THE SERUM LEVELS OF IRON, ZINC, CALCIUM AND SELENIUM IN CHILDREN WITH PICA

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Abstract: **Background & Objectives:** The present observational case and control study was done to seek the relation between pica and the serum Iron (Fe), Zinc (Zn), Calcium (Ca) and Selenium (Se) levels in children, while controlling for the confounding effect of hemoglobin levels. **Material & Methods:** Forty children with pica between 1 to 5 Years of age were studied (Pica Group). Eighty children within same age range and gender distribution without pica were taken as control (Control group). Each group was further stratified into hemoglobin level <9 gm/dl and ≥9 gm/dl respectively, to control for the confounding effect of iron deficiency anemia. The Iron (Fe), Zinc (Zn), Calcium (Ca) and Selenium (Se) levels in the serum were measured. **Results:** The plasma levels of iron and zinc in children with pica was significantly lower (P<0.001) than the control group. The children in Anemic pica group had low levels of mean plasma zinc level than the Anemic control group (P<0.001). Likewise, the children in Nonanemic pica group had low levels of mean plasma zinc level than the NonAnemic control group (P<0.001). The present study also showed that the plasma iron and zinc levels did not correlate with the age of onset, duration, frequency of ingestion or number of substances eaten. **Interpretation and Conclusion:** Pica is significantly associated with decreased serum iron and zinc. The observations of the present study further support the hypothesis that the low levels of plasma iron and zinc are the cause of pica, and not the effect of it.

Key Words: Anemia, Inedible Substance, Pica

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Introduction:

The name “pica” is derived from the Latin word Magpie -A bird -because of its omnivorous habit and craving for unnatural articles of food[1].

Pica is defined as persistent or compulsive perversion of appetite with ingestion of inedible or non-nutritive substances[2, 3]. It is associated with the passage of these substances unchanged in the stool, and with radiological evidence of their presence in the gut when they are radio-opaque[4]. The phenomenon of pica is reported to be more prevalent than commonly believed[5], and the problem is also widespread. It has been reported from all parts of the world[2] with prevalence varying from 10 % [6] to 32.5 % [7] of all the children surveyed and upto 73% of school children[8]. The difference in incidence was explained to be due to the difference in the ages of the populations studied - Pica being more prominent in younger children [6].The adverse effects of pica range from parasitic infestation, anemia, trichobezoar and intestinal obstruction[9] to life threatening hypokalemia[10] and lead and other poisoning[11, 12]. The etiology of pica is still controversial[13]. It may be viewed as a manifestation of Iron deficiency anemia[4], protein–caloric malnutrition[2], trace metal (zinc and copper) deficiency[14], habit disorder[15] or as a response to inconsistency in the psychosocial environment of the child[16].

It is still unclear, however, whether anaemia prompts geophagia (to compensate for iron deficiency) or whether geophagia is the cause of anaemia[17]. It is proposed that pica is a result of an instinctive ability to recognize a deficiency and to know which substances contain that vital nutrient[18, 19]. Cure of this compulsive behaviour with the therapeutic iron is the Hallmark of pica. Very little systematic research has been conducted on the association of pica with the serum levels of Iron (Fe), Zinc (Zn), Calcium (Ca) and Selenium (Se). The present observational case and control study will seek the relation between pica and the serum Fe, Zn, Ca and Se levels in children, while controlling for the confounding effect of hemoglobin levels.

Material and Methods:

The study was conducted in the Departments of Biochemistry and Paediatrics, SMS Medical College, Jaipur after taking permission from the Institutional Research Review Board. The study population was drawn from children brought to the outpatient and immunization services at Sir

Padampat Mother and Child Health Institute, Jaipur. A written informed consent was obtained from the parents of the subjects prior to the enrolment in the study.

Study Population: Forty children with pica between 1 to 5 Years of age who had been ingesting inedible Substances three or more times per week for 3 months or longer were studied (Pica Group). Eighty children within same age range and gender distribution without pica were taken as control (Control group).

