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'FESOFOR SPANSULE' CAPSULES IN PREGNANCY ANAEMIA

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The need for iron therapy arises when a diagnosis of an iron-deficiency anaemia has been made. Although this type of anaemia is common to all sexes and ages, it is in pregnancy that it is most often detected. Sometimes the symptoms are sufficiently evident for laboratory investigations to be made. Very often, however, an iron-deficiency anaemia is present, but remains untreated because the symptomatology was not obvious enough to arouse suspicion. Iron anaemia may be due to an inadequate absorption of iron from the intestines, or a loss of blood from haemorrhage, or an increased physiological demand for more haemoglobin (which usually means iron).

In pregnancy a woman may not be anaemic in the early stages, but with the increased needs resulting from the growth of the foetus, anaemia may readily develop. This anaemia may not be due to the demands of the foetus only, but may often be associated with nutritional deficiencies or impaired absorption of iron from the gut. Nutritional anaemia is directly associated with lack of food, improper diets, anorexia, diarrhoea, and some other more serious, but fortunately readily recognizable conditions.

Haemoglobin Levels in Pregnancy

The treatment of an iron-deficiency anaemia depends almost entirely on providing an adequate supply of iron which can readily be absorbed. However, in pregnancy there is the added complication of the growing foetus, so that it is generally recognized that prescribing iron to pregnant women is almost obligatory, no matter whether the haemoglobin at the beginning of pregnancy is well within normal limits or not. There are also certain geographic factors to be considered. A study at Ann Arbor, Michigan, showed that at an altitude of 800 feet above sea level the normal haemoglobin of pregnancy (in G. per 100 ml.) was: in the fourth month 11·4 - 15·0; fifth month 10·8 - 14·6; sixth month 10·2 - 14·0; seventh month 10·2 - 14·0; eighth month 10·4 - 14·2; ninth month 10·8 - 14·4; during labour 11·2 - 15·0; 10 days postpartum 11·4 - 15·4; and 42 days postpartum 12·0 - 16·0. In Johannesburg, however, where the altitude is 6,000 feet above sea level, these figures cannot apply, for here the normal haemoglobin levels are considered to be between 12·5 and 18 G. per 100 ml. It is obvious, then, that altitude is an important factor.

The haemoglobin levels in pregnant women cannot be considered static, even if they fall within normal limits when the initial assessments are made in the first few weeks of pregnancy. Benstead and Theobald[1] considered that there is no such condition as a 'physiological anaemia of pregnancy'. Accordingly, all pregnant women should receive iron as a routine from the onset of pregnancy until the end of breast feeding. This does not imply that other factors contributing to the production of an iron-deficiency anaemia can be neglected. In addition to whatever other therapy is necessary, iron should always be prescribed for the period already advised.

Requirements of Iron

Dietary iron is usually taken in the form of ferric hydroxide, which is often loosely combined with organic acids and amino acids. Ferric salts are, however, not as readily absorbed as ferrous salts. A daily requirement of 1·2 - 2 mg. of ionic iron will supply the requirements of an adult male, but in the female during pregnancy an intake of at least 3 mg. daily is required.

An added factor complicating simple iron therapy may be a failure to respond to treatment. This may be the result of an initially incorrect diagnosis, irregular treatment or inadequate dosage, or local conditions in the gastro-intestinal tract which may interfere with absorption. But in most cases it is the irregular and inadequate intake which probably produces the poor results. The factors influencing irregular intake depend a great deal on the social status and intelligence of the patients and on an adequate antenatal supervision. It is also caused in part by the necessity for prescribing preparations with ineradicable toxic side-effects; preparations which, in any case, must usually be taken three times a day.

The toxic effects of iron preparations are well known and are mostly the result of gastro-intestinal irritation and constipation. It is very important then to prescribe a preparation which can be taken easily by mouth, which is not taken more than once or twice a day, and which will not produce side-effects sufficiently unpleasant to stop the patient taking the drug regularly for what is, unfortunately, a very long period of time. Since iron must be given for such a long period, the choice of the drug becomes very important.

