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CONCISE COMMUNICATION

There is no clear association between low serum ferritin and chronic diffuse telogen hair loss

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Summary

Background Low iron stores are considered a possible cause of chronic diffuse telogen hair loss in women. Estimation of serum ferritin is recommended as part of the initial assessment when women present with chronic diffuse telogen hair loss, and iron supplementation therapy is commonly recommended for those found to have low iron stores.

Objectives To evaluate the relationship between low serum ferritin (≤ 20 μg L^{-1}) and chronic diffuse telogen hair loss in women.

Methods Between 1997 and 1999, 194 consecutive women who presented to a specialist hair clinic were assessed for diffuse telogen hair loss of greater than 6 months duration. All underwent biochemical investigations that included serum ferritin and had two 4-mm punch biopsies taken from the vertex of the scalp. One biopsy was sectioned horizontally and the other vertically.

Results Twelve women were found to have a serum ferritin of 20 μg L^{-1} or less (6·2%). Androgenetic alopecia was found on scalp biopsy in seven of these 12 women, while the other five women had normal histology. The five women with low iron stores and normal histology were treated with iron supplementation alone. This was continued until the serum ferritin was > 20 μg L^{-1}. Cessation or reversal of hair loss was not seen in any of these women.

Conclusions No direct relationship between low serum ferritin and hair loss can be established. The usefulness of serum ferritin in the routine investigation of women with chronic diffuse telogen hair loss is unclear, as is the role of iron supplementation therapy in the management of hair loss.

Key words: anaemia, androgenetic alopecia, ferritin, telogen effluvium

Iron deficiency is commonly listed as a possible cause of telogen effluvium;[1–4] however, this is controversial.[5,6] A recent case–control study found that mean serum ferritin levels in women with androgenetic alopecia and diffuse hair loss were significantly lower than in normal controls,[7] although in that study the mean serum ferritin levels were within the normal range in both groups.

There is debate over what is the normal serum ferritin level for women.[8] Serum ferritin < 15 μg L^{-1} is commonly used as the limit for iron deficiency, as this is the highest value of ferritin found in patients with iron-deficiency anaemia, and iron supplementation in women with serum ferritin of > 16 μg L^{-1} increases serum concentrations of ferritin but not of haemoglobin.[9] However, a serum ferritin level of > 70 μg L^{-1} is required for a 99% confidence interval for iron staining in the bone marrow, an alternative marker of adequate iron stores.[10] The confusion is compounded by the use of different reference ranges by different laboratories, based on their interpretation of the literature. The laboratory used for this study cited 20 μg L^{-1} as the lower limit of normal for women and that cut-off point was used in this study.

Diffuse hair loss lasting longer than 6 months in women is a common presentation to dermatologists. In Australia, androgenetic alopecia is the most common cause, followed by primary chronic telogen effluvium and drug-induced hair loss. Nutritional, metabolic and

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autoimmune diseases are uncommon causes.[11] Primary chronic telogen effluvium is considered a diagnosis of exclusion.[6,12]

Patients and methods

Between 1997 and 1999, 194 consecutive women who presented to a specialist hair clinic with diffuse telogen hair loss of 6 months or greater duration underwent extensive screening, including full blood count, serum ferritin, and scalp biopsy. All patients had two 4-mm punch biopsies taken from the vertex of the scalp. One biopsy was sectioned horizontally and the other vertically. Horizontally sectioned biopsies were used to calculate the ratio of vellus to terminal hair and patients with a ratio of $< 1 : 4$ were diagnosed as having androgenetic alopecia.[13]

Biochemical investigations included thyroid function tests, full blood count, renal and liver function tests, iron studies, serum testosterone, serum sex hormone-binding globulin, serum dehydroepiandrosterone sulphate, serum luteinizing hormone and serum follicle-stimulating hormone.

Patients diagnosed as having androgenetic alopecia were treated with either spironolactone 200 mg daily or cyproterone acetate 100 mg daily for 10 days each month. Topical minoxidil was not used by any patient during the course of this study.

Results

The age range was 11–72 years. One hundred and thirty-five (70%) women were premenopausal and 59 (30%) were postmenopausal. Overall, 117 (60%) were diagnosed as having androgenetic alopecia on histology.

Twelve patients (6%) were found to have a serum ferritin of 20 $\mu g\ L^{-1}$ or less (Table 1). The haemoglobin was normal in all cases and the low iron stores could be attributed on history to either heavy menstrual loss or low meat diet. None of the patients underwent further investigation for iron deficiency.

Of these 12 patients, none was found to have any associated biochemical abnormality. Seven of these 12 patients were diagnosed on biopsy as having androgenetic alopecia. The remaining five had no histological evidence of androgenetic alopecia and the differential diagnosis for their hair loss included primary chronic telogen effluvium and chronic telogen hair loss secondary to iron deficiency.