Each group was further stratified by hemoglobin level <9 gm/dl and ≥9 gm/dl into two subgroups pica-1 and pica-2 and control-1 and control-2 respectively, to control for the confounding effect of iron deficiency anemia.

Criteria for Selection:

Inclusion Criteria- Children of age between 1 to 5 years who had been ingesting inedible substances three or more times per week for 3 months or longer.

Exclusion Criteria- Children with evident developmental delay, acute/ chronic illness, thalassemia major and/ or children with moderate to severe malnutrition (weight for age <70%).

A detailed clinical history was taken and complete physical examination was done in all the cases. Venous blood (3 ml) was collected from a peripheral vein into a metal free plain plastic vial. Samples were left standing at room temperature for one hour. Subsequently the serum was separated by centrifuging at 3000 rpm for 15 minutes, and preserved at -20°C.

The Iron (Fe), Zinc (Zn) and Selenium (Se) levels in the serum of each subgroup were measured with the help of an Atomic Absorption Spectrophotometer (AAS 4141A) and the estimation of serum calcium was carried out on a fully automatic chemistry analyzer (OLYMPUS AU 400) in a standardized manner under set protocol in the Department of Biochemistry, SMS Medical College, Jaipur.

Results:

Following observations were obtained. All results are expressed in Mean ± S.D.

Table – 1 Distribution of Study and Control Groups

Hemoglobin	No of Pica cases	No of control subjects
<9 gm/dl	26 Pica-1 Anemic Pica Group	31 Control-1, Anemic NonPica Group
≥9 gm/dl	14 Pica-2, NonAnemic Pica Group	49 Control-2, Nonanemic NonPica Group
Total	40 Pica group	80 Control Group

Table- 2 Plasma Iron, Zinc, Calcium and Selenium in Different Groups (Mean ± S.D.)

Parameter	Pica	Control	Pica-1	Control-1	Pica-2	Control-2
Iron (µgm/dl)	43.3 ±10.4 (29.3-69.4)	51.4 ±10.7 (31.6-79.0)	38.4 ±7.6 (29.3-64.8)	44.2 ±11.4 (31.6-79.0)	52.4±8.8 (43.9-69.4)	55.9±7.4 (46.2-75.7)
Zinc µgm/dl)	58.8 ± 13.9 (41.3-79.7)	104.4 ±11.8 (82.3-126.3)	57.2±14.0 (41.3-79.0)	103.0±12.5 (82.3-122.4)	61.7±13.7 (43.6-79.7)	105.2±11.4 (84.5-126.3)
Calcium (mg/dl)	9.9 ± 0.59 (9.0-10.9)	9.8 ± 0.6 (9.0-10.9)	10.0 ± 0.6 (9.0-10.9)	9.8 ± 0.6 (9.0-10.9)	9.9 ± 0.5 (9.0-10.9)	9.8 ± 0.6 (9.0-10.9)
Selenium (µgm/dl)	11.3 ± 1.9 (9.1-15.7)	11.2 ± 2.2 (8.9-15.9)	11.4 ± 1.9 (9.1-15.6)	10.7 ± 1.9 (8.9-15.7)	11.2±2.0 (9.2-15.7)	11.6 ±2.3 (9.0-15.9)

On comparing all pica and all control groups, iron and zinc were low (P<0.001) in pica group. Whereas when anemic pica and anemic nonpica group were compared the difference was highly significant for zinc (P<0.001) and that for iron difference was only significant (P<0.05). In contrast when non anemic pica and non anemic non pica groups were compared only zinc showed highly significant P value. On comparing anemic pica and non anemic pica only iron showed highly significant difference (P<0.001). Whereas comparison of anemic non pica and non anemic non pica groups showed highly significant difference for iron only (P<0.001).

