Assessment of iron deficiency in rheumatoid arthritis

In a recent survey of 100 consecutive patients with rheumatoid arthritis (RA) attending a rheumatology outpatient department, over 75% had received a course of oral iron during their disease and 40% multiple (up to 12) courses (D R Blake and D G I Scott, unpublished observations). Since these figures almost certainly do not indicate the true incidence of iron deficiency, we have assessed the value of standard haematological indices of iron state to predict low iron stores. Serum ferritin concentration is a particularly sensitive index of low iron stores in RA,¹ and has, therefore, been accepted as the absolute iron state in our study. Patients with a low serum ferritin concentration were further investigated to assess the cause of their iron deficiency.

Patients, methods, and results

The standard laboratory profile used to predict iron state in clinical practice includes haemoglobin concentration; packed cell volume; the red-cell variables—mean cell volume, mean cell haemoglobin, and mean cell haemoglobin concentration (measured with a Coulter S automatic cell counter); and serum iron concentration and iron binding capacity (determined with a Technicon autoanalyser by the triazine method).

These variables were measured in 110 patients (34 men, 76 women), who fulfilled the criteria of the American Rheumatism Association for definite or probable RA² and who were currently attending medical and rheumatological outpatient departments. A sample of serum was stored at -20°C for independent estimation of ferritin concentration (immunoradiometric assay—Gammadab ¹²⁵I, Travenol Lab).

Of the 110 patients studied, seven (6%, three men and four women) had low iron stores as judged by serum ferritin concentration (< 12 µg/l). The table shows the standard haematological variables (mean ± 1SD) for these patients in contrast with the remainder, whose ferritin concentrations were normal or raised. Of the eight patients with low ferritin concentrations, two had a haemoglobin concentration above the accepted lower limit of normal for their age and sex.³ Fourteen patients had recently been prescribed iron, and subsequent estimations of their serum ferritin concentration showed that seven had values above, six had values within, and only one had a value below the normal range. Further analysis of the results in the patients with a low serum ferritin concentration detected no combination of variables that could have reliably or selectively predicted a low serum ferritin concentration.

Investigation of the eight patients with a low serum ferritin concentration disclosed that two had acute duodenal ulcers, one a benign gastric ulcer, and one presumed bleeding from a hiatus hernia. In two patients no specific cause for the low serum ferritin concentration was found, though both were women with a history of menorrhagia.

Comment

A moderate anaemia is the commonest systemic manifestation of RA, and its severity reflects the activity of the disease. Though the anaemia is often hypochromic and sometimes microcytic, it reflects the inability of the reticuloendothelial cells to release sequestered iron and, less commonly, a genuine iron deficiency. The avid retention of iron by the reticuloendothelial system is reflected by a rise in serum ferritin concentration, which has been observed to be high in inflammatory states,⁴ and the association between serum ferritin concentration and the activity of rheumatoid disease needs to be explored further.

The concentration of serum ferritin below which iron deficiency is said to occur is normally 12 µg/l.¹ Almost certainly this value is inappropriate for those with RA and should be adjusted upwards. We have shown, however, that even if a concentration of under 12 µg/l is accepted, at least 6% of our patients were genuinely iron deficient, and that none of the routine variables of iron state adequately predicted this group. The incidence of other diseases in patients with a low

serum ferritin concentration is disquieting, and the need for further investigation is clear. All patients in this study were receiving non-steroidal anti-inflammatory drugs capable of inducing gastrointestinal bleeding, but these should not be readily accepted as the cause of a low serum ferritin concentration.

The indiscriminate use of oral iron in patients with RA is inappropriate and dangerous. An estimation of serum ferritin concentration could usefully be incorporated as a routine measurement in the assessment of the rheumatoid patient, the cost being offset by a more rational prescribing policy.

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Raised blood urea concentration indicates considerable blood loss in acute upper gastrointestinal haemorrhage

Estimates of the amount of blood lost during acute upper gastrointestinal haemorrhage are known to be inaccurate because of the indirect and inadequate indicators available.^{1,2} The blood urea concentration has long been known to rise after upper gastrointestinal bleeding, but its value as an indicator of the volume of blood lost has been questioned because of uncertainty about the pathophysiology of its rise.

We undertook this study to see whether the blood urea concentration on admission allows prediction of the volume of acute blood loss. We also compared the creatinine clearance on admission with that at the time of discharge to establish whether hypovolaemia or absorption of blood are predominantly responsible for the rise.^{3,4}

Patients, methods, and results

We studied 57 patients admitted to hospital with a history suggesting upper gastrointestinal bleeding. Estimations of haemoglobin concentration, mean corpuscular volume, mean corpuscular haemoglobin, and blood urea and creatinine concentrations were made on a sample of blood taken on admission, and on samples taken 24, 48, and 72 hours after admission and on the day before discharge. Thirty-eight patients had creatinine clearance

Haematological variables in 110 patients with rheumatoid arthritis having low or normal iron stores (as shown by serum ferritin concentration). Results are given as means ± 1SD with ranges in parentheses

Haemoglobin concentration (g/dl)	Packed cell volume (%)	Mean cell volume (fl)	Mean cell haemoglobin (pg)	Mean cell haemoglobin concentration (g/dl)	Serum iron concentration (µmol/l) (normal range 14-36)	Iron binding capacity (µmol/l) (normal range 45-72)
Patients with low serum ferritin concentration (< 12 µg/l, n = 7)						
10.8 ± 1.6 (8.5-13.5)	32 ± 4 (27-35)	80 ± 7.7 (67-89)	26.5 ± 2.8 (21.4-29.6)	33 ± 0.95 (31-34)	8 ± 3.5 (2.7-14)	60.2 ± 7.6 (54-70)
Patients with normal serum ferritin concentration (> 12 µg/l, n = 102)						
11.2 ± 1.7 (8.6-17.4)	33 ± 5 (28-49)	80 ± 6.6 (66-94)	26.4 ± 2.6 (21.6-33.9)	33 ± 0.98 (31-35)	9.8 ± 5.4 (3-23)	63.6 ± 7.7 (55-73)