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The Role of Zinc in Senile Dementia

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Zinc deficiency has been reported in association with dementia and linked with its pathogenesis. A group of 45 elderly patients admitted to a mental hospital were given diagnoses in accordance with ICD-9, and their fasting plasma zinc levels were recorded. No difference was found in zinc levels between patients with diagnoses of senile dementia and those with other diagnoses.

Previous studies have shown the relevance of plasma zinc levels to psychiatric symptomatology, including acute syndromes associated with the administration of histidine (Henkin *et al*, 1975), prolonged total parenteral nutrition (Kay *et al*, 1976), acrodermatitis enteropathica (Nelder & Hambridge, 1975), and the continuing debate on the relationship of zinc to anorexia nervosa (Casper *et al*, 1980; Bryce-Smith & Simpson, 1984).

Srinivasan (1984) has summarised the role of trace metals in psychiatry, and Tiggelen (1983) reviewed the work linking zinc in the form of metallo-enzymes as a co-factor in the pathogenesis of dementia. However in much of the literature the diagnosis of dementia appears to have been based solely on the presence of cognitive impairment. The present study attempted to compare plasma zinc levels in patients with a diagnosis of senile dementia, using the ICD-9 definition (World Health Organisation, 1975), with those of a control group of patients with ICD-9 diagnoses.

Method

The sample comprised 45 patients over the age of 65, recently admitted to a mental hospital. They received a formal psychiatric interview, full cognitive assessment, and physical examination, and were given an ICD-9 diagnosis. Those with a diagnosis of dementia were rated on the Hachinski scale for arteriosclerotic dementia (Hachinski *et al*, 1974); in the absence of abnormal biochemical profiles, scores of less than 4 were taken as indicative of senile dementia and those of greater than 7 as of arteriosclerotic dementia. The Hachinski scale was thus used as an adjunct to ICD-9 to refine the diagnosis of senile dementia.

Fasting blood samples with minimal stasis were taken for a routine chemical screening, and for measurements of plasma zinc and plasma vitamin E levels (the latter is involved in the same oxidative pathways as zinc: the results of this part of the study will be reported in a later paper). Plasma zinc levels were measured using atomic absorption spectrophotometry (Whitehouse *et al*, 1982). The authors were blind to the results of the plasma zinc levels during the study.

Results

During the study period, eight patients were excluded for the following reasons: readmission (4), refusal to allow venepucture (2), immediate hospital transfer (2), of the remaining 45, 22 (18 female, 4 male; mean age 81.1 years) met the ICD-9 diagnosis of senile dementia (ICD-290.0). The comparison group (17 female, 6 male; mean age 75.3 years) had the following ICD diagnoses: manic-depressive states (ICD 296; $n=13$), arteriosclerotic dementia (ICD 290.4; $n=2$), paraphrenia (ICD 297.2; $n=2$) acute confusional state (ICD 293.0; $n=2$), organic psychosis unspecified (ICD 290.9 $n=2$) residual schizophrenia (ICD 295.6; $n=1$), and Korsakov's psychosis (ICD 291.1; $n=1$).

The numbers in each group receiving drugs affecting zinc bioavailability (i.e. steroids, diuretics, and lithium) were comparable. No patient suffered acute infection or trauma. One patient in the senile dementia group had malignant disease, compared with two in the control group. No patient had evidence of diabetes mellitus.

The plasma zinc results are shown in Table I. Analysis was undertaken using the Wilcoxon unpaired test; the difference between the senile dementia sample and the comparison sample was not statistically significant.

Discussion

The total body content of zinc is about 2g, 80% of which is bound intracellularly in metallo-enzymes and cell membranes. Those at risk of developing deficiency are diabetics, alchololics, pregnant and lactating women, and the elderly (Tiggelen, 1983).

