TRACE ELEMENT STUDIES IN KARACHI POPULATIONS PART III: BLOOD COPPER, ZINC, MAGNESIUM AND LEAD LEVELS IN PSYCHIATRIC PATIENTS WITH DISTURBED BEHAVIOUR

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Abstract

Blood levels of copper, zinc, magnesium and lead were determined in 29 males and 15 females suffering from disturbed behaviour. As far as we could ascertain they were under no medication and belonged to low income groups. Male patients had significantly higher levels than female patients for zinc ($0.05 > P > 0.01$) but there was no sexual difference for magnesium or copper. In patients copper and lead levels were higher than for normals ($P < 0.01$), but no difference could be found for Mg an Zn. At least one metal abnormality was observed female patients (JPMA 39: 235, 1989).

INTRODUCTION

To our knowledge, no real attempts have been made in the literature to explain comprehensively the effects of abnormal trace element levels in body fluids or body content in psychiatric disease. Even merely recorded observations are few and far between. It has been reported[1] that disturbed behaviour associated with Wilson's disease is accompanied by low blood copper levels. However, none of our patients had this disease. Otherwise, in disturbed behaviour of many other types including those labeled as having disorders like hypomania, psychomotor excitation, paranoia, and the manic phase of manic depressive illness, excitory neurotransmitter functions are dominant and one would expect to find raised blood copper and zinc[2] and low magnesium levels[3]. Lead can cause a whole range of neurological, physiological and behavioural problems ranging from raised hearing thresholds in children and adolescents at blood levels of 5 ug/dl[4] to acute encephalopathy, memory loss and death at 80 ug/dl[5] . Formerly, a safety limit of 40 ug/dl was set[6] but in 1985 levels above 25 ug/dl were regarded as elevated in U.S.A. [7] The half-life of lead in blood is only about 18 days and 90% of the lead burden is stored in the bones and release from the brain is very slow[8]. Although blood lead levels are therefore a measure of recent exposure only, there is no other easy way of assessing lead status. The effects of lead vary in severity between races e.g., black American children are less affected than white[4], and so we do not know if Pakistanis are affected as severely as Westerners or not. Individuals are affected differenfly at a given level e.g., 100 ug/dl may literally kill one person and have no obvious symptoms or in 19 (65.5%) of the males and 9 (60.0%) of the effects on another[9]. Recently, a protein has been isolated from red blood cells which confers protection from the effects of lead in some individuals with sustained high blood lead levels[10]. Lower income groups take up lead more readily and the effects are more severe[11]. Most of our patients happen to be from this group. The effects of metal abnormalities and high lead levels often enhance one another[2]. This study reports our findings concerning blood copper, zinc, magnesium and lead levels in psychiatric patients with disturbed behaviour.

MATERIALS, EQUIPMENT AND METHOD

Estimations were done on whole blood as it was impossible to achieve centrifugation promptly which is necessary if results in serum for zinc and magnesium are to be meaningful. Treatment of samples, standards, controls and blanks was done as previously described[12]. The preparation and calibration of standards for lead was similar to that described for copper and Sc, absorption versus concentration being linear. Precise details will be given later.

Patients:

A total of 29 males and 15 females were selected from low income groups who were attending the out-patients neuropsychiatric clinic at the Jinnah Postgraduate Medical Centre, Karachi, for the fir st time. They were not apparently taking any medicines at the time of blood sampling. In this group 18 males and 10 females were suffering from disturbed behaviour of incomplete diagnosis, together with 4 males and 1 female labeled as having hypomania, 2 males and 2 females with psychomotor excitation, 4 males and 1 female in the manic phase and 1 male, 1 female with paranoia. Statistical Analysis: For statistical evaluation of data obtained, the Wilcoxon Rank Sum Test[13] was used throughout as distributions were basically non-Gaussian in every case, thereby invalidating the student's 't' test.

RESULTS

Blood levels of copper, zinc and magnesium for this group of patients are given in Tables I and II

TABLE 1. Blood Copper, Zinc and Magnesium levels in the Disturbed Behaviour Group of Patients and comparisons with Normals.

Metal	Group	Sex	Range*	Mean*	Median*	S.D.	P
Copper	Patients	M	27–173	103.1	100.0	28.4	
		F	90–164	116.6	111.4	21.6	$<0.05^{++}$
		M+F	27–173	107.7	107.8	26.8	
	Normals[12]	M+F	71–116	93.5	94.5	11.25	$<0.01^{+}$
Zinc	Patients	M	554–2113	768.2	708.0	278.9	>0.05
		F	522–948	672.0	666.0	115.9	$>0.01^{++}$
	Normals	M	602.5–850	726.0	726.0	61.9	$>0.05^{+}$
		F	519–853	685.9	695.5	83.5	$>0.05^{+}$‡
Magnesium	Patients	M	0.84–5.11	3.77	3.86	0.82	
		F	2.87–6.23	3.77	3.67	0.86	$>0.05^{++}$
		M+F	0.84–6.23	3.77	3.85	0.82	
	Normals[12]	M	2.97–4.80	3.78	3.80	0.46	$>0.05^{+}$
		F	2.65–4.66	3.50	3.515	0.50	$>0.05^{+}$**

*Units for copper and zinc: ug/dl; magnesium: mg/dl.
+Significance of difference between normals and patients.
++Significance of difference between male and female patients.
‡Between male and female normals, $p < 0.01$.
**Between male and female normals $0.05 > p > 0.01$.
SD Standard Deviation.