Table - 3 Age of Onset, Duration of Pica, Number of Substances Eaten and Frequency of Ingestion in Children with Pica

Pica Characteristics		All (40)	Pica-1 (26)	Pica-2 (14)
A. Age of Onset (months)	<12	4 (10)	3 (11.5)	1 (7.1)
	12-24	33(82.5)	21 (80.7)	12 (85.7)
	>24	3 (7.5)	2 (7.7)	1 (7.1)
B. Duration of Ingestion (months)	3-12	29(72.5)	18 (69.2)	11 (78.5)
	13-24	8(20)	6 (23.0)	2 (14.2)
	>24	3 (7.5)	2 (7.7)	1 (7.1)
C. No.of Substances Eaten	1	17 (42.5)	11 (42.3)	6 (42.9)
	2-3	20 (50.0)	12 (46.2)	8 (57.1)
	4 and above	3(7.5)	3 (11.5)	0
D. Frequency of Ingestion	<3/day	7 (17.5)	3 (11.5)	4 (28.6)
	3-5/day	24(60.0)	17 (65.4)	7 (50.0)
	>5/ day	9 (22.5)	6 (23.1)	3 (21.4)

Table - 4 Plasma Fe and Zn Levels with respect to the Frequency or Number of Substances Eaten

		Frequency of Ingestion			No. of Non- nutritive substances		
		<3/day	3-5 /day	>5 /day	1	2-3	≥ 4
Iron in µg/dl	Pica-1	37.3±9.6 (n-3)	38.8±8.6 (n-17)	37.5±3.9 (n-6)	38.8± 9.1 (n-11)	37.6± 6.6 (n-12)	39.6± 7.7 (n-3)
	Pica-2	50.5± 7.7 (n-4)	54.6± 11.1 (n-7)	50.0± 3.7 (n-3)	52.0± 9.3 (n-6)	52.8± 9.0 (n-8)	-
	All	44.9± 10.5 (n-7)	43.4± 11.7 (n-24)	41.7± 7.2 (n-9)	43.5± 11.0 (n-17)	43.7± 10.6 (n-20)	39.6± 7.7 (n-3)
Zinc in µg/dl	Pica-1	57.4± 15.0 (n-3)	57.0± 14.5 (n-17)	57.6± 14.8 (n-6)	57.4± 15.9 (n-11)	57.2± 13.4 (n-12)	56.3± 14.6 (n-3)
	Pica-2	60.0± 16.3 (n-4)	62.6± 14.8 (n-7)	61.6±12.7 (n-3)	63.2± 15.1 (n-6)	60.5± 13.6 (n-8)	-
	All	58.9± 14.5 (n-7)	58.7± 14.5 (n-24)	59.0± 13.5 (n-9)	59.5± 15.4 (n-17)	58.6± 13.2 (n-20)	56.3± 14.6 (n-3)

The correlation coefficients (Pearson's Least Square) were calculated which showed that the plasma iron and zinc levels did not correlate with the age of onset (r = 0.125, P value =0.442 and r = - 0.137, P value = 0.401 respectively) and the duration of pica (r= - 0.056, P value = 0.731 and r = - 0.167, P value = 0.304 respectively).

P values by ANOVA were calculated to know whether plasma iron or zinc levels differ significantly with the frequency of ingestion or number of substances eaten. Results showed that plasma iron and zinc levels did not differ significantly with the frequency of ingestion or the number of inedible substances ingested.

Discussion:

The children in Pica and NonPica groups and their subgroups were comparable with respect to age, sex distribution and average weights (expressed as percentage of the weight expected for age and sex).Children with moderate to severe malnutrition (weight for age <70%) were excluded from the study as malnutrition is associated with significant changes in plasma levels of trace elements[20, 21].

In our study, mean hemoglobin levels of children in the pica group was found to be 8.4 ± 1.4gm/dl while the same for control group was 9.4 ± 1.4 gm/dl. Sunit Singhi et al (2003) studied 31 pica patients and 60 age and sex matched controls with the hemoglobin levels of 8.5 ± 1.3 gm/dl and 9.4 ± 1.1 gm/dl[14]. The difference between the two was found to be significant.

