then be better able to treat the whole person, rather than some faltering, failing bit of him or her, and be able to adapt treatments and recommendations to known domestic circumstances. Friendship builds up trust, trust induces confidence, and confidence can be three parts of the cure. In these matters the GP's family may be a great help.

And when all this is said and done there is one overriding principle without which much will be labour in vain. It may be

summed up in the latin tag: *non quod sed quomodo* (not what but how). It is not only what the GP does but how he does it. It is not what he does but what he is that often really counts in this challenging life, where the many occasions of suffering also provide opportunities of combating it. I would like to think that my doctor, unlike my accountant or solicitor, is a personal friend in addition to being a professional adviser. Perhaps this is asking too much, but I hope not.

Practice Research

Attitudes to prescribing iron supplements in general practice

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Abstract

In response to a postal questionnaire general practitioners in the Southampton and New Forest area indicated a considerable understanding of the principles of iron prescribing and use of laboratory tests to determine iron deficiency. Many respondents, however, chose slow release and compound iron preparations as first treatments for iron deficiency. The role of parenteral iron appeared to be poorly understood. The use of and response to laboratory investigations for iron deficiency were generally appropriate, but many practitioners probably do not check for a response to oral iron sufficiently early during treatment or stop prescribing supplements before iron stores have been replenished. There is scope for further education in the biology and management of iron deficiency in general practice.

Introduction

The treatment of iron deficiency is the only major recognised indication for iron supplements, and well defined guidelines are presented for their use.^{1,2} The prescribing data for iron supplements, which Callender reviewed,³ suggested that these guidelines are often not followed. Simple iron salts are recommended as the treatment of first choice, although many other iron preparations are available, including nearly 40 compound iron formulations on prescription.²

We therefore sent a questionnaire to general practitioners in Southampton and the surrounding area asking about their prescribing of iron supplements and use of laboratory tests for patients with iron deficiency.

Methods

Postal questionnaires were sent to 284 general practitioners who were on the mailing list for postgraduate activities at Southampton General Hospital. The area in which they practised included Southampton and the New Forest. A second questionnaire was sent to the practitioners who had not replied within six weeks. Aspects of current practice that were questioned were as follows: (a) The first and second choice oral iron preparations for iron deficiency, the usual daily dose, and the reasons for selecting the preparation. (b) Prescribing indications for oral and intramuscular iron. (c) Which laboratory tests were carried out before iron was prescribed and how often they were requested. (d) The duration of treatment in patients with proved iron deficiency and in patients not proved to have iron deficiency. (e) Monitoring of response.

The results were assessed using the χ^2 test.

Results

CHOICE AND DOSAGE OF IRON PREPARATION

Simple iron salts were indicated as the first choice formulation by nearly three quarters of all respondents, the commonest reason for the choice being their low cost. Among the simple iron preparations ferrous fumarate and gluconate in particular were thought by the practitioners who prescribed them to cause fewer side effects than ferrous sulphate ($p < 0.01$). The practitioners who chose slow release or compound formulations as first choice (74, 28%) claimed to do so because of convenient dosage, presentation of the tablet, and fewer expected side effects ($p < 0.01$ compared with ferrous sulphate). The compound preparations mentioned included a few preparations of iron and folic acid (14 responses, 5% of total respondents). In three cases only the practitioners stated that these were prescribed during pregnancy, although the questionnaire specifically requested information on their use in iron deficiency states. The daily dosage of elemental iron prescribed was lower in the group of doctors who prescribed slow release preparations when compared with ferrous sulphate ($p < 0.01$) (table I).

The pattern of prescribing for second choice preparations was similar, but with a higher proportion (96, 37%) of doctors choosing slow release or compound iron preparations. Sixteen (6%) respondents chose combinations of iron and folate. The reasons for the selection and the doses prescribed were similar within each group to those for the first choice preparations (table II).

LABORATORY ASSESSMENT OF IRON DEFICIENCY

Just over half (137) of practitioners replied that they always requested a laboratory test before prescribing iron. A slightly lower percentage (40%, 105) thought that they requested a laboratory test in at least three quarters of cases; 4.5% (13) admitted that they requested a laboratory test in under

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half of cases. Ten responses to this question could not be evaluated. The laboratory test most commonly used to determine a need for iron was the full blood count (93%, 246 of respondents); 81% (215) of doctors said that they often based prescribing on a blood film report of iron deficiency. Concentrations of serum iron and total iron binding capacity were used infrequently as a test for iron deficiency, and the ferritin concentration was rarely used (table III).

