

Low Plasma Zinc and Iron in Pica

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Abstract. Objective : To determine role of trace elements in causation of pica with specific reference to zinc and iron we studied plasma levels of iron (Fe), Zinc (Zn), calcium (Ca) and magnesium (Mg) and blood lead (Pb) levels by atomic absorption spectrophotometer in 31 children with pica (Pica Group) and 60 controls matched for age, sex and nutrition (Control Group) in an observational case and control study in the settings of outpatient clinic of a tertiary care, teaching hospital. **Methods :** Data from each group were further stratified by hemoglobin level <9 and >9 g/dl into two subgroups pica-1 and pica-2, and control-1 and control-2 respectively, to control for confounding effect of iron deficiency anemia. **Results :** The plasma Fe level (mean \pm SD) in children with pica (42.7 ± 9.2 mg/dl) was about 20% lower than that in controls (51.5 ± 10.0 mg/dl, $p < 0.001$). Plasma Zn levels in the pica group (60 ± 4.4 mg/dl) was about 45% lower than those in controls (110.2 ± 8.5 mg/dl, $p < 0.001$). Correlation of Zn and Fe levels with pica-related variables such as age at onset, duration and frequency and number of inedible objects ingested was not significant. **Conclusion :** These findings suggest that hypozincemia with low iron levels may be the possible cause of pica and contradict the contention that low levels of plasma Zn and Fe could be an effect of pica.

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Key words : Iron; Iron-deficiency; Pica; Zinc; Lead

Pica is defined as persistent or compulsive ingestion of inedible or non-nutritive substances.^{1,2} It has been reported from all parts of the world² with prevalence varying from 10³ to 32.5%⁴ of all children surveyed, and upto 73% of school children.⁵ It is more prominent in younger children.^{3,5} The adverse effects of pica range from parasitic infestation⁶ anemia⁷ and trichobezoar and intestinal obstruction^{7,9} to life threatening hypokalemia¹⁰ and lead and other poisoning.^{11,12} The etiology of pica is still controversial.¹³ Iron (Fe) deficiency anemia,¹⁴⁻¹⁵ hypozincemia,^{16,17} psychosocial stress in presence of anemia,¹⁸ and family distress-especially maternal¹⁹-have all been presented as causes. Very little systematic research has been conducted on the association of pica with the plasma/blood levels of iron (Fe), zinc (Zn), copper (Cu), magnesium (Mg), calcium (Ca) and lead (Pb). We have studied the relation between pica and plasma levels of Fe, Zn, Ca and Mg and blood Pb levels in children, while controlling for the confounding effect of hemoglobin levels.

MATERIALS AND METHODS

The study was conducted in the Department of Pediatrics, Nehru Hospital, Postgraduate Institute of Medical Education and Research, Chandigarh, India, over a period of one year. Informed consent was obtained from the parents of the subjects prior to enrolment in the study.

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Study Population

Thirty one children with pica (Pica-group) between 18 months to 48 months of age who had been ingesting inedible substances three or more times per week for 3 months or longer were studied. Sixty children within same age range and gender distribution without pica served as control group. The control and pica groups were drawn from children brought to the outpatient service for immunization and were free from any acute illness or symptoms. Children with evident developmental delay, chronic illness and thalassemia major were excluded from the study. Children with moderate and severe malnutrition (weight for age <70%) were also excluded as malnutrition is associated with significant changes in plasma Zn and Fe levels.²⁰ Sociodemographic data and details of pica viz.,-the objects eaten, frequency of ingestion, amount ingested each time, associated symptoms and relevant medial history-were recorded on a predesigned form. A detailed physical examination and hemoglobin estimation was done in all the cases.