What is required is a preparation which should be long-acting and with few side-effects. 'Fesofor spansule' capsules were made available for this purpose. Each spansule capsule contains 150 mg. of exsiccated ferrous sulphate in a sustained-release form. The release of the drug is timed so that only a small amount is set free in the stomach and the remainder is freed in the upper part of the small intestine. A dose of 1 capsule (150 mg. of ferrous sulphate) has been shown to give the same haemoglobin response as the normal daily dose of 600 mg. required in tablet form.[2,3] In addition, since small quantities of iron are released at a time, the mucous membrane is not unduly irritated; thus the side-effects of the iron in this form should be less frequent than with ordinary tablets. A dose of 1 capsule given daily, or at the most twice a day, was

considered a great advantage in ambulant women and in those who might be away from home during the day.

METHODS

In this series 74 pregnant patients were investigated. The average age of each patient was 25·5 years and the range varied from 17 to 35 years. All the patients were White. Their nutritional state was satisfactory, and advice on an adequate and proper dietary régime was always given when they were first seen. A routine examination was carried out at their first attendance, and 1 capsule of fesofor a day was prescribed. In only 1 or 2 patients was the dose increased to 2 capsules a day. Especial care was taken to remind the patients to adhere to this régime, and regular haemoglobin checks were made throughout pregnancy. In addition, multivitamin tablets were given until the end of the pregnancy.

Complete blood counts were done when the patient was first seen, but the haemoglobin level was the only estimation that was repeatedly done, using the American Optical Haemoglobinometer. The normal range in Johannesburg varies from 12·5 to 18 G. per 100 ml. Since the same technicians made all the assessments, errors were practically insignificant. The patients were seen regularly, and their clinical state was assessed each time, of course, in addition to the haemoglobin estimation.

RESULTS

In 59 patients seen in the 9 weeks from the 5th to the 14th week of pregnancy, the mean haemoglobin level was 15·1 G. per 100 ml. ± 0·14 G. There were 10 patients with haemoglobin levels between 13 and 14 G.; 20 between 14 and 15 G.; 18 between 15 and 16 G.; 8 between 16 and 17 G.; and 4 between 17 and 18 G. per 100 ml.

In 64 patients (in whom the previous 59 are included) investigated between the 17th and 28th weeks of pregnancy, the mean haemoglobin level was 14·1 G. per 100 ml. ± 0·12 G. In this group there were 9 patients with haemoglobin levels between 12 and 13 G.; 24 between 13 and 14 G.; 18 between 14 and 15 G.; 12 between 15 and 16 G.; and 1 between 16 and 17 G. per 100 ml.

In 49 patients (carried over from the other 2 sections) investigated between the 29th and 40th weeks of pregnancy, the mean haemoglobin level was also 14·1 G. per 100 ml. ± 0·12 G. In this group there was 1 patient with a haemoglobin level between 11 and 12 G.; 3 were between 12 and 13 G.; 19 between 13 and 14 G.; 20 between 14 and 15 G.; 5 between 15 and 16 G.; and 1 between 16 and 17 G. per 100 ml.

These results show that at the onset of pregnancy all the patients had haemoglobin levels above the lowest limits of normal. From the 17th to the 28th week 9 patients had haemoglobin levels at or about the lowest limit of normal, and between the 29th and the 40th weeks 1 patient was below, and 3 at, the lowest limit of normal. This indicates that throughout the course of treatment it was only towards the end of pregnancy that 1 patient had a drop in her haemoglobin level in spite of the treatment given.

Fig. 1 shows the variations in the haemoglobin levels in 5 selected patients throughout pregnancy. These patients

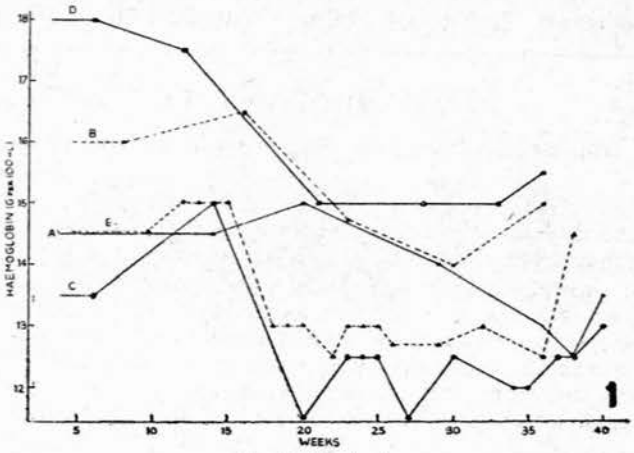

Fig. 1. See text.

