Sensitivity of reticulocyte indices to iron therapy in an intensely training athlete

Michael J Ashenden, Geoffrey P Dobson, Allan G Hahn

Abstract

Iron deficiency anaemia, and its debilitating effect on performance, is an area of concern for many female athletes. Automated technologies that analyse individual reticulocytes may provide a sensitive measure of bone marrow response to iron supplementation. The reticulocyte characteristics of a female volleyball player with frank iron deficiency anaemia, and her subsequent response to oral iron therapy, are reported.

(*Br J Sports Med* 1998;32:259-260)

Keywords: iron deficiency anaemia; reticulocytes; female athletes; Technicon H*3

Department of Physiology and Applied Nutrition, Australian Institute of Sport, Canberra, Australia

M J Ashenden
A G Hahn

Department of Physiology and Pharmacology, James Cook University of North Queensland, Townsville, Australia
G P Dobson

Correspondence to:
Michael J Ashenden,
Department of Physiology
and Applied Nutrition,
Australian Institute of Sport,
PO Box 176, Belconnen,
ACT 2616, Australia.

Accepted for publication
13 February 1998

Female athletes have been regarded as being susceptible to iron deficiency anaemia based primarily on the low serum ferritin values often encountered in this population.¹ Reliance on low serum ferritin values as a single indication of iron deficiency is an unreliable diagnostic tool² since it is susceptible to several pathological and physiological conditions that may confound interpretation.³

An alternative to biochemical indices has been to diagnose iron deficiency anaemia on the basis of mature red blood cell parameters. However, iron deficiency has to be present for a long time before the indices of the mature cell population change sufficiently to be detectable by traditional haematology analysers.⁴ Many modern automated blood cell counters now permit similar red cell parameters to be measured directly in reticulocytes, which have only recently been released from the bone marrow and thus provide a more current indication of bone marrow status.⁵ One such analyser, the

Technicon H*3 (Bayer Diagnostics, Tarrytown, New York, USA), stains and identifies the remnant RNA within reticulocytes, and performs cell by cell analysis of 20 000 individual reticulocytes measuring the haemoglobin concentration (corpuscular haemoglobin concentration mean; CHCMr) and cell volume, from which is derived the haemoglobin content (corpuscular haemoglobin content; CHr) of the newly released cells.

The amount and concentration of haemoglobin within reticulocytes has been shown to differ between healthy subjects and iron deficient patients,^{5,6} and the amount of haemoglobin contained in each cell was found to increase in female patients with iron deficiency anaemia after oral iron therapy.⁴ It would be highly desirable if similar results were found in highly trained athletes, since early detection of iron deficient erythropoiesis can prevent the long term consequences of iron deficiency anaemia⁴ and so avoid any performance impairment. This technology has only recently been applied to athletic populations, and it is unclear whether reticulocyte indices are sensitive to iron deficiency in intensely training athletes.

Case report

An 18 year old female international level volleyball player provided a venous blood sample for routine monitoring at the beginning of her scholarship at the Australian Institute of Sport. Haemoglobin concentration was 11.4 g/dl and serum ferritin 10 µg/l (day 1). It was found on dietary counselling that the athlete had an aversion to consuming animal flesh. She was prescribed 350 mg/day Ferrogradumate (ferrous sulphate, equivalent to 105 mg elemental iron; Abbott, Sydney, NSW, Australia) and encouraged to consume two or three servings of red meat per week. Reticulocyte characteristics were monitored weekly using earlobe blood samples (days 7, 16, and 22). A progressive increase in CHCMr and CHr was clearly observed, which was noted within seven days of iron therapy (fig 1). A follow up venous sample taken about four weeks later showed that serum ferritin had increased substantially, together with an increase in haemoglobin concentration (day 36).

No further monitoring was undertaken until a subsequent routine blood sample was taken about two months after iron therapy had commenced (day 75). This showed a sharp decline in ferritin almost to values seen before iron supplementation (fig 1). There was no concomitant decrease in haemoglobin concentration. However, CHCMr and CHr had declined

Figure 1 Concentration (CHCMr, left axis) and amount (CHr, right axis) of haemoglobin in reticulocytes of an iron deficient female volleyball player receiving oral iron supplementation. Hb, serum haemoglobin.

to values almost identical with initial values when the subject first presented with iron deficiency anaemia. An interview with the subject revealed that compliance with oral iron therapy had diminished compared with the initial weeks; iron tablets were taken on average only once per week. Unfortunately, a seven week overseas sporting tour prevented any further blood monitoring.

