

## SERUM AND TISSUE IRON AND MENORRHAGIA

by

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Haden *et al* (1933) drew attention to the menstrual disturbances due to simple achlorhydric anaemia. They suggested that simple achlorhydric anaemia and iron deficiency should be suspected in all cases of unexplained menstrual disturbances.

Taymor *et al* (1960 and 1964) presented reports on a group of patients with menorrhagia in whom the aetiological factor appeared to be chronic iron deficiency and in whom a satisfactory improvement in menorrhagia was noted after iron therapy, either oral or parenteral. They suggested that chronic iron deficiency can be a cause as well as the result of menorrhagia, as they noted that there is very high rate of response to iron therapy in menorrhagia, high rate of organic pathology in patients who failed to respond to iron medication, associated rise in serum iron level in majority of the patients who show response to iron and decreased response to iron therapy when initial serum iron levels were high.

### Material and Methods

The present study was carried out on the patients attending the Out-patients' Department and those admitted in Hos-

pital for Women, Patna Medical College Hospital, Patna.

Two chief criteria for inclusion in the initial phase of study, in addition to menorrhagia were the absence of gross pelvic pathology and an initial serum iron level of 90 mcg/100 ml. or below and absence of any haematological disorder. Every case had an endometrial biopsy to exclude dysfunctional uterine haemorrhage, and organic pathology. Eighty cases fulfilled the above criterion and another 30 cases of menorrhagia were also studied who had no pelvic pathology but had serum iron level above 90 mcg./100 ml. to compare the results of iron therapy.

Besides routine examination, serum iron was estimated in each case and depending upon the serum iron level, the cases were divided into two broad groups for the purposes of comparative study to assess the result of iron therapy. Bone marrow examination was done to find out the presence and amount of tissue iron. The grading was done according to the method described by Rath and Finch (1949). This was done to find out the correlation between serum iron and tissue iron since tissue iron has been considered to be a more sensitive index of iron level in the body. Oral iron therapy was administered. In cases where oral iron was not tolerated or where the initial iron level was very low, medication was

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TABLE I  
Shows the Range of Haemoglobin and Serum Iron in 110 Cases of Menorrhagia

Haemoglobin in gm. %	80 cases with serum iron below 90 mcg./100 ml.		Haemoglobin in gm. %	30 cases with serum iron above 90 mcg./100 ml.	
	No. of cases	Serum iron		No. of cases	Serum iron
4-5	3		4-5		
5-6	5	30-40	5-6	90-95	2
6-7	9	40-50	6-7	95-100	4
7-8	13	50-60	7-8	100-105	6
8-9	16	60-70	8-9	105-110	12
9-10	12	70-80	9-10	110-115	6
10-11	8	80-90	10-11		
11-12	8		11-12		
Above 12	6		Above 12		

Table I shows in 80 cases with serum iron level of 90 mcg./100 ml. or below 90 mcg./100 ml., haemoglobin ranged from 4 gm. to over 12 gm. In maximum number of cases (61.25%) it ranged between 7-11 gm.%. In 6 (7.5%) cases haemoglobin was above 12 gm.%. In 30 cases with serum iron level above 90 mcg. the haemoglobin level varied between 8-9 gm.% or above 12 gm.%.

changed to intramuscular route. After a varying period of treatment for two or four months, the cases were reviewed and the results of iron therapy assessed taking into consideration mainly the improvement in menorrhagia along with serial estimation of haemoglobin percentage and serum iron determination.

Therapeutic response was graded as 'improved', if there was improvement in the menorrhagia, irrespective of the rise of serum iron and 'failed' where there was no or little clinical improvement.

ligible, the response to iron therapy was good. When the tissue iron store was at + level in 5 cases even with low serum iron of 70—80 mcg./100 cc the response to iron therapy was unsatisfactory. Out of 20 cases with serum iron of 80—90 10 improved. In these cases bone-marrow iron was low while in 90 cases with bone-marrow iron level at + level there was failure or iron therapy. This shows that tissue iron as well as serum iron play an important role in the control of functional menorrhagia where organic patho-

TABLE II  
*Shows Serum Iron, Bone marrow Iron Level in 80 Cases with Menorrhagia*

No. of cases	Serum iron	Bone marrow	Therapeutic response
5	30 - 40	0	Excellent response
8	40 - 50	0	Excellent response
10	50 - 60	0	Good response
6	60 - 70	0	Good response
10	60 - 70	0	Failed
15	70 - 80	0	Improved
5	70 - 80	+	Failed
12	80 - 90	0	Improved
9	80 - 90	+	Failed

Table II shows serum iron level and bone marrow iron level in 80 cases with menorrhagia. The serum iron level varied from 30—90 mcg/100 ml.