Estimation of Trace Elements and Minerals

Blood (3 ml) was collected from a peripheral vein into trace element-free, heparinized plastic vials using disposable plastic hubbed needles. One milliliter of heparinized whole blood was set aside in a trace element-free vial; the remainder was centrifuged at 3000 rpm for 10 minutes. The separated plasma was stored until analysis in another trace element-free vial at 4°C, as were the whole blood samples. Samples were digested using

the standard method adopted in our laboratory.²¹ Plasma Zn and Cu levels were determined with the help of an atomic absorption spectrophotometer (Perkin Elmer model 4000), while a direct current photometer (Spectrospan V₁, Beckman) was used for estimation of plasma Fe, Mg, Cu and blood Pb levels. The spectrophotometer was calibrated with the standards obtained from Sigma Co. USA. The reference materials that were used to check the accuracy of analytical method were obtained from International Atomic Energy Institute, Vienna, Austria and National Bureau of Standards, USA. The accuracy for Pb, Zn, Fe and Mg was above 99%. The precision of the method for Pb, Zn and Fe was upto 1 mg/dl and for Mg 0.1 mg/dl.

Data Analysis

Data obtained on Pica and Control was compared using

chi-square test for categorical variables and t-test and analysis of variance (ANOVA) for continuous variable. Within each group data was further categorized into two subgroups i.e. Pica-1 and Pica-2 and Control-1 and Control-2 based on hemoglobin levels. Pica-1 and Control-1 group had hemoglobin levels <9 g/dl and Pica-2 and Control-2 had levels >9 g/dl. Correlation coefficients (Pearson's least square) were calculated to look for possible interrelationship between plasma Fe and Zn levels on one hand and age at onset of pica and duration of pica on the other. SPSS version 7.5 was used for data analysis.

Results

The groups and the subgroups were comparable with respect to age and sex distribution and average weights (expressed as percentage of the weight expected for age

TABLE 1. Clinical Data in Different Groups

Group	Number	Sex Ratio (M : F)	Age (months)	Weight (%)	Hemoglobin (g/dl)
Pica	31	21:10*	27.3 ± 10.3† (18-46)	88.2±7.8†	8.5±1.3 (6.5-11.5)
Control	60	39:21	29.4 ± 8.0 (18-48)	86.3±6.1	9.4±1.1 (7.2-12.1)
Pica-1	21	14:7	27.0 ± 10.3 (18-46)	88.4±7.9	7.8±0.8 (6.5-8.9)
Pica-2	10	7:3	27.9 ± 9.6 (18-44)	87.1±8.0	10.0±0.8 (9.1-11.5)
Control-1	22	14:8	27.1 ± 8.3 (18-48)	86.1±6.3	8.2±0.4 (7.2-8.9)
Control-2	38	25:13	30.7 ± 8.9 (18-48)	86.3±6.0	10.0±0.8 (9.0-12.0)

Figures in parenthesis represent range

*P = n.s., by χ^2 -test, between Pica and Control group

†P=n.s., by t-test, between Pica and Control groups.

TABLE 2. Age of Onset and Duration of Pica, Number and Frequency of Non-nutritive Substances Ingested in Children with Pica

Pica characteristics	All n=31	Pica-1 n=21	Pica-2 n=10
A. Age of onset (months)			
<12	3 (9.6)	3 (14)	-
12-24	26 (84)	17 (81)	9 (90)
>24	2 (6.4)	1 (5)	1 (10)
B. Duration (months)			
3-12	23 (74)	15 (71)	8 (80)
13-24	6 (19)	5 (25)	1 (10)
>24	2 (6.5)	1 (5)	1 (10)
C. No of substances eaten			
1	13 (42)	9 (43)	4 (40)
2-3	17 (55)	11 (52)	6 (60)
4 and more	1 (3)	1 (5)	
D. Frequency of ingestion			
< 3/day	4 (13)	1 (5)	3 (30)
3-5/day	21 (68)	15 (71)	6 (60)
<5/day	6 (19)	5 (24)	1 (10)

*Percentages in brackets

Low Plasma Zinc and Iron in Causation of Pica

and sex). On physical examination no abnormal sign was detected in any of the study subjects except the presence of pallor in children with hemoglobin <9 g/dl.

Age at onset, duration of pica, number of substances eaten and frequency of ingestion in children with pica is shown in Table 2. The mean \pm SD age at onset of pica was 16.4 \pm 7.2 months and the duration 10.8 \pm 7.7 months. Both pica subgroups were comparable in this respect. Eight-four percent were 1-2 years old at the onset of pica, 74% had pica for 3-12 months and 81% ingested inedible substances up to five times per week. All the children with pica had geophagy; other inedible substances ingested were bricks, cement, ash, plaster, coal and soap.

