COMPARATIVE STUDY OF IRON DEXTRAN IN SEVERE AND MODERN IRON DEFICIENCY ANAEMIA OF PREGNANCY

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The adequacy of oral iron therapy and the benefits and safety of total dose infusion using diluted iron dextran without any serious adverse effects have been reported by several authors. Undiluted iron dextran infusion which has been lately introduced has many advantages over the diluted mode of administration.

(a) The time required is reduced from several hours to half an hour or a few minutes.

(b) The danger of circulatory overload in cases of congestive failure associated with severe anaemia is eliminated.

(c) Blood transfusions have been drastically decreased.

(d) Incidence of local reactions like thrombophlebitis are practically absent.

According to Stiengold (1962) the incidence and the intensity of reactions rose if the anaemia was complicated by folic acid deficiency, respiratory, cardiac diseases or chronic infections. When any of the above conditions were present the incidence of reaction rose from 5 to 24%. In such cases the author has recommended very small doses to be administered.

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We report here our experience with total dose infusion of undiluted iron dextran in 50 patients with severe anaemia (Group A) and 110 patients with moderate anaemia (Group B). The aim of this study was to assess whether severely anaemic patients i.e. less than 5 gms: are prone to increased hazards after undiluted total dose infusion.

Material and Methods

Patients suffering from iron deficiency anaemia who were admitted in the antenatal wards of the Irwin Hospital, New Delhi, were selected for study. All patients were investigated before commencing treatment. Haemoglobin, peripheral smear, serum iron, unsaturated iron binding capacity (UIBC) and reticulocyte count were done in every case. Bone marrow examination was carried out in a few selected cases only. All patients were weighed and the amount of iron dextran required in each case was calculated with the help of the manufacturers formula

$$\frac{0.3 \times \text{Wt. in lbs} \times (100 - \% \text{ Hb.}) \text{ No. of Amp.}}{100}$$

Pulse, blood pressure were recorded repeatedly before during and after the infusion. Twenty-five mgms of iron dextran was given intravenously very slow-

ly as a test dose. Patients were then observed for a minimum of 30 minutes and if no untoward reaction occurred, the total undiluted dose of iron dextran was administered intravenously. Only autoclaved glassware was used to avoid unnecessary reactions. With an autoclaved syringe the drug was administered at an average rate of 1 ml/minutes increasing to 2-3 ml/minute, when no reactions were observed after more than half the dose had been given in both the groups. Total dose was administered to patients with cardiac decompensation only when signs like increased jugular venous pressure, cardiac dilatation and rales at the lung bases had subsided or improved markedly. This was achieved by initial treatment with intravenous furesamide, salt restricted high protein diet, morphine and oxygen therapy. No reduction in fluid intake was found necessary. The weight, intake and output were charted daily and patients reassessed clinically every day (Table I). In five cases where signs of congestive failure did not improve sufficiently or the patient remained dyspnoeic, one unit of packed cells was transfused. Undiluted iron dextran was then administered slowly the next day. All measures to combat severe reactions or shock were kept ready at hand.

TABLE I

Output and Weight Loss After Initial Furesamide Therapy in 36 Cases with Congestive Heart Failure in Both Groups

Day of treatment	DAY 1		DAY 2		DAY 3		DAY 4		DAY 5	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
Output in mls.	2600-3000	2800	1500-2600	2000	780-1000	870	650-800	670	600-780	612
Weight loss in Kgs.	0.9-1.4	1.2	0.6-1.0	0.8	0.2-0.5	0.4	0.0-0.3	0.2	0.0-0.3	0.2

Observations

The age was similar in both the groups i.e. 18 to 40 years. In group (A) the mean haemoglobin was 3.17 gm% with a range of 1.5 gm. to 5 gm%. In group (B) the mean haemoglobin was 6.5 gm% with a range of 5 to 8 gm%. Details regarding other initial investigation are given in Table II. In group A, on clinical examination 50% i.e. 25 cases had signs and symptoms of congestive heart failure the latter being frank in the majority of the