INDICATIONS FOR IRON SUPPLEMENTS

Oral iron was most often prescribed when hypochromic microcytic anaemia was reported or in response to a report suggesting iron deficiency based on a blood film examination. A high proportion of practitioners also prescribed iron for mild normocytic anaemia or for patients with chronic diseases such as rheumatoid arthritis or renal failure (table IV). The perceived indications for prescribing intramuscular iron were varied; 91%

TABLE I—First choice oral iron preparation

Iron preparation	No (n=265)	Reasons for choice*					Daily dose of elemental iron (mg)			
		a	b	c	d	e	Not stated	<100	100-200	>200
<i>Simple iron salts:</i>										
Ferrous sulphate	144	142	46	4	43	29	27	6	110	1
Ferrous fumarate	26	16	12	7	11	5	3	1	22	0
Ferrous gluconate	20	19	8	1	15	4	4	5	11	0
Ferrous succinate	1	0	1	0	1	1	0	0	1	0
Total %	72	93	35	6	37	20	18	6	75	<1
<i>Slow release iron salts:</i>										
Feospan	21	3	19	7	16	3	1	19	1	0
Ferro-Gradumet	17	3	15	8	10	1	1	0	16	0
Slow Fe	4	1	3	2	2	0	0	4	0	0
Ferrocontin	1	0	1	0	1	0	0	0	1	0
Total %	16	16	88	40	67	9	5	54	42	0
<i>Compound iron preparations:</i>										
	31	9	25	8	21	8	1	8	22	0
Total %	12	29	81	26	68	26	3	26	71	0

* (a) It is cheap; (b) convenient dosage; (c) well packaged tablet; (d) minimal side effects; (e) more effective than other preparations.

TABLE II—Second choice oral iron preparation

Iron preparation	No (n=265)	Reasons for choice*					Daily dose of elemental iron (mg)			
		a	b	c	d	e	Not stated	<100	100-200	>200
<i>Simple iron salts:</i>										
Ferrous sulphate	44	43	10	1	4	6	9	1	33	1
Ferrous fumarate	39	39	17	4	23	6	13	11	32	1
Ferrous gluconate	57	47	18	1	35	6	6	4	29	0
Ferrous succinate	1	1	1	0	0	0	0	0	1	0
Ferrous glycine sulphate	1	0	1	0	0	0	0	0	1	0
Total %	54	91	33	4	44	13	20	11	68	2
<i>Slow release iron salts:</i>										
Feospan	34	1	27	11	25	1	5	29	0	0
Ferro-Gradumet	30	3	26	13	18	4	4	0	25	1
Slow Fe	6	1	5	2	5	0	0	6	0	0
Ferrocontin	3	0	2	1	3	1	1	0	2	0
Total %	28	7	83	37	70	8	14	48	37	1
<i>Compound iron preparations:</i>										
	23	7	15	4	18	3	2	13	8	0
Total %	9	30	65	17	78	13	9	57	35	0
<i>No response or unclear:</i>										
	27									
Total %	10									

* See table I.

TABLE III—Use of laboratory tests before prescribing iron (n=265) (percentages in parentheses)

	Often	Infrequently	Never	Not evaluable
Full blood count	246 (93)	5 (2)	2 (<1)	12 (5)
Blood film report	215 (81)	20 (7.5)	1 (<1)	28 (10.5)
Iron concentration and total iron binding capacity	63 (24)	164 (62)	11 (4)	27 (10)
Ferritin concentration	5 (2)	50 (19)	160 (60)	50 (19)

TABLE IV—Reasons for prescribing oral iron (n=265) (percentages in parentheses)

	Often	Infrequently	Never	Not answered
As a tonic	2 (<1)	70 (26)	180 (68)	13 (5)
Patient asks for iron	2 (<1)	100 (38)	146 (55)	17 (6)
Tiredness	3 (1)	74 (28)	165 (62)	23 (9)
Mild normocytic anaemia	45 (17)	142 (54)	60 (23)	18 (7)
Hypochromic microcytic anaemia	236 (89)	17 (6)	8 (3)	4 (2)
Laboratory report of iron deficiency on film	242 (91)	20 (8)	2 (<1)	1 (<1)
Chronic disease, such as rheumatoid arthritis	42 (16)	164 (62)	44 (17)	15 (6)

