Hematologic Disturbances in Infantile Malnutrition

Values for Copper, Iron, Paraphenylene Diamine Oxidase and Iron-Binding Capacity in the Serum

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DIFFERENT kinds of diets produce different types of infant malnutrition. Of these, the two principals are (1) marasmus or calorie-protein malnutrition, in which the cause is an insufficient calorie and protein intake; and (2) "distrofia pluricarencial" or kwashiorkor, in which the cause is an insufficient protein intake with an adequate or even increased caloric intake, especially as carbohydrate. From the clinical point of view, these two syndromes are clearly recognizable because the kind of alteration that they produce is very different.[1–5]

In Chile and other South American countries kwashiorkor seems to be less frequent than marasmus, which generally sets in during the first few months of life.

In kwashiorkor, macrocytic anemia, and to a lesser extent hypochromic anemia associated with bone marrow alterations reflecting defects of the maturation factors, is a common finding.[6] Recently, in kwashiorkor, several authors have described a diminution of serum iron-binding capacity, serum paraphenylene diamine oxidase and serum copper associated with this type of anemia.[7–9]

In marasmus, there is no morphologic alteration of the erythrocytes and serum proteins are normal or slightly diminished.[6] The present report gives the results of studies on paraphenylene diamine oxidase activity, iron-binding capacity and serum iron and copper values in children under one year of age affected by calorie-protein malnutrition (marasmus) of different degrees.

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PATIENT MATERIAL AND METHODS

Twenty-one infants with marasmus, who ranged in age from five to twelve months and had been admitted to the Hospital Manuel Arriarán of Santiago, were studied. They were divided into two groups. Group I consisted of ten infants who had attained only 40 to 60 per cent of their calculated ideal weight (second degree malnutrition according to Gómez et al.[5]). Group II consisted of eleven infants who had attained only 35 per cent or less of their ideal weight (third degree malnutrition). Fifteen normal infants were used as controls (group III). Special care was taken in order to obtain similar age averages in the three groups (7.1, 7.4 and 7.3 months, respectively).

The malnutrition in these children was caused by an insufficient calorie and protein intake as determined by social and economic factors. These children had received a very diluted skim milk as their sole nourishment; some with the addition of carbohydrate some without. Not one of them had been breast-fed for more than two months.

Up to the time the blood sample was obtained, and twenty days prior to it, there were no associated pathologic conditions that might have interfered with the results. There was no evidence of edema and the changes in the skin and hair were minimal or nonexistent.

The following determinations were made in all three groups: hemoglobin, blood counts and total protein. Copper was estimated using the method

TABLE I

Group I				Group II				Group III			
Age (mo.)	Weight (kg.)	Red Blood Cells (million)	Hemoglobin (gm. %)	Age (mo.)	Weight (kg.)	Red Blood Cells (million)	Hemoglobin (gm. %)	Age (mo.)	Weight (kg.)	Red Blood Cells (million)	Hemoglobin (gm. %)
6	3.5	4.2	11.6	5	2.9	3.7	11.5	5	7.3	4.2	12.1
4	3.0	5.0	11.6	4	2.8	3.3	10.6	5	6.6	4.3	12.2
8	5.0	5.0	12.2	9	3.4	4.4	13.7	5	6.4	4.4	11.6
6	4.3	3.1	9.9	4	2.7	3.8	11.4	9	9.1	4.3	11.3
9	5.2	3.2	9.9	4	2.8	3.9	10.4	7	8.5	4.8	12.0
8	4.5	4.8	10.8	8	3.9	3.7	10.6	10	9.2	4.0	10.2
9	5.1	4.1	9.6	9	3.4	3.7	10.8	9	9.0	4.2	12.3
8	4.6	3.9	10.3	12	5.1	4.1	11.0	3	6.0	4.2	11.6
12	6.0	4.4	10.9	7	3.1	3.3	10.8	3	6.0	4.1	10.4
4	3.6	5.1	12.6	12	6.4	3.7	10.7	3	5.8	4.3	10.7
				4	3.5	3.4	10.3	9	8.7	4.3	12.3
								9	8.5	8.4	12.0
								9	9.5	4.0	12.0
								11	10.5	4.3	9.6
								12	12.0	3.8	11.7
7.4	4.4	4.2	10.9	7.1	3.6	3.7	11.1	7.8	8.2	4.3	11.6
2.4	0.8	0.7	0.9	3.8	1.4	0.2	0.9	2.8	1.7	0.4	0.6