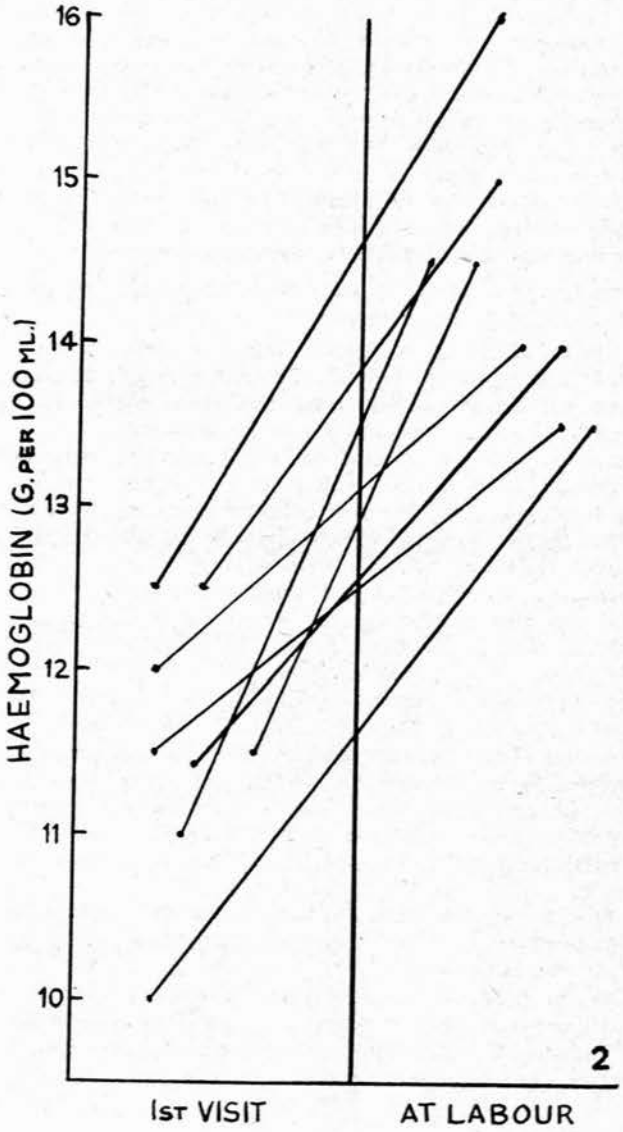

Fig. 2. See text.

were chosen to show the variations in haemoglobin levels in the blood, relevant to the initial levels in the early weeks of pregnancy. Patient A started at a level of 14·5 G. per 100 ml. at the 6th week and maintained her level satisfactorily at 13·5 G. per 100 ml. at labour. Patient B started at a level of 16 G. per 100 ml. at the 8th week and maintained her level at 15 G. per 100 ml. at the 36th week. Patient C started at 13·5 G. per 100 ml. at the 6th week and maintained her level up to labour at 13 G. per 100 ml. Patient D, at the first week of pregnancy, had a haemoglobin level of 18 G. per 100 ml.; at the 36th week it was 15·5 G. per 100 ml. Patient E had a haemoglobin level of 14·5 G. per 100 ml. at the 10th week, and a level of 15·5 G. per 100 ml. at labour.

Fig. 2 shows the results obtained in 8 patients who were considered to be anaemic at the onset of pregnancy. The results show the difference in haemoglobin levels at the onset of pregnancy and at labour, and it can be seen that in every instance the anaemic patient had a rise of haemoglobin to within normal limits by the onset of labour.

As a rule, in patients starting from a low haemoglobin level, it was after 4 - 6 weeks' treatment that the level reached was considered to be normal. The response to treatment showed a rise of haemoglobin of the order of about 1% a day until a satisfactory level was obtained.

Symptomatically, all the patients treated were free from complaints related to a low haemoglobin level. There were no signs of iron deficiency and breathlessness; pallor and swelling of the extremities were noticeably diminished and did not exceed what would be found in a normal pregnancy with normal blood findings.