(240) of respondents claimed to use parenteral iron. This was most common if the patient had failed to respond to oral iron (157, 59%), including poor patient compliance (146, 55%). About a third (80) of respondents expected a more rapid effect in raising haemoglobin or replacing iron stores (88). Other indications mentioned were severe anaemia (three), gastric side effects from oral iron (two), anaemia discovered in late pregnancy (two), postpartum anaemia (one), and malabsorption syndromes (one). Only 9% (25) indicated that they never prescribed parenteral iron or that they did so only on request from a hospital specialist.

MONITORING RESPONSE TO IRON TREATMENT

In proved cases of iron deficiency most practitioners (169, 64%) continued to prescribe oral iron until several weeks after a normal blood count had been achieved, and 25.5% (68) indicated that they stopped iron when the blood count returned to normal. Iron was occasionally stopped when the symptoms resolved (three replies) or was continued indefinitely (two replies). Eight per cent (25) of the responses to this question could not be evaluated.

The timing of assessment for response to iron showed wide variation, with stated periods ranging from two weeks to over three months; 51% (137) of practitioners indicated that they would check for a response in a month or less, a further 34% (91) assessed for response between one and two months, and 4% (10) assessed after two months or longer. Twenty seven (10%) responses could not be evaluated. In cases where "iron deficiency" was not proved 34% (89) indicated that they prescribed iron for at least a month, and a few prescribed iron for longer periods.

Discussion

The absorption of ferrous iron from the gut depends on the dose of oral iron and the state of the iron stores. Increasing the dose of supplemental iron will increase the amount absorbed but decrease the fraction absorbed.^{4,5} As the iron deficiency state is corrected total iron absorption from the gut is gradually reduced.^{6,7} Increasing the daily dose of iron from 100 mg to 400 mg in experimental iron deficiency increases the rate of accumulation of iron stores, but doses greater than 200 mg daily do not affect the rate of the rise in haemoglobin.⁸ The amount of iron absorbed from different simple ferrous iron salts is similar and is therefore not a factor in response to iron.⁹ Iron absorption is greatest in the duodenum and proximal jejunum; many sustained release iron preparations may release iron beyond these sites and thus absorption is reduced.^{10,11} Gastrointestinal intolerance, particularly nausea and epigastric pain, is dependent upon the soluble elemental iron content^{12,13} and psychological factors^{11,12} rather than the preparation used. Use of the highest tolerated dose of a simple inexpensive iron preparation is therefore generally advised to initiate treatment.¹² The recommended replacement dose of iron in iron deficiency states is 100-200 mg of elemental iron. Doses lower than this may be necessary if gastrointestinal intolerance is a problem. Higher doses are useful only if iron treatment is short, but they carry the risk of increased side effects.

The results of our survey show that a high proportion of the general practitioners whom we questioned adhere to recommended guidelines regarding the use and appropriate dose of simple iron salts. Their perception, however, that there are fewer unwanted effects with ferrous fumarate and gluconate compared with ferrous sulphate is not supported by the evidence.¹²

The use of slow release and compound formulations by many

respondents as a first (28%) or second (37%) choice seemed to be largely governed by convenient dosage and better tolerance by the patient. The questionnaire did not attempt to differentiate between clinical cases. The use of these formulations as a first choice is not supported by experimental evidence. If there is a reduced incidence of gastrointestinal intolerance with slow release preparations it may result either from a lower dose of elemental iron prescribed compared with prescribing simple salts or because some sustained release formulations may release the iron incompletely.^{5,10} Nevertheless, initiating treatment with a low dose of simple iron salts, reducing the dose in patients who experience unwanted gastrointestinal effects, or giving the iron with food allows many patients to continue treatment without resorting to more expensive preparations.¹³ Compared with the prescribing figures for Britain in 1979 presented by Callender,³ the proportion of compound and slow release iron formulations claimed as first choice treatment in our survey is much lower.