TABLE II

Pre-treatment Blood Values in Both Groups

Initial investigations	Group A		Group B	
	Mean	Range	Mean	Range
Haemoglobin	3.17 Gm.%	1.5-5 gm.%	7.1 gm.%	5.1-8 gm.%
Serum iron	40 ugm.%	25-80 ugm.%	65 ugm.%	40-110 ugm.%
UIBC	230 ugm.%	120-500 ugm.%	300 ugm.%	100-495 ugm.%
Reticulocyte	1.2	0.5	1	0.5

patients. In group B only 10% i.e. 11 cases presented with signs and symptoms of cardiac decompensation which were minimal in some. Amongst the 25 cases in group A, 5 patients in whom the Hb was between 1.5 to 3 gm% and signs and symptoms of right sided failure were marked and did not subside with intravenous furesamide, one unit of packed cells was transfused. Total dose infusion of iron dextran was then administered very slowly taking great care. The remaining 20 cases were only given undiluted iron dextran.

The Hb. rise per week ranged between 1.5 to 2.2 gm%, values observed in group A were higher compared to group B. There was no difference in the haemoglobin response amongst the patients who received an initial packed cell transfusion followed by total dose infusion and only total dose infusion. The haemoglobin levels in both the groups reached nearly normal levels within 4-6 weeks. In most of the cases one unit of packed cells only raised the haemoglobin by 0.5 gm to 0.7 gm%.

Mean serum iron level ten minutes after the infusion was 20900 ugm% in group A and 11200 ugm% in group B, Marchesin and Wallerstein (1964) recorded very high levels like 95000 ugm% at 10 minutes. Such high initial levels were not observed after total dose infusion in the present study. The mean serum iron level 6 weeks after infusion was 75 ugm% in group A and was 74 ugm% in group B. In both the groups 50% of clearance was observed around 36 hours and as much as 90% of plasma iron was cleared by the 7th day. Wood *et al* (1968) used iron dextran complex labelled with iron 59 and demonstrated that 50% clearance was observed by 2.5 to 4 days and complete clearance by the 10th day. Will and Gordon (1968) also used iron 59 labelled iron dextran and observed 50% clearance between 29 to 62 hours, mean being 49 hours. In all patients serum iron had fallen to normal levels by the 14th day. The above observations are in agreement with those of the present study in which 50% iron clearance was observed by 36 hours and 90% by the 7th day.

Reactions

In group A, 30% of the patients developed reactions as opposed to 29% in group B. None of the patients developed anaphylactoid reactions as reported by Mehta *et al.* All these patients showed variable degree of palpitation, dyspnoea, vomiting, giddiness, headache, bodyache, joint pains and fever.

During Infusion

Systemic reactions during infusion were more frequently observed in group A as compared to group B. The details are given in Table III. Nausea was the

TABLE III

Reactions During Infusion

Reactions	Group A		Group B	
	No. of patients	Percentage	No. of patients	Percentage
Nausea	5	10	9	8.1
Vomiting	1	2	6	5.4
Burning	4	8	2	1.8
Flushing	4	8	6	5.4
Headache	-	-	2	1.8
Giddiness	4	8	7	6.3
Dyspnoea	-	-	-	-
Chest pain	2	4	1	0.9
Techycardia	-	-	4	3.6
Bradycardia	-	-	-	-
Anaphylactoid reaction	-	-	-	-

most frequent reaction observed in both the groups (8.1% and 10% in group B and group A respectively). On the whole reactions during infusion were observed with higher frequency in group A as opposed to group B, Patients with minimal signs of heart failure did not present a higher intensity or incidence of untoward reactions. None of the patients who showed reactions required discontinuation of the drug.

Post Infusion Reactions

Local reactions in the form of thrombophlebitis occurred in one patient in group B and none in group A (Table IV). None of the patients in these groups developed other local reactions like urticaria, etc. Systemic reactions after the infusion were also more frequent in group A. Bodyache was significantly observed in group A and may have some correlation with the severity of the anaemia and generalised malnutrition.