SIDE-EFFECTS

There were no side-effects from taking fesofor. Although indigestion and constipation were seen in several patients, these complaints could not be attributed to the therapy, and were usually dispersed by prescribing antacids or mild aperients.

DISCUSSION

Most obstetricians will agree that it is a common finding that patients who are anaemic at the beginning of pregnancy must be treated with iron, not only to compensate for deficiencies in the diet, but also to maintain the haemoglobin level within normal limits. Normal women who are not anaemic at the onset of pregnancy, very often become anaemic as pregnancy progresses. It has been suggested that the incidence of anaemia in normal women, owing to the 'drain' of the foetus, may be as high as 70%.

It is obvious, then, that all pregnant women should be given iron, in order not only to maintain an already normal haemoglobin level within normal limits, but also to raise an anaemic haemoglobin level to a normal level and to keep it there. From the results obtained, fesofor can be shown, in the first place, to have maintained a haemoglobin level in normal women within normal limits throughout pregnancy; and, in the second place, to have raised the haemoglobin to normal levels in 8 patients in whom anaemia was established before therapy was begun, and to have maintained it there right up to labour.

Benstead and Theobald[1] have claimed that 20 - 30% of patients cannot tolerate treatment with ordinary iron tablets, such as ferrous sulphate. Indigestion, constipation, and complaints of an unpleasant taste, are some of the few and regular reasons given to obstetricians for stopping iron tablets. In this series of patients there were no complaints whatsoever on these grounds. The fact that it was possible also, almost invariably, to maintain treatment on one capsule a day, was found to be of great advantage. It is my opinion that treatment should be commenced with 1 - 2 capsules daily at the first visit of the patient, no matter what the haemoglobin level is, and treatment should be continued up to labour and, if possible, for as long as the mother is breast-feeding the child. There is a possibility that the incidence of miscarriages might be lowered if the haemoglobin levels of pregnant women were maintained within normal limits. In the antenatal clinic iron should be prescribed, no matter what other advice may be given with regard to diet, hygiene and other matters.

In this trial the patients also received, as a routine, multivitamin preparations for very nearly the same reason as they were given iron. An investigation of this nature is rather tedious, but the results show that it has been worth while, since we have demonstrated that iron therapy throughout the period of pregnancy should be obligatory and that fesofor spansule capsules are valuable for ensuring a steady intake of iron in an easily assimilated form, in which side-effects have been shown to be more or less eliminated.

It is interesting to note that, when the patients were examined 6 weeks after labour, not only were the haemoglobin levels within normal limits, but the infants were also found to be vigorous and healthy to an extent not usually encountered where anaemia had developed during the pregnancy.

SUMMARY

1. Iron was given as a routine to 74 patients, in the form of a long-acting preparation (fesofor spansule capsules) throughout the pregnancy and for the duration of lactation.

2. In only 8 patients was the haemoglobin level below the accepted limit of normal when these patients were first seen.

3. All but 1 of the patients came to labour with haemoglobin levels within the normal accepted limits.

4. No side-effects of any kind related to iron therapy were encountered in this investigation.

5. At the 6-week follow-up after labour all the patients examined showed haemoglobin levels within the normal limits.

6. It is suggested that all pregnant patients should be treated with iron regularly from the onset of pregnancy to the end of lactation. It is also suggested that, because of their long-acting properties and complete lack of side-effects, fesofor spansule capsules have been shown to be the treatment of choice.

I wish to thank Messrs. SKF Laboratories for an initial supply of fesofor spansule capsules, and also for their assistance in providing information in this field.

Vitamin supplements used ('pramilets', 'gestatabs', 'en-

cebrin', 'filibon' and 'prelafol forte') were kindly donated by Abbott Laboratories, White Laboratories, Inc. (Scherag Pty. Ltd.,), Eli Lilly & Co., Lederle Laboratories and Ayerst Laboratories, respectively.

ADDENDUM

Thirty-nine patients seen 6 weeks after labour had a follow-up haemoglobin estimation done. The values varied from 12·5 - 17 G. per 100 ml., with an average of 15 G. per 100 ml.

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