



**SERUM TRACE ELEMENTS (COPPER, MANGANESE AND ZINC) STATUS OF
PSYCHIATRIC PATIENTS OF FEDERAL NEUROPSYCHIATRIC HOSPITAL, ENUGU
NIGERIA.**

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ABSTRACT

Introduction. Trace elements play major roles in various metabolic pathways and are usually associated with an enzyme or another protein as an essential component or they function as cofactors. Alterations in the optimum levels of trace elements may adversely affect biological processes and are associated with many diseases. A few investigators have reported serum trace element levels in some psychiatric disorders. **Aim.** In this study, we determined the trace element status of psychiatric patients and the effect of drug treatment. **Result.** The mean serum copper and manganese of the controls were significantly lower than those of the drug-naïve subject ($p < 0.0001$) while it showed no significant difference from that of the patients on drugs, ($p > 0.05$). A similar result was obtained for manganese. The mean serum zinc level of the control was higher than that of the drug-naïve patients, ($p < 0.0001$) and almost same as that of the patients on drugs, ($p > 0.05$). **Conclusions.** Drug-naïve psychiatric patients have elevated mean copper and manganese levels but decreased zinc level while those on drugs have near normal levels of all three elements when compared with control values. Since drugs that relieve symptoms affect the serum levels of these trace elements, one can surmise that these elements play some role in the pathogenesis or pathology of mental disorders. Their routine measurement, therefore may aid in the drug management of mental disorders.

KEY WORDS: psychiatric disorder, trace elements, psychotic drugs, copper, manganese, zinc.

INTRODUCTON

Trace elements play major roles in various metabolic pathways and are usually associated with an enzyme (metallo-enzyme) or another protein (metallo-protein) as an essential component or they function as a cofactor^[1, 2]. Alterations in the optimum levels of trace elements may adversely affect biological processes and are associated with many diseases^[3]. A few investigators have reported serum trace element involvement in some psychiatric disorders such as schizophrenia, mania, depression and anxiety disorder^[4]. Copper, manganese and zinc have been commonly implicated^[5]. These have neurological functions and play roles in neurotransmitter metabolism^[6, 7, 8]. Neuropsychiatric disorder may arise from serum trace element imbalance.

This study measured the serum levels of copper, manganese and zinc in psychiatric patients (on drugs and

drug naïve) of Federal Neuropsychiatric Hospital, Enugu Nigeria to determine their trace element status and the effect of drug administration on this.

SUBJECTS, MATERIALS AND METHODS

Subjects

The test population was made up of 100 subjects (54 males and 46 females) diagnosed of mental disorders by Consultant Psychiatrists. Their ages ranged between 21 and 45 years. Fifty of them were in-patients and on drugs, usually, chlorpromazine, haloperidol and olanzapine, while fifty of them were drug naïve patients seen in the Emergency Unit of the Hospital. Fifty age and gender matched subjects with no family history of mental illness served as controls.

Patients on diuretics, (loop agents), and mineral supplements were excluded from the study. For the

controls, pregnant subjects, lactating mothers, persons on mineral supplements and those with recent history of surgery or acute infection were also excluded. Ethical approval was given by the Ethics Committee of the Federal Neuropsychiatric Hospital, Enugu, (ref No. FNHE/HCS&T/011/ETHICS006).

Sample collection

Special attention was given to sample collection to avoid contamination of samples. Fresh disposable needles, vacutainer syringes and commercially prepared plain tubes were used for sample collection. The blood samples were allowed to clot at room temperature and spun at 3000 rpm for 5 minutes and serum was transferred into eppendorf tubes and stored frozen until analysis which took place usually within 1 week of sample collection.

Laboratory Analysis

Copper, manganese and zinc levels of samples were determined using Varian AA240 Atomic Absorption Spectrophotometer. A 1 in 10 dilution of serum was made before introduction into the Spectrophotometer.

Statistical Analysis

Data were grouped into four; - controls, all patients, patients on drugs, and drug-naïve patients. Excel 2002, (Microsoft, Seattle WA, USA) and SPSS for window 16.0, (SPSS Inc. Chicago, IL, USA) were employed for data analysis. Data were also grouped according to gender and age and analyzed using student's 't' test and ANOVA. Level of significance was set at $p \leq 0.05$.