Acharya et al (2007) studied 50 pica patients with a hemoglobin level 9.28 ± 2.25 gm/dl, as compared to 50 NonPica control subjects with a hemoglobin level of 9.30 ± 2.31gm/dl[22].

Coltman et al (1969)[23] demonstrated, as had Carlander (1959)[24], that when pica patients begin iron therapy the pica stops long before the anemia is repaired. Pica is related to iron deficiency and not to anemia.

In the present study plasma iron levels in pica group were 43.3 ± 10.4 µgm/dl which is significantly low (P<0.001) as compared to NonPica group in which mean iron levels were 51.4 ± 10.7 µgm/dl.

Relation between pica and low plasma iron was reported by many authors in the past. Earlier studies showed an association between pica and low plasma iron levels[4, 23, 24, 25]. Many authors also documented that pica is cured by giving iron therapy[4, 26]. Lanzkosky (1959)[4] first proposed a theory that iron deficiency is the major cause of pica and Crosby (1971)[26] stated that cure of this compulsive behavior with therapeutic iron is the hallmark of pica.

On the contrary, Minnich et al (1968)[27] and Okcuoglu et al(1966)[28] felt that pica results in malabsorbtion of iron from the diet. They proposed that clay or starch may prevent the absorption of iron from the intestine and iron deficiency is a result of pica.

Coltman (1969)[23] reported iron deficiency in patients with pica for substances which could not conceivably decrease the absorption of iron. These findings again created controversy that whether decreased plasma iron levels cause pica or is an effect of pica and the cause effect relationship is yet not resolved.

Singhi et al (2003)[14] conducted an observational case control study comprising of 31 pica children and 60 controls matched for age, sex and nutrition. The results showed that mean plasma iron level in pica group (42.7 ± 9.2 µgm /dl) was about 20% lower than that in controls (51.5 ± 10.0 µgm /dl, p<0.001).

Acharya et al (2007)[22] also reported low plasma iron levels in children with pica. The study group comprised of 50 children having pica with ages between 18 months and 6 years and compared them with fifty age and sex matched children without pica who were essentially normal. The mean plasma iron in pica group was 48.64 ± 10.50 µgm/dl which was significantly lower (p<0.001) than that of NonPica group (93.32 ±7.95µgm/dl).

The other significant finding of our study was that the mean plasma Zinc level in children of pica group (58.8 ± 13.9 µgm/dl) was almost 45% lower as compared to control groups (104.4 ± 11.8µgm/dl) which were showing plasma zinc levels within normal range. The findings indicate a strong association between hypozincemia and pica. Prasad et al (1963)[29] was the first author who reported low plasma zinc levels in children with a syndrome of geophagy, iron deficiency anemia, hepatosplenomegaly, growth retardation and hypogonadism. Okcuoglu et al (1966) [28] studied this syndrome among village children in turkey and confirmed the association between hypozincemia and pica. Danford et al (1982)[30, 31] studied 66 mentally retarded individuals, 60 with and six without pica. The Results showed a decreased plasma zinc levels in pica patients as compared to controls.

In contrast to these studies, our study group comprised of children with pica who were neither significantly growth retarded nor mentally retarded.

Sunit singhi et al (2003)[14] reported that mean plasma zinc levels in pica group (n=31) was (60.0 ± 4.4 µgm/dl) significantly lower as compared to controls (110.2± 8.5µgm/dl). The study also paid attention to plasma zinc levels after systematically controlling for hemoglobin and iron levels. They found that plasma zinc levels were lower in children with pica compared to controls with similar hemoglobin and iron levels.

Acharya et al (2007)[22] reported that mean plasma zinc levels in children with pica (57.52± 15.77µgm/dl) were significantly lower (P<0.001) as compared to controls (103.72± 10.92µgm/dl) which were within normal limits.

In the present study plasma calcium levels in the pica group was 9.9 ± 0.59 mg/dl while the same in the control group was found to be 9.8± 0.6 mg/dl. The difference between the two was statistically nonsignificant (p>0.05).