TABLE II. Normal and Abnormal Blood Levels for Copper, Zinc and Magnesium in the Disturbed Behaviour Group of Patients.

29 Males and 15 Females

Metal	Sex	Number (Percentage) of patients with Levels		
		Low	Normal	Raised
Copper	M	2(6.9)	18(62.1)	9(31.0)
	F	0	10(66.7)	5(33.3)
	M+F	2(4.5)	28(63.6)	14(31.8)
Zinc	M	1(3.4)	26(89.7)	2(6.9)
	F	0	14(93.3)	1(6.7)
	M+F	1(2.3)	40(90.7)	3(6.8)
Magnesium	M	3(10.3)	24(82.8)	2(6.9)
	F	0	14(93.3)	1(6.7)
	M+F	3(6.8)	38(86.4)	3 (6.8)

together with those for normal subjects reported previously[12]. Twenty eight (19 males, 9 females) out of 44 patients (63.6%) had at least one metal abnormality. The term "metal abnormality" is used here to denote one of the following: allow or raised blood level of copper, zinc or magnesium or a lead level of over 40 ug/dl. Sixteen (10 males, 6 females) out of the 44 cases (36.4%) had no abnormalities at all but an extra 10 (6 males, 4 females) or 22.7% had a lead abnormality only. Seven patients (6 males, 1 female) or 15.9% had lead plus at least one other metal abnormality and 11 patients (7 males, 4 females) or 25.0% had at least one metal abnormality other than lead.

TABLE III. Number and Percentage of Metal Abnormalities among the Patients.

29 Males + 15 Females

Sex	Number (Percentage) of Patients with the stated no. of Metal Abnormalities.							
	0*	0+Pb+	1*	1+Pb+	2*	2+Pb+	3*	3+Pb+
M	10(34.5)	6(20.7)	5(17.2)	3(10.3)	1(3.4)	2(6.9)	1(3.4)	1(3.4)
F	6(40)	4(26.7)	3(20)	1(6.7)	0	0	1(6.7)	0
M+F	16(36.4)	10(22.7)	8(18.2)	4(9.1)	1(2.3)	2(4.5)	2(4.5)	1(2.3)

*Copper, zinc and or magnesium but lead below 40 ug/dl.
+Copper, zinc and/or magnesium and lead over 40 ug/dl.

Further details are in Table III including the fact that 1 male and 1 female had abnormalities in copper, zinc and magnesium and 1 male was abnormal in all four blood metal levels. Blood copper levels for our group of patients were significantly higher ($P < 0.01$), than for normals. As with normals[12], there

was no significant difference between the sexes. Nine males and 5 females were individually above the normal range, while 2 males were below it, one of whom was known to be in the manic phase of manic depression. As with normals[12] ($P < 0.01$), our male patients had significantly higher levels of zinc than females ($0.05 > P > 0.01$) but there was no significant difference either by sex or in total between patients and normals. Two male patients and one female were above the normal range and one male patient having auditory hallucinations had a low level. Blood magnesium levels are significantly higher for normal males than females ($0.05 > P > 0.01$) but there was no significant difference in our group of patients. There was no significant difference in levels between normals and our patients either by sex or in total. Three males had levels below the normal range. Two males and one female were above; one male was in an acute psychotic state and the female and the other male were in the manic phase of manic depresion. Blood lead levels were estimated for 28 of the 29 male patients and 14 of the 15 females. Levels were significantly higher than for controls ($P < 0.01$) and 18 (13 males, 5 females) of the 44 patients (42.9%) had levels of 40 ug/dl or above. Regression analysis was carried out as previously[12], results being in Table IV.

TABLE IV. Intermetallic Regression Equations and Correlation Co-efficients for Patients and Normals.