Twenty-nine cases where serum iron was between 30-70 mcg/100 ml., tissue iron store was negligible and response to iron therapy was excellent. In 10 of these cases, though the serum iron was between 30—70 mcg/100 cc. and tissue iron was nil, there was no improvement in menorrhagia. These cases later on were subjected to thorough curettage and 7 out of these 10 had tuberculous endometritis and 3 had non-specific chronic endometritis. In 15 cases with serum iron level of 70—80 mcg./100 cc. with tissue iron store neg-

logy or hormonal disturbances are not involved.

The response to iron therapy in the total group of patients complaining of menorrhagia has been shown in Table III. Cases were divided into 3 groups according to serum iron level less than 70 mcg./100 ml., 70—90 mcg./100 ml. and above 90 mcg./100 ml. The perusal of above table indicates that a high order of improvement (74.36% and 65.85%) was obtained in both the groups having serum iron below 90 mcg./100 ml. In the group of 30 cases which had serum iron level above 90 mcg./100 ml. improvement was noted only in 46.6% cases, showing that the improvement fell as the serum level rose.

TABLE III  
Showing Improvement in Menorrhagia with Iron Therapy

	Serum iron level		
	In 80 cases	In 30 cases	
	70 or below 70 mcg./100 ml.	70 - 90 mcg./100 ml.	90 - 120 mcg./100 ml.
No. of cases	39	41	30
Improved	29 (74.36%)	27 (65.85%)	14 (46.6%)
Failed	10 (25.64%)	14 (34.15%)	16 (53.4%)

TABLE IV  
Showing Serum Iron Levels Before and After Iron Therapy Associated with Improvement in Menorrhagia in 56 Cases

Increase of more than 50%	— 30 (53.57%)
Increase less than 50%	— 20 (35.71%)
Increase below 10%	— 6 (10.72%)

The above table shows the degree of rise of serum iron in 56 cases of menorrhagia whose therapeutic response was graded as 'improved' with adequate iron therapy. In 30 (53.57%) there was rise of more than 50% and in 20 (35.71%), the rise was between 10—50% and in the remaining 6 (10.72%) there was less than 10% or no rise at all, although the cases had showed clinical improvement.

TABLE V  
Showing Response to Iron Therapy in 80 Cases of Menorrhagia

Total	— 80 cases
Improved	— 56 (70%) cases
Failure	— 24 (30%) cases
(a) No pathology	— 14 (17.5%) cases
(b) Organic causes	— 10 (12.5%) cases

Table V shows high percentage of improvement (70%) with iron therapy. Amongst the 'failure' group nearly half had underlying uterine pathology which

remained undetected on initial screening examination.

Discussion

Response to iron therapy, carried out in 110 cases of the present series, was quite significant. For purpose of study the cases were divided into 3 groups viz. 70 or below 70 mcg./100 ml. (39 cases), between 70—90 mcg./100 ml. (41 cases), and those above 90 mcg./100 ml. (30 cases). The response to iron therapy in the first two groups was quite high (74.36% and 65.85%) as compared to 46.6% success in the third group having serum iron level above 90 mcg./100 ml. The improvement is more marked when tissue iron level is negligible. There is high failure rate (53.4%) in cases with initial high serum iron level. In the pathogenesis of menorrhagia resulting from chronic iron deficiency, the factor of tissue resistance seems to play a major role. The local factors in uterine endometrium or possibly myometrium might play a role here. Taymor *et al* (1964) suggested that iron deficiency may cause menorrhagia by interfering with the enzymatic production, lack of which weakens the muscular elements of the uterus affecting particularly the spiral arterioles. Beutler (1957 and 1959) has shown that in ani-

mals deficient in iron, cytochrome oxidase iron and succinic dehydrogenase iron are depleted before there is any manifestation of clinical deficiency. These enzymes play an important role in the function of muscles and this fact lends considerable weight to the theory that menorrhagia may be caused by a weakness of muscular elements in the uterus due to tissue iron deficiency. This weakness particularly affects the spiral arterioles and often occurs without significant anaemia. Thus, iron deficiency from whatever cause may lead to menorrhagia and menorrhagia in turn produces a more average iron deficiency. Therapy with iron breaks the vicious cycles.

It is suggested therefore, that in patients with menorrhagia and no demonstrable organic pathology, serum iron determination and needle biopsy of the bone marrow should be a part of investigation in each case.

#### Summary

Eighty cases of menorrhagia, having serum iron level of 90 mcg./100 ml. or

below, and 30 cases with serum iron level above 90 mcg./100 ml. and without any demonstrable organic pathologic findings on initial examination, were studied in detail with special reference to serum iron, tissue iron, and response to iron therapy.

70 per cent of cases with serum iron level below 30 mcg./100 ml. gave a good response to iron therapy with the improvement of menorrhagia. With serum iron above 90 mcg./100 ml. the improvement with iron therapy was only 46.6 percent.

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