

Magnesium, zinc and copper in acute psychiatric patients *)

By D. P. Srinivasan ¹⁾, S. Marr ²⁾, R. A. Wareing ²⁾, N. J. Birch ²⁾, ³⁾,

¹⁾ Department of Psychiatry, St. James' University Hospital, LEEDS, U. K.

²⁾ Department of Biochemistry, University of Leeds, LEEDS, U. K.

³⁾ Department of Biological Sciences, The Polytechnic, Wolverhampton, U. K.

Zusammenfassung

Magnesium, Zink und Kupfer wurden im Plasma von Patienten mit einer Vielzahl psychiatrischer Symptome einer psychiatrischen Abteilung untersucht, die zum Teil eine Lithium-Therapie erhielten. Es handelte sich um stationäre wie ambulante Fälle. Die Diagnose wurde vom Psychiater gestellt, die Elektrolytbestimmungen erfolgen unter Blindbedingungen. Nach Vorliegen der Daten wurden die Ergebnisse in Beziehung gesetzt zu Alter, Geschlecht, Diagnose und Medikation. Die Ergebnisse dieser vorläufigen Studie lassen deutliche Unterschiede in der Elektrolytverteilung erkennen bei Aufteilung der Patienten nach diagnostischen Kriterien auf neun verschiedene Gruppen.

Summary

Plasma Mg, Zn & Cu determinations were carried out on samples from patients presenting with a wide variety of psychiatric symptoms at a psychiatric unit in a large general hospital and also at a lithium clinic in a psychiatric hospital. Both in- and out-patients were studied. The patients were selected and assessed by the psychiatrist and analysis of the blood samples in the biochemistry laboratory was carried out 'blind'. After analysis of the complete set of samples, the data was re-identified with the patient and statistical analysis carried out in relation to age, sex, psychiatric diagnosis and medication. The results of this preliminary study will be reported to reveal apparent differences in metal ion concentrations between the nine diagnostic categories considered.

Résumé

Des déterminations plasmatiques du Mg, du Zn et du Cu ont été effectuées sur des échantillons provenant de patients avec une large variété de symptômes psychiatriques, dans une unité psychiatrique d'un hôpital général et également dans un service clinique de traitement par le lithium d'un hôpital général. Nous avons étudié des patients hospitalisés et non hospitalisés. Les patients ont été sélectionnés par le psychiatre et l'analyse des échantillons de sang dans le laboratoire de biochimie a été effectuée «en insu». Après l'analyse de l'ensemble complet des échantillons, les données ont été réidentifiées avec le patient et une analyse statistique a été effectuée en rapport avec l'âge, le sexe, le diagnostic psychiatrique et la médication. Les résultats de cette étude préliminaire ont fait apparaître des différences manifestes dans les concentrations des ions métalliques entre les 9 catégories considérées de diagnostic.

* * *

A broad spectrum metabolic screening of the whole population of a large psychiatric hospital (about 1 400 patients) has indicated that many of the in-patients had a moderate abnormality in serum trace-metals and in particular Magnesium (Mg), Zinc (Zn), and Copper (Cu) [1]. The preliminary data suggest that the abnormal results were seen, not as a result of changes following long-term hospitalization, but frequently occurred in recently admitted patients and were associated with other biochemical changes indicative of protein-energy deficit. This suggested that the trace metal changes were associated with the mental state, either primarily or secondarily, and were not due to the quality or quantity of the hospital diet.

To investigate the incidence of trace metal disturbances in recently admitted patients, and those attending a hospital on a daily basis, we have studied consecutive admissions to an acute psychiatric unit in a large District General Hospital. The patients were unselected and represent most of the admissions and referrals to one specific psychiatric team over a six-week period (January to March, 1981).

Blood was taken with minimal stasis from an antecubital vein into plain tubes and after clotting was transferred to the Biochemistry Department where it was immediately separated. Metals were determined later using atomic absorption spectrometry (IL 157, Instrumentation Laboratories Ltd.) the instrument being fitted with background correction facilities which were used for the determination of Zn and Cu. All samples were diluted with solutions containing appropriate concentrations of salts, to obviate interferences, prior to analysis.

Statistical analysis of the results was carried out by means of the Students' 't' test and the data was compared with control data obtained from 85 members, male and female, of the hospital staff who were without overt psychiatric symptoms, in good health and of a wide range of ages.

* Results presented at the 3rd International Symposium on Magnesium, Baden-Baden, 22.—28. 8. 1981.

Results and discussion

The results are displayed in the accompanying Tables 1 and 2. Table 2 shows the results of trace metal analyses expressed as percentages of the corresponding control group indicated in Table 1. Significant differences indicated by the 't' test are also shown.