The mean plasma Fe level in children with pica was about 20% lower than that in the controls (P<0.001) Table 3; however, mean Fe levels were similar in Pica and control subgroups made on the basis of hemoglobin level.

The mean plasma Zn level in children with pica was significantly lower than that of controls (p<0.001, t-test)

Table 3; the difference persisted between subgroups pica-1 and control-1 and pica-2 and control-2 (p<0.001; t-test). The Zn levels were similar in subgroup pica-1 and pica-2 and control-1 and control-2 Table 3. Plasma CU, Mgn, Ca, and blood Pb levels were similar in both the groups and their subgroups (Table 3).

Plasma Fe and Zn levels in Pica group did not correlate with the age at onset (r=0.99 and 0.126 with Fe and Zn respectively) or duration of pica. (r=0.009) with Fe and Zn. Plasma Zn and Fe levels did not differ significantly with the number of inedible substances ingested or frequency of ingestion (Table 4).

DISCUSSION

Mean hemoglobin and plasma Fe levels were significantly lower in children with pica compared to controls. Others^{14,14,22-27} have reported similar findings. In view of the overwhelming consensus in the literature on low

TABLE 3. Plasma Iron, Zinc, Copper, Magnesium, Calcium and Blood Lead in Different Groups (Mean \pm SD)

	Pica (n-31)	Controls (n-60)	Pica-1 (n-21)	Control-1 (n-22)	Pica-2 (n-10)	Control-2 (n-38)
Iron mg/dl	42.7 \pm 9.2 (30-67)	51.5 \pm 10 (33-76)	37.6 \pm 5.2*	39.7 \pm 4.3 (33-45)	53.5 \pm 5.5*	57.8 \pm 6.2 (50-76)
Zinc mg/dl	60.0 \pm 4.4 (53-70)	110.2 \pm 8.5 (96-130)	60.2 \pm 4.5†	107.6 \pm 7.6 (98-118)	59.5 \pm 4.6†	111.7 \pm 8.7 (96-130)
Copper mg/dl	123.2 \pm 8.4 (110-140)	124.0 \pm 6.8 (105-140)	122.5 \pm 9.4 (110-140)	123.5 \pm 6.8 (112-140)	124.6 \pm 7.8 (113-140)	124.3 \pm 6.8 (105-136)
Magnesium mg/dl	2.4 \pm 0.5 (1.9-3.9)	2.3 \pm 0.3 (1.7-3.0)	2.4 \pm 0.3 (1.9-3.0)	2.4 \pm 0.3 (1.7-2.8)	2.5 \pm 0.5 (2.0-3.9)	2.3 \pm 0.3 (1.8-3.0)
Calcium mg/dl	10.0 \pm 0.2 (9.2-11.2)	10.2 \pm 0.5 (9.1-11.1)	10.0 \pm 0.6 (9.1-11.2)	10.1 \pm 0.4 (9.3-11.0)	9.9 \pm 0.3 (9.4-11.0)	10.3 \pm 0.6 (9.1-11.1)
Lead mg/dl	26.9 \pm 5.0 (17.6-34)	27.8 \pm 3.2 (18.4-32)	27.5 \pm 5.0 (17.6-3.4)	28.6 \pm 2.1 (24-32)	25.5 \pm 5.0 (18.9-32)	27.6 \pm 3.8 (18.4-32)

Figures in parenthesis represent the range

*P<0.05; by t-test, as compared to corresponding subgroup within the same group[.

