0163-4984/95/4701-3-0235 $05.20

Serum Aluminum Levels in Alzheimer's Disease and Other Senile Dementias

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ABSTRACT

The exact cause of Alzheimer's disease and the part played in it by aluminum is still speculative. We have studied serum aluminum in 356 healthy people, and we have observed that serum aluminum concentration is increased in aging people in relation to age. We suggest that this could be associated with an enhanced gastric permeability or by an increase in metal accumulation proportional to age. We have measured serum aluminum levels in patients with probable Alzheimer's disease, patients with other senile dementias, and age-matched group. Patients with probable Alzheimer's disease have statistically significant higher serum aluminum levels than patients with other types of senile dementias (alcoholic, vascular, multi-infart) and an age-matched control group. When we compare serum aluminum of patients with senile dementias from other causes with the age-matched control group, we do not find significant differences.

Index Entries: Aluminum; Alzheimer's disease; serum aluminum in healthy people; aluminum and age; aluminum and renal function.

INTRODUCTION

Aluminum (Al), although present on much of the earth's surface, has no known biological function and is not considered essential to the diet *(1)*; indeed, it has been clearly demonstrated that it is neurotoxic to animals *(2)*. The exact cause of Alzheimer's disease (AD) and the part played in it by Al is still speculative, although the detailed pathological

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manifestations of the disease differ from those of dialysis dementia. Al has been identified within disease neurons, and colocalized with silicon as amorphous aluminosilicates, has been found as a feature at the core of senile plaques in the brains of sufferers of the disease *(3,4)*.

The evidence that links Al in drinking water to AD is derived to a large extent from epidemiological studies that compare rates of the disease in populations that are supplied with water containing different amounts of Al *(5,6)*. These studies have also been criticized because of inaccuracy both in the diagnostic classification of cases and in the measurement of population exposure to Al.

A uniform set of diagnostic criteria, evolved by a consensus of clinicians and researchers, has been published. For the physician, the most definitive diagnosis in most instances is "probable Alzheimer's disease." This is a terminology where the probability rate of true Alzheimer's disease is about 90–95%. The "possible Alzheimer's disease" is useful to express the situation where potentially causative factors, e.g., alcoholism, are present, and where there is the possibility of being concurrent true Alzheimer's disease. The only criteria for diagnosis of "definitive Alzheimer's disease" is histopathologic evidence from biopsy or autopsy *(7)*.

In 1980 Shore and associates *(8)* did not show increased Al concentrations in Alzheimer's disease. However, later studies *(9,10)* showed significantly elevated Al levels in the serum or whole blood of Alzheimer's disease patients.

Fernandez et al. *(11)* have shown a significant serum Al increase proportional to the increase of age. The known decline of renal function observed with the increasing of age and, therefore, the likely decrease in Al clearance could be responsible for the serum Al increase.

In this survey, we have evaluated the Al serum level in normal healthy aging people, and we have made a case-control study between Al serum level in patients with probable Alzheimer's disease and patients suffering from other senile dementias as control group.

MATERIAL AND METHODS

Sample Population

Healthy People

This was a sample population of 356 adults ages 20–80 yr. The mean age of the population was 49.8 yr with an SD of 17.6 yr. There were no significant illnesses registered in the group.

Group 1

People with probable Alzheimer's disease: a sample population of 17 patients. The mean age of the population was 69.7 yr with an SD of 7 yr.

Group 2

People with other senile dementias (alcoholic, vascular, multi-infart): a sample of population of 15 patients. The mean age of the population was 65.6 yr with an SD of 8.1 yr.

Group 3

Age-matched control group: A sample of population of 189 healthy adults. The mean age of the population was 63.7 with an SD of 9.4.

There were no significant differences for age among groups 1, 2, and 3: ANOVA ($F = 2.59$; $p = 0.077$).

Analytical Procedure

Serum Al determinations were carried out by atomic absorption spectroscopy with a Perkin Elmer 1100 spectrometer with HGA 500 graphite oven with L'vov platform and deuterium background correction. Serum urea concentration were analyzed by an enzymatic conductivity rate method employing a Beckman™ conductivity electrode. A precise amount of sample is injected into the urease reagent in a reaction cup containing an electrode that monitors solution conductivity as urease catalyzes the hydrolysis of urea to ammonium carbonate.

Aluminum Quality Control

Our laboratory participates in Al determination in the "Worldwide Interlaboratory Quality Control" run by the Societé Francaise de Biologie Clinique. Reproducibility of the procedure was ± 6%; detection limit (2 SD of determinations of the zero standard) has been 0.35 µg/L; characteristic mass: 9.6 pg. The normal range for serum Al in our laboratory was 2–14 µg/L.

RESULTS

Aluminum in Healthy People and Age

We have studied serum Al concentrations in healthy adults in relation to age and physiological renal function ($n = 356$) (age range 20–80 yr). The distribution of serum Al values is symmetric and Gaussian. Applying Kolmogorov-Smirnov goodness of fit test, we have obtained the following results: (mean = 0.271 µmol/L ± SD = 0.142 µ mol/L KS-Z $p > 0.05$).