Plasma calcium levels in children with pica have not been extensively reported in the literature. Sunit Singhi et al (1982)[32] studied 180 cases of pica for the significance of the type of material eaten in relation to socio-economic environment and nutritional deficiencies. Results showed that Geophagy (75%) was the commonest form of pica, followed by wall plaster 58%), coal (44%) and chalk or slate-pencil (38%). Most of the articles eaten were crunchy. Statistically significant association was seen between eating of calcium containing articles and clinical evidence of rickets (p<0.01). These findings suggested that pica may be a need based behavior whereby the child is trying to supplement the deficient nutrient by eating nonfood articles. They said that the effort to maintain a constant internal environment constitutes one of the most universal and powerful drives and it was postulated that by instinct, child seeks to supplement deficient nutrient in his diet, by eating nonfood articles. There are experimental evidences to suggest this in the animals, both in the laboratory and in the field. Osteomalatic cattle have been observed to have osteophagia, but they ceased to do so when fed with phosphorus rich diet. Children with parathyroid deficiency are known to crave for chalk and plasters, and patients with Addison's disease crave salt.

Singhi et al (2003)[14] studied plasma calcium levels in 31 pica patients (mean 10.0 ± 0.2 mg/dl) and compared them with plasma calcium levels in 60 controls(mean 10.2 ± 0.5). They reported that plasma calcium levels were similar and within normal range in all the children and clinically overt rickets was not seen in any of the children. Our findings are consistent with these findings.

In the present study mean plasma selenium levels in the pica group was 11.3 ± 1.9 µgm/dl which is statistically not different from the plasma selenium concentration in the NonPica group (11.2 ± 2.2µgm/dl: p>0.05).

S. Yetgin et al (1992)[33] investigated serum selenium concentration in 40 children with iron deficiency anemia and 40 control subjects matched for age, sex and geographical origin. It was found that significantly lower (p<0.001) levels were found in patient group, which consisted of both normally developed and malnourished children. Patients also having pica had higher levels of selenium compared to patients without pica.

Our findings of plasma selenium concentration did not correlate with S. Yetgin et al (1992)[33]. The possible explanation of this may be that S. Yetgin et al[33] included the malnourished children in the study group, while pica patients in our study were not malnourished.

Present study was also aimed to investigate the cause-effect relationship between pica and plasma levels of iron and/or zinc levels in pica patients. Controversy still exists around the question that whether the low plasma levels of iron and/or zinc are cause of pica or it is an effect of it.

Prasad et al (1963)[29] and Okcuoglu et al (1966)[28] felt that pica results in malabsobption of iron and/or zinc from the diet. In contrast Federman et al (1997)[13], Lanzkowasky (1959)[4] and Danford et al (1982)[30, 31] believe that iron deficiency can cause pica while Hambidge et al (1971)[34], Bhalla et al (1983)[35] and Chen et al (1985)[36] believe that zinc deficiency can be the cause of pica.

If pica is the cause of iron and/or zinc deficiency, plasma iron and zinc levels should show a positive correlation with the age of onset of pica or they should show a negative correlation with the duration of pica. Moreover, the plasma levels of iron and zinc should be lower in children who ingested more number of non-nutrient substances as well as in children who ingested them with higher frequency.

Results of the present study showed that the plasma iron and zinc levels did not correlate with either age of onset of pica or with duration of pica and did not differ significantly with the frequency of ingestion or number of substances eaten.

Our findings are consistent with those observed by Singhi et al (2003)[14]. They also showed that plasma iron and zinc levels in pica group did not correlate with the age of onset (r=0.99 and 0.126 with Fe and Zn respectively) or duration of pica (r=0.009) with Fe and Zn.

The observations of the present study further support the hypothesis of Singhi et al (2003) that the low levels of plasma iron and zinc are the cause of pica, and not its effect.

Conclusion:

Pica is significantly associated with decreased serum iron and zinc. The observations of the present study further support the hypothesis that the low levels of plasma iron and zinc are the cause of pica, and not the effect of it.

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