Although there are significantly decreased serum Mg concentrations in female schizophrenics and elderly, demented female patients and in a very small group of male epileptic patients who were receiving anti-epileptic drugs, the major changes seen in this group of acutely ill patients were in the concentrations of Zn. All groups had a mean serum Zn lower than a comparable normal control group determined concurrently by our laboratory. The most significant decreases in serum Zn were seen in schizophrenics, dementias and most significantly in alcoholics.

Such differences have been reported previously by Pfeiffer [2, 3] although in our laboratory we have been unable to confirm the concomitant rise in serum Cu reported by this author. Our results

Tab. 1: Concentrations of Mg, Cu and Zn in serum for a control series comprising members of nursing and other hospital staff. All subjects were free from overt psychiatric or physical illness. Mean \pm S. D.

Controls

	n	Mg(mM)	Cu(μ M)	Zn(μ M)
Male	28	0.86 ± 0.10	18.74 ± 4.50	15.61 ± 3.34
Female	57	0.82 ± 0.10	21.33 ± 5.45	14.36 ± 2.08
Total	85	0.83 ± 0.10	20.54 ± 5.26	14.74 ± 2.57

Tab. 2a—2g: Mean Concentrations of Mg, Cu and Zn in serum of patients classified according to psychiatric diagnosis. All results are expressed as the percentage of the mean concentration of the respective control group as listed in Table 1. The significance is indicated following Students' 't' test * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.005$.

Tab. 2a:

Schizophrenia

% Control	n	Mg	Cu	Zn
Male	31	102.9	108.5	80.1***
Female	12	92.3*	90.1*	88.1**
Total	43	100.3	97.8	85.1***

Tab. 2b:

Affective psychoses

% Control	n	Mg	Cu	Zn
Male	8	94.5	111.2	88.0*
Female	19	106.8*	104.6	94.5
Total	27	103.2	105.7	91.1*

Tab. 2c:

Alcoholism

% Control	n	Mg	Cu	Zn
Male	7	95.2	110.7	72.3***
Female	1	94.5	85.0	53.5***
Total	8	98.1	99.3	73.5***

Tab. 2d:

Dementias

% Control	n	Mg	Cu	Zn
Male	5	94.1	104.5*	79.7*
Female	12	112.4***	109.9	84.8*
Total	17	107.1*	113.5	83.2***

Tab. 2e:

Subnormalities

% Control	n	Mg	Cu	Zn
Male	4	87.9*	96.0	85.3
Female	2	124.1	93.0	95.6
Total	6	101.7	90.6	91.3

Tab. 2f:

Epilepsy

% Control	n	Mg	Cu	Zn
Male	4	85.4**	98.0	87.2
Female	0			

Tab. 2g:

Neuroses

% Control	n	Mg	Cu	Zn
Male	3	84.8	88.1	82.7
Female	7	103.5	101.6	99.1
Total	10	96.8	96.1	93.1

overall were, however, skewed towards decreased Zn and elevated Cu (Figures 1, 2, 3). Zn deficiency has been reported previously in association with alcoholic pancreatitis. [4]. *Moynahan* [5] has drawn attention to the psychiatric sequelae of Zn deficiency in children with *acrodermatitis enteropathica* and it is clear that our results suggest major abnormalities in Zn metabolism in adult psychiatric patients.

The changes demonstrated in serum Mg were few and inconsistent and may indicate the efficiency of the homeostatic mechanisms for this ion [6]. Indeed, the well recognized Mg deficiency of alcoholism [7] was not reflected in *all* patients in

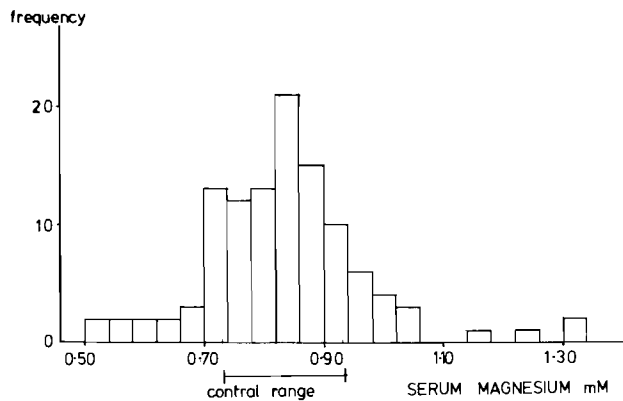


Fig. 1: Distribution of serum Mg results obtained in 112 patients admitted or referred to St James' University Hospital Psychiatric Unit. Control range shows upper and lower extremes of results obtained from the normal control group described.