†P< 0.001; by t-test, as compared to correspond controls

TABLE 4. Plasma Iron and Zinc in Children with Pica Related to Frequency and Number of Non-nutritive Substances Eaten

		Frequency of ingestion			No. of non-nutritive substances eaten		
		< 3/day	3-5/day	>5/day	1	2-3	>3
Iron in μ g/dl	P1	30.0 (n-1)	38.0 \pm 5.0 (n-15)	38.4 \pm 5.8 (n-5)	38.0 \pm 3.9 (n-9)	36.6 \pm 4.3 (n-11)	45.0 (n-1)
	P2	51.7 \pm 7.6 (n-3)	53.0 \pm 3.9 (n-6)	62.0 (n-1)	52.0 \pm 7.7 (n-4)	52.8 \pm 5.9 (n-6)	-
	All	46.2 \pm 12.5 (n-4)	42.2 \pm 8.5 (n-21)	42.3 \pm 10.9 (n-6)	42.3 \pm 9.1 (n-13)	42.9 \pm 9.8 (n-17)	45.0 (n-1)
Zinc in μ g/dl	P1	56.0	59.2 \pm 8.2	59.4 \pm 5.0	60.3 \pm 5.5	60.1 \pm 3.8	60.0
	P2	61.0 \pm 7.0	59.5 \pm 3.4	56.0	56.5 \pm 2.5	60.5 \pm 5.6	-
	All	59.8 \pm 6.2	59.3 \pm 7.1	58.8 \pm 4.7	59.1 \pm 5.1	60.9 \pm 4.1	60.0

*P= not significant, by ANOVA, for plasma iron or zinc level with respect to the frequency or the number of substances eaten within Pica group or each subgroup

levels of hemoglobin and Fe in pica, we decided to control for the confounding effect of these variables while studying plasma levels of Zn, Cu, Mg, Ca and blood Pb levels by stratifying data on the basis of hemoglobin level.

The most significant finding of the study was that the mean plasma Zn level in children with pica was almost half that of controls, suggesting a strong association between hypozincemia and pica. The first report of hypozincemia in pica came from Prasad *et al.*¹⁶ They described syndrome of geophagy, Fe deficiency anemia, hepatosplenomegaly, growth retardation and hypogonadism in association with hypozincemia, which was later confirmed by Okcuolgu *et al.*²⁴. Since, then, more authors have reported low levels of Zn in pica^{17,28-30} but little attention had been paid to Zn after systematically controlling for hemoglobin and Fe levels. We found that plasma zinc levels were lower in children with pica compared to controls with similar hemoglobin and iron levels.

Do low plasma levels of Zn and/or Fe cause pica or is it an effect of pica? Controversy surrounds the answer to this question. Some investigators feel that pica results in malabsorption of Fe and/or Zn from the diet^{16, 24,25,31,32} while others believe that Fe deficiency^{13,14,27,33} and Zn deficiency^{17,28,29} can cause pica. If indeed pica causes Fe and/or Zn deficiency plasma Fe and Zn levels should correlate positively with age at onset of pica and negatively with duration of pica. Further, levels of these trace elements would be lower in children who ingested more non-nutrient substances more frequently. We did not find such as association. The correlation between plasma Fe and Zn and age at onset and duration of pica was not significant; as also of Fe and Zn. In a recent study, induction of zinc deficiency in sheep led to pica, then pica so induced relieved Zn-deficiency.³⁴ In our opinion, these observations support the hypothesis that low levels of Fe and Zn are the cause of pica, and not its effect.

Plasma levels of Cu and Mg in otherwise healthy and mentally normal children with pica were studied perhaps for the first time. These were within normal limits in both the groups and their subgroups. Earlier studies on mentally retarded adults³³ and children with iron deficiency anemia, geophagy, hepatosplenomegaly, dwarfism and hypogonadism²⁴ have yielded variable results. Ca levels in children with pica have not been reported in the literature. In a previous study we found that rickets was significantly more prevalent in children with pica for plaster or chalk than for other substances.³⁵ Clinically overt rickets was not seen in any of our children, and plasma Ca levels were similar and within normal range in all children. High Pb levels in children with pica have been traced to painted toys, discarded battery castings, paint peelings from ceilings and window sills, house dust and soil contaminated with Pb.^{6,12,36} However, none of the children in this study had high Pb levels, probably because they did not ingest any

substances rich in Pb.

To conclude, we found that children with pica had low level of plasma Zn and Fe, which in our opinion was the likely cause of their pica. These data should form the basis for an intervention trial comparing efficacy of Fe and Zn therapy for treatment of pica.

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Low Plasma Zinc and Iron in Causation of Pica

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