All 12 patients were given oral iron supplementation for a minimum of 3 months, whereupon their iron studies were repeated. After 3 months, four patients were found to have serum ferritin below 20 $\mu g\ L^{-1}$; in these, iron therapy was continued for a further 3 months and the blood test repeated. After 6 months, all 12 patients had serum ferritin $> 20\ \mu g\ L^{-1}$. In addition to the iron replacement, the seven patients diagnosed as having androgenetic alopecia were treated with spironolactone 200 mg daily. Four had symptomatic improvement (a reduction of hair shedding and an increase in hair volume over a 6-month period), while three noted no change in hair density. These results were similar to the response rates seen in the other 108 patients who received oral antiandrogen therapy for androgenetic alopecia (unpublished observation).

Table 1. Patients with diffuse telogen hair loss and low serum ferritin ($\leq 20\ \mu g\ L^{-1}$)

Patient no.	Age (years)	Clinical diagnosis	Duration of hair loss	Initial ferritin ($\mu g\ L^{-1}$)	V:T ratio	Diagnosis	Treatment	Response
1	42	Ludwig 2	4 years	18	1 : 2·2	AGA	Spironolactone + iron	Nil
2	37	Ludwig 1	16 years	14	1 : 2·4	AGA	Spironolactone + iron	Nil
3	43	Ludwig 1	3 years	16	1 : 3·5	AGA	Spironolactone + iron	Nil
4	48	Ludwig 1	1 year	20	1 : 3·5	AGA	Spironolactone + iron	Improved
5	39	Ludwig 1	3·5 years	20	1 : 2·6	AGA	Spironolactone + iron	Improved
6	37	Ludwig 2	4 years	18	1 : 2	AGA	Spironolactone + iron	Improved
7	15	Ludwig 1	1 year	12	1 : 3·4	AGA	Spironolactone + iron	Improved
8	41	Ludwig 1	6 months	15	1 : 12	CTE	Iron supplementation	Nil
9	23	Ludwig 1	16 months	15	1 : 29	CTE	Iron supplementation	Nil
10	46	Ludwig 2	1 year	20	1 : 9	CTE	Iron supplementation	Nil
11	27	Ludwig 1	1 year	17	1 : 5	Indeterminate	Iron supplementation	Nil
12	48	Ludwig 1	6 years	8	1 : 5·2	Indeterminate	Iron supplementation	Nil

V:T ratio, the ratio of vellus to terminal hairs at the level of the mid-isthmus on horizontally sectioned scalp biopsy. AGA, androgenetic alopecia (V:T $< 1 : 4$); CTE, chronic telogen effluvium (V:T $> 1 : 8$). The hair loss was deemed indeterminate when $1 : 4 \leq$ V:T $\leq 1 : 8$.

The five patients with no histological evidence of androgenetic alopecia and low serum ferritin received iron replacement therapy alone. Cessation of hair shedding or an increase in hair density was not seen in any of these patients.

Discussion

If low iron stores cause reversible hair loss, then iron replacement should lead to cessation of hair loss and/or hair regrowth.

In our cohort of 194 patients, low iron stores were found in 12 (6%) patients. However, these iron stores could not be linked aetiologically to hair loss as in no case did iron replacement clearly lead to cessation of hair loss or improvement in hair density. Seven of these 12 women were found to have androgenetic alopecia and the iron deficiency was not felt to be the cause of their hair loss. In five women, iron deficiency was considered in the differential diagnosis of their hair loss; however, none of these women responded to iron replacement therapy. While four of the seven women with both low iron stores and androgenetic alopecia responded to therapy, it was felt that their response was due to oral antiandrogens rather than the iron replacement, as a similar response rate to oral antiandrogen monotherapy was seen in the 108 patients with androgenetic alopecia and normal iron stores.

It cannot be discounted that a response to iron replacement therapy may have been seen if the therapy had been continued longer. Serum ferritin levels of $> 40\ \mu g\ L^{-1}$ have been advocated for women undergoing treatment for hair loss.[14] While a significant role of low iron in the cause of diffuse hair loss cannot be totally excluded, it is not supported by the study.

The rate of hair loss in androgenetic alopecia fluctuates, particularly in the early stages. Many patients initially present with self-limiting episodes of telogen effluvium, although the recovery is often incomplete. The incidental finding of iron deficiency does not negate the possibility of underlying androgenetic alopecia in these patients. Without further investigation and observation, neither the clinician nor the patient should assume that such hair loss is solely attributable to the low iron stores and that iron replacement alone will reverse the hair loss.

Androgenetic alopecia is common in women. The potential for reversal of androgenetic alopecia with oral antiandrogens is limited. If oral antiandrogens are to be used to treat androgenetic alopecia, then they are likely to be of greatest benefit if instituted early, with the aim of delaying or arresting progression of the hair loss. It is therefore in the patients' interest not to attribute hair loss too readily to low iron stores and to ensure that alternative causes of hair loss have been excluded.

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