The advent of automated blood counting machinery during the 1960s transformed the ease and accuracy with which a full blood count result could be produced. Excellent reviews of the validity of diagnostic tests in iron deficiency have been published by Cavill and Cook.^{14,15} Haemoglobin is the largest and most easily assessed iron store in the body¹⁴; a fall in haemoglobin concentration with microcytic hypochromic features is the most readily available test of iron deficiency anaemia. The mean cell volume, however, is probably the most sensitive index of iron deficiency in a full blood count, falling before the haemoglobin concentration does.¹⁵

Measurements of serum or plasma iron concentrations and total iron binding capacity are simple and inexpensive, and the results are available to general practitioners within 10 days. But from a general practitioner's point of view they are probably seen as a "secondary" screen after anaemia has been identified. Interpretation of the serum iron concentration and total iron binding capacity is not always straightforward: diurnal fluctuations occur in serum iron concentrations, and the total iron binding capacity may be influenced by various acute and chronic diseases. Ferritin is a water soluble iron storage complex, and many forms are found in the body. Measurement of ferritin in serum or plasma has only just become available in the Southampton area. The results of extensive studies, reviewed by Worwood,¹⁶ have shown that serum ferritin is an accurate reflection of whole body iron stores.

The full blood count was the test preferred by the general practitioners for the diagnosis of iron deficiency anaemia, although many also used a blood film report. Iron, total iron binding capacity, and ferritin, the "secondary" tests, are used infrequently, perhaps when there is doubt as to the certainty of the diagnosis of iron deficiency anaemia.

Surprisingly, only half of the practitioners carried out a laboratory test in all cases before prescribing iron. Over 90% of respondents requested a laboratory test in three quarters or more of cases. A small percentage appear to use laboratory tests inadequately.

The prescribing of iron for iron deficiency on the basis of laboratory reports was usually appropriate. Early iron deficiency may present as a mild normochromic normocytic anaemia.⁶ Prescribing iron in response to such a laboratory report, however, which was done at least occasionally by nearly three quarters of the respondents, is likely to result in the treatment of many patients with no iron deficiency. Up to 40% of practitioners claimed to prescribe iron on some occasions for non-specific complaints or because the patient requested iron. In most cases in the absence of proved iron deficiency treatment is prescribed for no longer than a month. Short term administration of a cheap preparation may be harmless for a placebo effect or while awaiting results of laboratory tests. The widely held belief that iron is good for the blood as a general tonic will not disappear overnight, as shown by the variety of iron and vitamin preparations that are available without a prescription.

Whether or not it is appropriate to prescribe iron in the anaemia of chronic disorder is difficult to determine. In some conditions, notably rheumatoid arthritis, an iron deficient state may coexist, and the anaemia may be alleviated by iron supplements.¹⁷ Repeated

assessment of the response in such patients is desirable before continuing treatment indefinitely.

The recommended indications for parenteral iron differ from the reported use in this survey. Although failure to respond to oral iron was the commonest reason for prescription, this is not an indication per se without analysing the reasons.¹⁸ If adequate oral iron supplements are given the rate of response to oral and parenteral iron is similar,^{19,20} and the more rapid replacement of stores has no real therapeutic benefit. About a third of respondents, nevertheless, considered that a faster response was a reason for prescribing parenteral iron.

Assessing the failure or success of treatment received a varied response. The questionnaire did not seek to relate the timing of the follow up test to the severity of anaemia. Any degree of iron deficiency is an important sign which needs appropriate treatment and adequate investigation. The initial response rate in iron deficiency anaemia is said to be a rise in haemoglobin of 2 g/l in the first three weeks of treatment or >0.1 g/l per day.²¹ A test repeated after three weeks of appropriate treatment is probably optimum^{21,22} so that non-responders can be seen and managed appropriately.

Roughly a quarter of the general practitioners stopped prescribing iron when a normal haemoglobin concentration was achieved. Though it has been contested,²³ it is desirable to continue to replenish iron stores, especially in view of the high recurrence rate.^{24,25} Many general practitioners may therefore be giving inadequate courses of oral iron.

The results of this survey in general practice suggest that, although iron supplements are often prescribed in accordance with the principles in standard reference texts, there is scope for improvement. Through education programmes in the biology of iron deficiency and its treatment²⁶ it should be possible to reduce the cost of iron prescribing by encouraging a more thoughtful approach to investigation and treatment of iron deficiency.

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