CONCISE REPORT

Effect of Iron Therapy on Serum Ferritin Levels in Iron-Deficiency Anemia

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The level of serum ferritin is a reliable indicator of body iron stores. Exceptions include liver disease, malignant diseases, and treatment of iron-deficiency anemia. The latter was noted in iron-deficient infants who showed a rise of serum ferritin to normal levels in the first week of treatment. To evaluate this in adults, 14 patients with iron-deficiency anemia were studied prior to and after beginning treatment with oral ferrous sulfate in standard dose.

In the first week of treatment, serum ferritin was assayed by radioimmunoassay. No rise occurred in the first 3 wk in 5 patients treated with standard dose, although hematologic response occurred. With double dose, 7 of 9 showed a ferritin rise in 2 days with return to subnormal levels within 6 days of discontinuing iron. This study indicates that standard treatment of iron deficiency anemia in adults does not cause a rise in serum ferritin until hemoglobin levels are normal. The early rise seen with double dose is most likely due to absorption of iron in excess of utilization for erythropoiesis resulting in temporary storage. When iron is discontinued, stores are rapidly depleted as reflected by the prompt decrease in serum ferritin.

IN THE LAST 7 yr, sensitive immunologic techniques have shown that small amounts of ferritin normally are present in serum. The level of serum ferritin has been shown to correlate very well with the amount of body iron stores. In uncomplicated iron-deficiency anemia, the level of serum ferritin is found to be less than normal in virtually all cases. Based on these observations, many hematologists now feel that serum ferritin assay may be used in place of a marrow examination when the only indication for the marrow examination is to estimate iron stores.

Certain clinical states present exceptions to this approach, e.g., active liver disease and some malignant diseases. In these conditions, serum ferritin does not reflect the size of body iron stores.

More of a practical problem from a clinical standpoint in the assessment of body iron stores is the report by Simmes et al. in 1974. They found that in infants, the following study was done.

The present study was undertaken to see if the findings described in infants also occurred in adults.

MATERIALS AND METHODS

For the studies using oral iron, the 14 adult patients had iron-deficiency anemia established by the presence of a microcytic hypochromic anemia, serum ferritin measurements less than 10 ng/ml, and full correction of the anemia by treatment with ferrous sulfate tablets only. Erythrocyte indices were obtained using a Coulter Model S. Hypochromia was determined from a smear of peripheral blood. Serum ferritin was measured by radioimmunoassay using a commercially available kit (Clinical Assays, Cambridge, Mass.). Results using this kit were reproducible with an interrun coefficient of variation of 11% using pooled serum with a mean value of 9 ng/ml. A number of serum samples from this study were also assayed by Dr. James Cook, Kansas City Medical Center and the results were virtually identical.

RESULTS

Standard Dose Treatment

Five patients with iron-deficiency anemia were given ferrous sulfate tablets containing 60 mg of iron 3 times a day. Serum ferritin was measured numerous times during the treatment period. Figure 1 illustrates the results. No patient showed a rise of serum ferritin into the normal range during the first 4 wk of treatment, although all achieved the expected hematologic response. By the time the patients attained a serum ferritin level within the low normal range, they had reached a normal hematocrit.

Since these results differed from those reported in infants, the following study was done.

Double Dose Treatment

Nine patients with iron-deficiency anemia received 120 mg of iron as ferrous sulfate t.i.d. and their serum ferritin levels were followed at intervals (Fig. 2). Seven of 9 patients so treated showed a prompt rise of serum ferritin into the low normal range within the first days of treatment. This response was not as great as that reported in infants, although the dose calculates to be approximately 6 mg elemental iron/kg,
Intravenous Iron Treatment

Serum ferritin response following administration of intravenous Imferon was determined in 5 patients who had clinical indication for use of parenteral iron. Two patients fulfilled the original definition of iron-deficiency anemia. Three patients had initial serum ferritin levels in the low normal range and were anemic as a result of acute blood loss. All 5 patients showed a prompt rise of serum ferritin within the first 5 days of treatment (Fig. 4).

DISCUSSION

From a clinical standpoint, it is useful to know that standard doses of oral iron used in treating iron-deficient adults does not result in a rise of serum ferritin into the normal range until the anemia is corrected. The prompt rise in serum ferritin noted following initiation of oral iron in iron-deficient infants was seen, although to a lesser extent in our
adult patients given a similar dose of iron on a body weight basis.

The mechanism underlying this interesting phenomenon is unclear. One possibility is that intestinal mucosal cells produce and release ferritin during the process of iron absorption. It has been shown previously that intestinal mucosal cells exhibit two pathways for iron during the absorptive process. Most of the iron absorbed is rapidly transported across mucosal cells by a mechanism not involving ferritin. As the amount of iron available for absorption is increased, the rapid transport mechanism is saturated and the mucosal cells store iron as ferritin. If some of the ferritin, with or without iron, is released to the blood, this could explain the possible dose-related rise in serum ferritin.

Bypassing the gastrointestinal tract by giving iron dextran intravenously resulted in a prompt rise in serum ferritin in our study. One would expect this result, since iron administered in this way is cleared from circulation by reticuloendothelial cells. Even though the amount of iron given to these patients greatly exceeds the amount absorbed from the oral route, this observation suggests an alternative and more likely explanation for the rise in serum ferritin following the larger oral dose, i.e., the iron-deficient subject absorbs more iron than can be used immediately for erythropoiesis. This would result in a transient buildup of stored iron and, as a consequence, an increase in serum ferritin. As Hallberg has shown, the larger the dose of iron administered to the iron-deficient patient, the greater the amount of iron absorbed, thus, the more likely this sequence is to occur with the larger doses used in infants and our 7 patients. Recent work by Norrby, using oral iron in doses up to 400 mg daily, indicates that some iron-deficient subjects do in fact absorb more iron than can be used immediately for erythropoiesis. He found stainable iron in marrow reticuloendothelial cells as early as 3 wk after beginning iron treatment, before anemia was fully corrected. He did not report on bone marrow studies done earlier in treatment.

If this were the explanation for the rise in serum ferritin, one would expect a fall to pretreatment levels within a few days of stopping oral iron, since the patients are still iron deficient and should utilize the small amount of stored iron for erythropoiesis. This did occur in 3 of 4 patients who had shown an early rise with the larger dose of iron. These 3 were quite anemic, while the fourth was only mildly so—a male with an hematocrit of 40%.

Serum ferritin assay appears to be reliable in evaluating an adult patient suspected of iron-deficiency anemia even when the patient is receiving oral iron if the dose is no more than 60 mg of iron t.i.d. and if treatment is within the first 2–3 wk.

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REFERENCES


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