RESULTS

The mean serum copper of controls, $96.41 \pm 8.10 \mu\text{g/dl}$, was significantly less than that of the drug-naïve patients, $121.70 \pm 20.90 \mu\text{g/dl}$, ($p < 0.0001$) while it showed no significant difference from that of the patients on drugs, $95.77 \pm 71 \mu\text{g/dl}$, ($p > 0.05$). The mean serum manganese of the controls, $5.78 \pm 2.57 \mu\text{g/dl}$ was significantly less than that of the drug-naïve patients, $9.30 \pm 7.51 \mu\text{g/dl}$ ($p < 0.001$) while it showed no significant difference from that of the patients on drugs, $5.72 \pm 2.58 \mu\text{g/dl}$, ($p > 0.05$). The mean serum zinc level of the control, $86.95 \pm 5.64 \mu\text{g/dl}$ was higher than that of the drug-naïve patients, $59.20 \pm 18.44 \mu\text{g/dl}$, ($p < 0.0001$) and almost same as that of the patients on drugs, $86.75 \pm 5.39 \mu\text{g/dl}$, ($p > 0.05$).

Similar pattern of variations in the serum trace element concentrations of male and female patients and their corresponding controls were observed except in the case of manganese of female subjects which showed no significant difference between the control and drug-naïve patients, (Table 1). Statistical analyses based on age groupings did not reveal any significant differences in serum levels of the trace elements either in the control or patients, ($p > 0.05$).

DISCUSSIONS AND CONCLUSIONS

Values obtained for the trace elements in this study for both the test and control subjects were within the lower half of their reference ranges yet there were significant increases and decreases. It would appear that there is a need for the determination of the reference ranges of these elements for the locality since the control figures used for the comparison of data were not generated locally. The significant differences seen in the mean values of these elements between the control and the patients combined were due to those between the control and the drug-naïve patients since in each case the mean control values were very close to those of the patients on drugs.

The elevated copper level in the drug-naïve patients seen in this study agrees with the findings of Andra *et al.*, (2000), Herran *et al.* (2000) and Narang *et al.*, (1991)^[10,11,12]. Some studies have found increases in serum copper concentrations in patients with schizophrenia^[13, 14, and 15]. Drug treatment tends to normalize the increase. Copper is a cofactor for many enzymes and plays an important role in central nervous system development. The bound copper can be redox active and participate in redox reactions including the production of free radicals that may in turn lead to increased dopaminergic activity in psychiatric disorders. Alternatively, initial increase in neurotransmitter activity can induce stress in the systems and lead to increase in serum copper. However, both processes may not be exclusive. The later might have a positive feedback effect on the former both of which can be reversed by drugs.

The elevated mean serum manganese of drug-naïve patients observed in this study is in contrast with the finding of Yanik *et al.*, (2004)^[5] but agrees with those of Hossain, (2007)^[16] and Barceloux, (1999)^[17]. The levels fall very close to the control values with drug treatment. Antipsychotic drugs such as chlorpromazine are known to raise the level of manganese in the central nervous system and decrease those of copper^[18]. The conflict in reported values may arise from the time of sampling since the commencement of ill health.

Mean serum zinc concentration of the drug-naïve patients was significantly lower than that of the control. There are studies that reported no difference between the levels of serum zinc of psychotic patients and control or even elevated levels in patients^[11]. It is not known whether there is a cause-effect relationship between trace elements and mental disorder or whether the physiological levels of these elements in the patient are only modified by some events in the illness which the drugs now tend to correct. In the latter case, the serum trace element level may change depending on the chronicity or acuity of the illness and time of blood sampling in relation to commencement of therapy. It is also known that higher serum copper level, as found in this study, may disturb zinc absorption.

In this study, alterations in trace element metabolism in mental disorders were affected by drug treatment. There were no sex or age -dependent significant differences and the patterns of alterations were similar in both sexes except in the case of manganese in which illness did not alter the mean concentration in the female patients. However, there are conflicting reports on the actual effects of the illness on the levels of individual serum trace elements. While serum zinc was lowered, copper and manganese were raised. These changes may be due to oxidative stress brought about by disordered neurotransmitter activities especially dopamine and serotonin. Since drugs that relieve symptoms affect the serum levels of these trace elements, one can surmise that these elements play some role in the pathogenesis of mental disorders. Their routine measurement, therefore may aid in the drug management of mental disorders.

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