NOTE: Group I, ten infants with second degree malnutrition. Group II, eleven infants with third degree malnutrition. Group III, fifteen normal infants aged three to twelve months.

described by Eden and Hamilton,[10] iron by the method of Rath and Finch,[11] paraphenylenediamine oxidase by the method of Honckin,[12] and iron-binding capacity by the method of Rath and Finch.[11]

RESULTS

Hematologic Data

Confirming previous observations, the degree of anemia seen in the children with advanced malnutrition (group II) was not very severe when compared with the infants in group I or with the normal infants (group III) (Table I). This is also true for the hemoglobin levels which showed average values of 11.6 gm. per cent for group III, 10.9 gm. per cent for group I and 11.1 gm. per cent for group II (Table I).

Serum Protein Data

The average values for serum protein were 6.5 gm. per cent for group III, 6.1 gm. per cent for group I and 5.9 gm. per cent for group II. This confirms previous findings which showed that the decrease in the serum protein concentration is not very marked in malnourished infants. The difference was significant only in the children with advanced malnutrition (group II) as compared with the normal ones (group III) (Table II).

Biochemical Data

The average level of iron in the serum was 79 μg. per cent in the normal infants (group III), similar to that observed by others. In this age group, the concentration of both serum iron and hemoglobin is low.[6-17] In group I, the average value was slightly lower (69 μg. per cent) but the difference was not significant (Table II). On the other hand, in group II the average value was clearly lower (54 μg. per cent) and the difference was significant when compared with the values in group III (Table II).

Iron-Binding Capacity

In group III the average value for iron-binding capacity was 260 mg. per cent; in group I, 185 mg. per cent; and in group II, 148 mg. per cent (Table II). The total iron-binding capacity was calculated by adding the value of the serum iron plus the value of the iron-binding capacity; the resulting figure was very low in the infants with malnutrition (group II) (Table II). The percentage of saturation

TABLE II

Determination	Mean ± S.D.		
	Group I	Group II	Group III
Plasma copper (μg. %)	71 ± 27 P < 0.1	64 ± 21 P < 0.01	89 ± 19
Plasma iron (μg. %)	69 ± 12 P < 0.1	54 ± 16 P < 0.01	79 ± 16
Total plasma proteins (gm. %)	6.1 ± 0.6 P < 0.1	5.9 ± 0.6 P < 0.01	6.5 ± 0.4
Iron-binding capacity (μg. %)	185 ± 23 P < 0.001	148 ± 35 P < 0.001	260 ± 37
Total iron-binding capacity	259 ± 36	201 ± 32	337 ± 31
% saturation of iron-binding capacity	26%	25%	23%
Paraphenylene diamine oxidase activity (mg. %)	61 ± 13 P < 0.01	59 ± 16 P < 0.01	80 ± 15

was obtained by dividing the value of serum iron by the total iron-binding capacity; the resulting values were very close in the three groups (Table II).

Copper

The average value of the concentration of serum copper was 89.7 μg. per cent in the normal group, somewhat lower than the value pointed out by Sturgeon.[17] This author observed that the serum copper levels, as contrasted with iron, are high during the first months of life. In the malnourished infants (groups I and II), the values were even lower (69 and 54 μg. per cent, respectively). The value of P <0.01 in group II in relation to group III (Table II).

