marrow.

The bone marrow is only a part of the body iron stores. Therefore, it is not possible to calculate from our results the exact proportion between ferritin in iron stores and serum. On the assumption that the ferritin concentration in the bone marrow corresponds to the concentration in the other iron stores, our results would indicate that the total iron stores contain approximately 1 g ferritin. In the serum are approximately 0.3 mg ferritin. The relation between ferritin in the iron stores and serum would then be 3300:1. The mechanism of the release of ferritin from the iron stores is not yet clear. Serum ferritin in iron overload contains less iron than ferritin from normal tissue [15]. It is not clear, whether serum ferritin is a secretory isoferritin or whether it is due to nonspecific release from damaged cells.

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