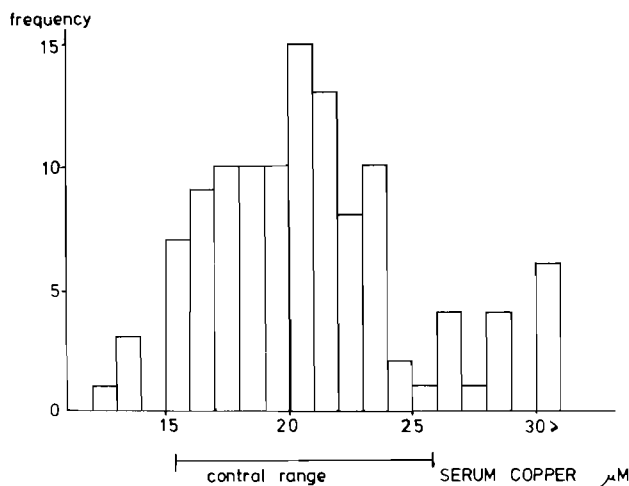


Fig. 2: Distribution of serum Cu results obtained in 112 patients admitted or referred to St James' University Hospital Psychiatric Unit. Control range shows upper and lower extremes of results obtained from the normal control group described.

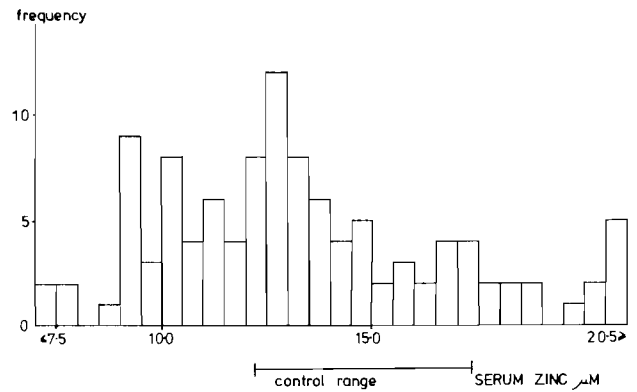


Fig. 3: Distribution of serum Zn results obtained in 112 patients admitted or referred to St James' University Hospital Psychiatric Unit. Control range shows upper and lower extremes of results obtained from the normal control group described.

decreased serum Mg though the lowest values overall were found in this group ($Mg_{pl} = 0.50 - 1.17$ mM) and the mean values of both males and females were below those of the normal controls. Possibly the psychiatric definition of alcohol abuse employed in this unit was not sufficiently precise to isolate only the severe alcoholics and the group may have included alcohol abusers with only anecdotal case-histories.

There was evidence of decreased serum Mg in neurotic patients, both male and female.

Our results confirm, in acute psychiatric patients, our previous finding of widespread abnormality in serum trace-metals. However, further studies are required to define the role of such metals in the psychopathological process. In particular it is important to discover the role of Mg and its effects on the interactions between Zn and Cu. Whatever the molecular mechanism, however, it is clear that psychiatric patients acutely admitted may be in a sub-optimal nutritional state and that the trace metal concentration in serum may reflect this. Whether such nutritional deficit is the primary cause of the psychiatric illness, or is a result of the disability to care adequately for themselves due to the illness, is a question which must receive urgent attention.

Acknowledgements

We wish to thank Dr. *R. P. Hullin*, Metabolic Research Unit, High Royds Hospital, Menston, Ilkley, Yorkshire, for continued encouragement

and support and Dr. *J. Roberts* for permission to study patients under his care at St James' University Hospital, Leeds. This work was supported by The Medical Research Council.

References

- [1] *Birch, N. J., Hullin, R. P., Kajda, P. K., Morgan, D. B., Srinivasan, D. P. Wareing, R. A.*: Plasma Zn, Cu & Mg in 1400 Psychiatric In-Patients. Manuscript in Preparation.
- [2] *Pfeiffer, C. C., Iliev, V.*: A study of zinc deficiency and copper excess in the schizophrenias. In: *Pfeiffer, C. C.* (ed): Neurobiology of Trace Metals Academic Press, New York, (1972) pp 141—165.
- [3] *Pfeiffer, C. C., Bacchi, D.*: Copper, Zinc, Manganese, Niacin and Pyridoxine in the schizophrenias. *J.Appl.Nutrit.* **27**—9 (1975) 39.
- [4] *Williams, R. B., Russell, R. M., Dutta, S. K., Giovetti, A. C.*: Alcoholic Pancreatitis — Patients at high risk of acute Zinc deficiency. *Am.J.Med.* **66** (1979) 889—893.
- [5] *Moynahan, E. J.*: Zinc deficiency and disturbances of mood and visual behaviour. *Lancet* **i** (1976) 91.
- [6] *Cantin, M., Seelig, M. S.* (eds): Magnesium in Health and Disease. Spectrum Press, New York. (1980) 995p.
- [7] *Flink, E. B., Stutzmann, F. L., Anderson, A. R.*: Magnesium deficiency after prolonged parenteral fluid administration and after chronic alcoholism complicated by delirium tremens. *J.Lab.Clin.Med.* **43** (1954) 169.

(For the authors: Dr. N. J. Birch, Reader in Biological Sciences, Department of Biological Sciences, The Polytechnic, Wulfruna Street, WOLVERHAMPTON, WV1, 1LY, England.