TABLE I
Plasma zinc measured in sample groups: μmol/litre

	Senile dementia ($n=22$)	*Functional and other* ($n=23$)
Median	10.45	11.20
25th–75th percentiles	9.3–12.5	10.1–12.5
Mean	10.92	11.21
Range	8.3–17.7	9–13

TABLE II
Comparison of results with literature results

Study	*No. of patients*	*Mean plasma zinc level: μmol/litre*	*s.d.*
Present study			
Senile dementia	22	10.92	2.26
Other diagnoses	23	11.21	1.27
Hullin (1983)[1]			
Dementia			
Male	64	13.6[2]	2.6
Female	176	13.6[2]	2.6
Healthy control			
Male	22	15.9	3.1
Female	54	14.5	1.8
Tigellen (1983)			
Dementia (DSM-III)	23	15.81[2]	1.78
Healthy elderly control	28	18.05[2]	1.85
Bunker (1984)			
Healthy elderly	24	11	1.2
Healthy Adults	50	13	1.8

1. Long stay mental hospital (all ages).
2. Serum zinc levels.

Although widely used, doubt has been cast on the validity of plasma zinc as a sole indicator of total body zinc status (*British Medical Journal*, 1981); Abdulla (1983) concluded that liver zinc may be a more accurate parameter of deficiency. Prasad (1983) states that plasma zinc is a useful indicator, provided the specimen is not haemolysed or taken in conditions of acute stress or infection. As plasma zinc is mainly protein-bound, levels of albumin and binding protein (α_2 macroglobulin) will affect estimations. No patient in this study had an elevated white cell count (taken as indicative of infection) or hypo-albuminaemia. In a younger age-group (23–62 years), Halsted & Smith (1970) found no instance of an elevated plasma zinc level in a variety of disease states.

The normal level of plasma zinc in adults is 12–22 μmol/litre; recent work has suggested mean levels in healthy elderly adults of 11 μmol/litre (s.d. 1.2) and in healthy adults of 13 μmol/litre (s.d. 1.8 (Bunker *et al*, 1984). The levels in the present study compare well with Bunker's elderly group (Table II). The work of Kosman *et al* (1979) showed a small but not statistically significant difference between plasma and serum zinc. Direct comparisons between studies using either measure are thus valid.

Burnet (1981) hypothesised a genetically based, age-related progressive inability of neurones to incorporate zinc ions into DNA-handling enzymes, leading to an Orgel 'error catastrophe', producing defective protein synthesis and cell death. Thus 'pathological ageing' occurs. This has led to the current research interest in the role of zinc as a co-factor in the aetiology of senile dementia.

Previous workers have found evidence of lowered zinc levels in patients with dementia. In a study of recently admitted elderly patients with dementia, compared with those with depression, Hullin (personal communication) found significant lowering of plasma zinc in patients with dementia, with the albumin-bound fraction accounting for this difference. The serum levels were of an order similar to the present study. When screening a chronic hospital population, Hullin (1983) found a significant lowering of serum zinc in patients with dementia compared with patients with schizophrenia and affective disorder and controls (Table II).

In neither of these studies, however, were the types of dementias classified. Hullin also noted (personal communication) that patients with dementia in the latter study had average body weights lower than the other patients and some 20 kg lower than normal elderly people living in the community. This raises the possibility that the drop in serum zinc

could be concurrent with a nutritional defect or be an abnormality of metabolism as a consequence rather than a cause of dementia.

Tiggelen (1983) found similar results (Table II) in acutely admitted dementia patients (according to DSM-III classification), compared with healthy controls, but 70% of these had abnormal dexamethasone suppression tests. He therefore questioned the diagnosis of DSM-III dementia in his study group. He also suggested a superimposed undiagnosed depressive illness, and postulates that an abnormality of the hypothalamic-pituitary adrenal axis caused by, or could cause, zinc deficiency.

There are no obvious reasons why the levels of plasma and serum zinc quoted in the various studies differ so widely. The most comparable study to this one is that by Hullin (personal communication) and, aside from the differences in classification mentioned, it is unclear why the two studies have produced contrasting results. Further research into this area is clearly warranted.

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