Discussion

Red blood cells have a finite lifespan, and about 1% of the red cell population is removed from the circulation every day.⁷ Virtually all of the iron contained in these senescent cells is recycled and available for subsequent haemoglobin production, which must match the rate of removal to maintain constant haemoglobin levels in the blood.⁷ If, through accelerated iron loss or inadequate dietary iron intake, body iron stores become depleted, haemoglobin production may be impaired. This will lead to a state of iron deficiency anaemia if left untreated.

This case confirms that reticulocyte characteristics in an intensely training athlete with iron deficiency anaemia respond to iron supplementation in a similar manner to those of sedentary subjects and could be utilised as an indication of a positive response to iron therapy. The increase in CHCMr and CHr occurred within seven days of supplementation, significantly reducing the one month interval required to detect a positive response in haemoglobin concentration.⁸

In addition, it provides a valuable illustration of the potential for reticulocyte indices to pre-empt a decline in haemoglobin concentration during the early stages of iron deficiency. As the

serum ferritin, CHCMr, and CHr values on day 75 were similar to those measured on day 1, it would appear that iron stores had again become depleted to such an extent that normal rates of haemoglobin production could not be maintained. This had not yet become evident from haemoglobin concentration, which showed no decline between days 36 and 75. On the basis of a decline in reticulocyte characteristics, an intervention strategy could be implemented before the early stages of iron depletion develop into iron deficiency anaemia.

Reticulocyte characteristics appear to be a valuable tool for detecting a positive response to iron therapy in intensely training athletes. This inexpensive test, which can be performed on skin prick blood samples,⁹ is also ideal for regular monitoring of athletes considered susceptible to developing iron deficiency anaemia.

- 1 Telford RD, Bunney CJ, Catchpole EA, *et al.* Plasma ferritin concentration and physical work capacity in athletes. *Int J Sport Nutr* 1992;**2**:335–42.
- 2 Weight LM. 'Sports anaemia' Does it exist? *Sports Med* 1993;**16**:1–4.
- 3 Borch-Iohnsen B. Determination of iron status: brief review of physiological effects on iron measures. *Analyst* 1995;**120**: 891–3.
- 4 Brugnara C, Laufer MR, Friedman AJ, *et al.* Reticulocyte hemoglobin content (CHr): early indicator of iron deficiency and response to therapy. *Blood* 1994;**83**:3100–1.
- 5 Buttarello M, Bulian P, Venudo A. Laboratory evaluation of the Miles H³ automated reticulocyte counter. *Arch Pathol Lab Med* 1995;**119**:1141–8.
- 6 d'Onofrio G, Chirillo R, Zini G, *et al.* Simultaneous measurement of reticulocyte and red blood cell indices in healthy subjects and patients with microcytic and macrocytic anemia. *Blood* 1995;**85**:818–23.
- 7 Smith JA. Exercise, training and red blood cell turnover. *Sports Med* 1995;**19**:9–31.
- 8 Oski FA. Iron deficiency in infancy and childhood. *New Engl J Med* 1993;**329**:190–3.
- 9 Ashenden MJ, Parisotto R, Dobson GP, *et al.* Reticulocyte parameters can be obtained from capillary blood samples. *Aust J Med Sci* 1997;**18**:78–83.

Commentary

Iron deficiency anaemia is a common condition particularly in women and probably affects 10% of normal women at any one time. It may be more common among athletes especially those whose diet is low in iron and who use non-steroidal anti-inflammatory medicines, which can cause gastro-intestinal tract blood loss through a combination of gastric irritation and reduced platelet function.

Diagnosis of iron deficiency anaemia in athletes can be complicated by co-existent sports anaemia which is in fact a dilutional pseudo-anaemia caused by increased plasma volume. Most of the new generation of automated blood cell counters can measure the haemoglobin content and concentration of reticulocytes (immature red cells). As these cells are the latest to be released from the bone marrow, they are the best indication of iron stores within the bone marrow; they will show a reduction in haemoglobin content and concentrations as iron deficiency occurs and an increase in these parameters in response to iron treatment. They are not affected by sports anaemia. Clinical experience with these measurements is accumulating, and they show great promise as early indicators of iron deficiency anaemia and response to treatment.

E J WATTS
Basildon, Essex