Discussion

Total dose therapy in microcytic hypochromic anaemia with iron dextran com-

TABLE IV

Post Infusion Reactions

Reactions	Group A		Group B	
	No. of patients	Percentage	No. of cases	Percentage
Fever	-	-	3	2.7
Bodyache	9	18	7	6.3
Joint pain	1	2	11	9.9
Chest pain	-	-	-	-
Giddiness	2	4	1	0.9
Vomiting	-	-	-	-
Abdominal pain	-	-	1	0.9
Headache	-	-	1	0.9
Rash	-	-	-	-
Thrombophlebities	-	-	1	0.9

plex is now well established. It has also been reported to be safe by a number of workers (Basu, 1965; Bhatt, 1966; Bonner, 1965; Dass, 1967; Elhence, 1966; Lane, 1964; Mehta, 1968; Nissim, 1964; and many others). It has, however, been contraindicated in cardiac and pulmonary diseases. In our study, we have tried to make a comparison between cases of severe and moderate anaemia as regards the haematological response and side-effects, whether total dose infusion therapy could be used as a substitute for repeated blood transfusions in patients who are severely anaemic and showing signs of congestive failure. After total dose infusion the haematological response showed that almost normal levels of haemoglobin were achieved in both the groups within 4-6 weeks. A higher level of haemoglobin was observed in group A as opposed to group B, the cause of which is not clear, but may be the initial lower haemoglobin causing an improved response. Patients who were given both blood and total dose had no better response in comparison to those who received total dose only. The plasma iron turnover was more or less similar in both the groups. The plasma iron turnover was not affected by the initial haemoglobin levels. This had been proved by Dass *et al* in their previous studies.

None of the patients in the present study had anaphylactoid reactions, whereas Mehta *et al* have reported as high as 3.5% in their studies. Thrombophlebitis was observed in only one patient. The incidence in the present study as well as in our previous studies was very low compared to that reported by Basu 1965; Grimes, 1957; Mehta 1965; Bhatt, 1966 and others.

During infusion the reactions were mild to moderate in both the groups, not requiring discontinuation of the infusion. Reactions were more frequent in patients with severe anaemia, but certainly not alarming. In both groups nausea was the most common side-effect. In the post-infusion period, the overall incidence of side effect was higher in group B, but the number of reactions were more frequent in group A. It is evident that as larger doses of iron dextran were administered in group A, i.e. in severely anaemic patients, the reactions also tended to be more frequent. Twenty-five cases with severe anaemia and minimal signs of congestive failure at the time of infusion did not exhibit any serious side-effects even though the incidence of untoward reactions showed an increase. None of these patients exhibited any signs of circulatory overload after the infusion. The total infusion however, did not exceed 60 cc. in any case. There was a marked reduction in the total blood transfusions. It may be concluded that packed cell transfusion would be necessary only in very few selected cases of severe anaemia with pregnancy. Iron dextran can be safely administered in severe iron deficiency anaemia. The incidence of side-effects and reactions were seen more frequently with increasing severity of anaemia, but still within the safe limits for administration of the infusion. In the present study groups, it was not necessary to resuscitate the patient or to discontinue the infusion on account of the severity of side reactions.

Summary

Total of 160 patients of iron deficiency anaemia were taken up for intravenous undiluted total dose iron dextran therapy. Fifty patients were severly anaemic, 25 of them were showing signs of congestive heart failure and 110 patients were mode-

rately anaemic, 11 of them were showing signs of congestive heart failure. 30% of the group A developed reactions as opposed to 29% in group B. Blood transfusion was used in a very small number, the remaining having only iron dextran infusion. Mean rise of haemoglobin per week varied between 1.5 to 2.2 gm.% in both groups with a little higher response in group A. Iron dextran can be safely administered in both severe and moderate iron deficiency anaemia. Blood transfusion should be used in very few selected cases only.

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