Paraphenylene Diamine Oxidase Activity

The average value of the plasma paraphenylene diamine oxidase activity was 80 mg. per cent, a normal figure for the method employed. In the malnourished infants, the average values were lower, 61 mg. per cent in group I and 59 mg. per cent in group II (P was <0.01 in both groups) (Table II).

COMMENT

In group II the serum concentration of both iron and copper was significantly decreased. Although we do not know the actual intake of these elements, we assume that it was low since the malnutrition resulted from underfeeding in all the infants studied. In our patient population, breast feeding is rarely prolonged beyond the third month of life, at which time, small amounts of cow's milk and, sometimes, flour in special preparations are substituted.[13] Although the ingestion of copper and iron is very low, the tissue concentrations are probably normal, since the requirements during retarded growth are also lower than normal (e.g., the iron required for hemoglobin formation in a malnourished infant is less than that required by a normal infant; for a same given age, the normal infant has a higher weight and blood volume and, consequently, a higher level of hemoglobin). On the other hand, copper and iron are stored in the infant's liver during pregnancy,[14–17] thus these elements are provided in normal amounts during the first months of life.

Deficiency of iron produces, among other alterations, a decrease in the plasma iron concentration, an increase in the percentage of saturation of the iron-binding capacity and microcytic-hypochromic anemia of different degree.[17] Our results differ from this situation since the percentages of saturation are similar in the three groups; the hemoglobin is normal and the erythrocytes are morphologically normal.

Different authors have pointed out that a deficiency of copper would produce an anemia similar to that caused by a deficiency of iron.[18,19] This fact has been related to certain types of infantile anemia accompanied by decreased serum copper.[20–23] However, it has not been possible to reproduce copper deficiency in children,[14,15] probably because of the congenital deposit mentioned previously.

Based on these data, we do not believe in the existence of a copper or iron deficiency in our infants related to their "requirements" and that this explains the absence of anemia or the decrease in the hemoglobin concentration. Anemia appears when growth and development are reinicyated or when the malnutrition begins later in life. [2,5,6,8–10]

The decreased concentration of copper and iron in the plasma could be explained as a consequence of the decrease in the protein to which these elements are bound. In our patients, the "siderophilin" was determined by adding the iron-binding capacity, plus the total iron-binding capacity, which is thought to represent siderophilin.[11,24] The "ceruloplasmin" was determined by a method based on the property of this protein to oxidize paraphenylene diamine.[12] According to these methods, both proteins were diminished (Table II). The total iron-binding capacity was lowered in 23 per cent of the infants in group I and in 30 per cent of the infants in group II. The paraphenylene diamine oxidase was also reduced by about 23 and 36 per cent lower than normal in the same groups. It is a well known fact that the serum proteins are significantly altered in "distrofia pluricarencial,"[25–29] but these alterations are seldom seen in the calorie malnutrition of small infants. The total serum protein was decreased in 6 per cent of the infants in group I and in 9 per cent of the infants in group II. These facts suggest that the decrease in total iron-binding capacity and paraphenylene diamine oxidase is not a consequence of a generalized hypoproteinemia, since the decrease in their values is much more significant than the decrease in the total serum protein.

Mitchell et al.[29] point out that the levels of siderophilin are not constant in the circulating plasma and may vary under certain circumstances; they even suggest that these proteins are present in two phases: one circulating in the plasma and the other retained inside the cell. This statement is also true for ceruloplasmin which varies its concentration under different pathologic conditions.[30] Thus, the selective decrease in the concentration of these two proteins may represent an unknown accommodation mechanism to the requirements of the undernourished infant.

SUMMARY

In two groups of infants with malnutrition of different degree due to underfeeding, determinations of the serum values of copper, iron, total iron-binding capacity and paraphenylene diamine oxidase were performed. The resulting figures were significantly decreased, but despite this, no anemia or signs of iron or copper deficiency were observed. A brief discussion of the results is given.

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