Metals	x	y	Sex	Regression Equation	Correlation Coefficient (Patients)	Correlation Coefficient (Normals)[12]
Zn V.Cu Cu	Zn	M		$y = -4.233x + 1206.7$	–0.432	–0.247
		F		$y = 2.292x + 404.75$	0.428	0.095
		M+F		$y = -3.027x + 1062.6$	–0.340	–0.108
Mg V.Cu Cu	Mg	M		$y = 0.0142x + 2.297$	0.496	0.320
		F		$y = 0.014x + 2.125$	0.354	–0.209
		M+F		$y = 0.0134x + 2.318$	0.439	–0.042
Mg V.Zn Zn	Mg	M		$y = -1.593 \times 10^{-3}x + 4.992$	–0.545	–0.0479
		F		$y = 5.261 \times 10^{-3}x + 0.237$	0.707	0.367
		M+F		$y = -1.010 \times 10^{-3}x + 4.512$	–0.294	0.249

Metal abnormalities on an individual basis and grouped according to diagnosis or the manifestations of disease are given in Table V.

TABLE V. Metal Abnormalities in diagnosed cases and in some individual manifestations.

Diagnosis or Manifestation	Sex	N	Number of Metal Abnormalities				
			None	One	Two	Three	Four
Manic Phase	M	4		(1)Pb ↑ (2)Cu ↓	(3)Cu ↑ Pb ↑ (4)Mg ↓ Pb ↑		
	F	1				Cu ↑ Zn ↑ Mg ↑	
Hypomania	M	4	(1,2)	(3,4)Cu ↑			
	F	1		Pb ↑			
Paranoia	M	1		Pb ↑			
	F	1		Pb ↑			
PsychomotorRetardation	M	2	(1,2)				
	F	2	(1,2)				
Violent, aggressive	M	7	(1)	(2–5) 4xPb ↑	(6)Cu ↑ Mg ↓	(7)Cu ↑ Zn ↑ Pb ↑	
	F	4	(1)	(2)Cu ↑ (3)Pb ↑	(4)Zn ↑ Pb ↑		
Hallucinations	M	2		(1)Cu ↑		(2)Cu ↑ Zn ↓ Mg ↓	
	F	1	(1)				
Ac. Psychosis	M	3	(1,2)			(3)Cu ↑ Mg ↑ Pb ↑	
Other Hyperexcited States	M	2	(1)		Cu ↑ Pb ↑		
	F	1		Cu ↑			
Other Manifestations	M	4	(1,2)	(3)Cu ↑			(4)Cu ↓ Zn ↑ Pb ↑ Mg ↓
	F	4	(1,2)	(3)Cu ↑ (4)Pb ↑			

Numbers in brackets refer to patient number.
Circled arrows indicate disagreement with the literature.

DISCUSSION

In disturbed behaviour which is not associated with Wilson's disease excitoryneurotransmitter functions are dominant and one would expect to fmd raised blood copper and zinc[2] and low magnesium[3] levels. Levels of lead higher than those in controls would not be unexpected. As expected, blood copper levels were significantly higher for this group of patients than for normals (Tables I and II), although two males had low levels. Unexpectedly, there was no significant difference in zinc and magnesium levels between patients and normals although three patients had zinc levels above the normal range and one had a level below; three had low magnesium levels and three had raised. Blood lead levels for the patients were significantly higher than for controls. All patients had elevated levels [above 25 ug/dl[7]] but 18 of the 44 patients (42.9%) as compared with 13 out of 62 (21.0%) controls were above the former safetylimit [40ug/dl[6]], i.e. abnonnal in our context. Intermetallic correlation coefficients (r, Table IV) were higher numerically in every case for the patients than for normals. Perhaps these are to some degree influenced by the lower nutritional status of the patients or by the higher lead levels. Of note is the fact that for copper versus zinc for females, the coefficient is fairly high and positive, whereas it is close to zero for normal females. As for normals it is negative for males and for males plus females. Consideration of the results on a more individual patient basis (Table V) reveals that all five lebelled as being in the manic phase of manic depressive illness had metal abnormalities, the results of three wholly agreeing with that in the literature2'3. Three of five patients with hypomania and both paranoiacs had expected metal abnormalities (the female paranoiac had a lead level of 76.4 ug/dl) but none of those with psychomotor excitation had an abnormality. The remainder of the patients had either not been admitted to the wards or had discharged themselves

before a diagnosis had been confirmed and were therefore categorised according to theft presenting condilions or manifestations. Ofthese9out of 11 patients (81.8%) exhibiting violent or aggressive behaviour had metal abnormalities, all of which conformed to previous literature reports[2,3]. Of those with auditory or visual hallucinations, an acute psychotic reaction, or other hyperexcited manifestations, five of nine patients had metal abnormalities of which three agreed with the literature. Of the eight remaining patients, four had metal abnormalities of which one partly contravened previous reports[2,3] having blood copper 27.0 (normal range[12] 71-116), zinc 2113 (602.5-850), lead 42.1 ug/dl, magnesium 0.84 g/dl (2.97-4.80). A total of 28 (63.6%) of our patients had at least one metal abnormality and of these 21 (75.0%) or 47.7% of the total number of patients were totally in agreement with results quoted in the literature[2,3].

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