In the same sample population, we have also measured serum urea levels to evaluate renal function (mean = 6.14 mmol/L ± SD = 1.78 mmol/L). Urea levels increase in relation with age, because of the physiological decline of renal function (Fig. 1) ($r = 0.42$; $F = 68.7$; $p = 0.0001$; $r^2 = 0.17$).

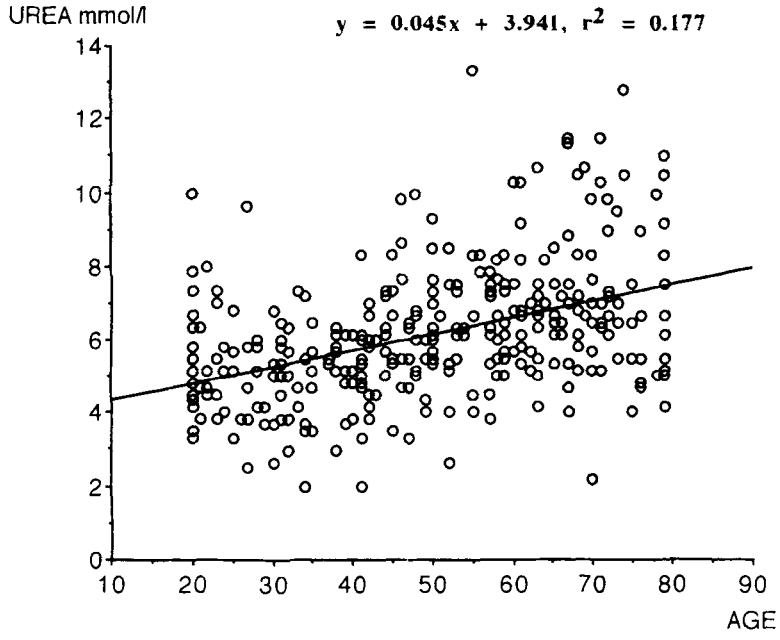

Fig. 1. Relationship between urea and age in healthy people.

To investigate the increment of the serum Al in relation to age as observed in Fig. 2, we have considered that Al can rise owing to a decrease in the renal clearance or an increment in the gastrointestinal absorption and in this way cause a higher accumulation.

We have calculated by linear regression the relationship between serum Al levels with both age ($r = 0.27$; $F = 22.83$; $p = 0.0001$; $r^2 = 0.067$) and urea ($r = 0.12$; $F = 5.08$; $p = 0.002$; $r^2 = 0.015$). We can observe a better correlation between serum Al and age.

Aluminum in Alzheimer's Disease and Other Senile Dementias

The general prolongation of life expectancy has increased the prevalence Alzheimer's disease. We have made a case-control study between 17 patients diagnosed as probable Alzheimer's disease and two control groups: Patients with other senile dementias (alcoholic, multi-infart, and so forth) and an age-matched control group. To verify if there were statistically significant differences between group 1 and group 2, we applied a nonparametric test (U-Mann Whitney), and have found significant differences (U-Mann Whitney $p = 0{,}001$).

A statistically significant difference is evident when we compare the age-matched control group with patients with probable Alzheimer's disease (U-Mann Whitney $p = 0.023$), but not when we compare with senile dementias owing to other causes (U-Mann Whitney $p = 0.812$) (Fig. 3).

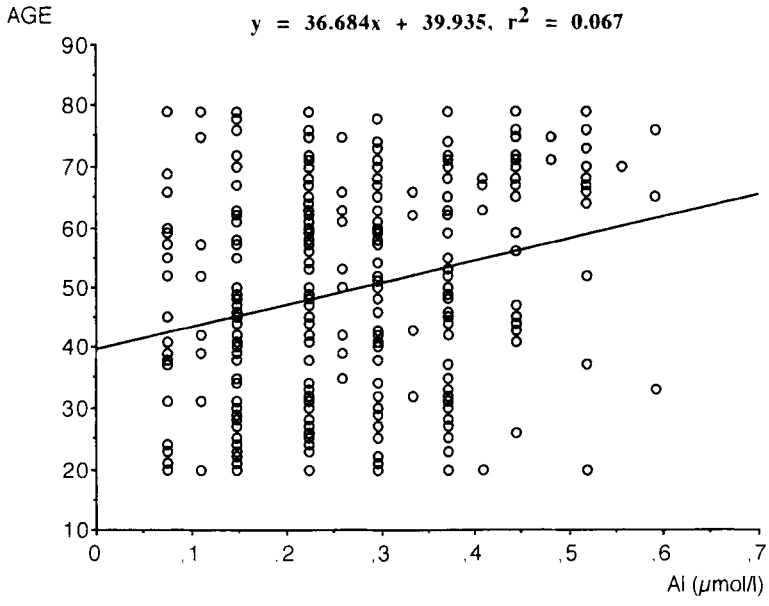

Fig. 2. Serum Al and age in healthy people.

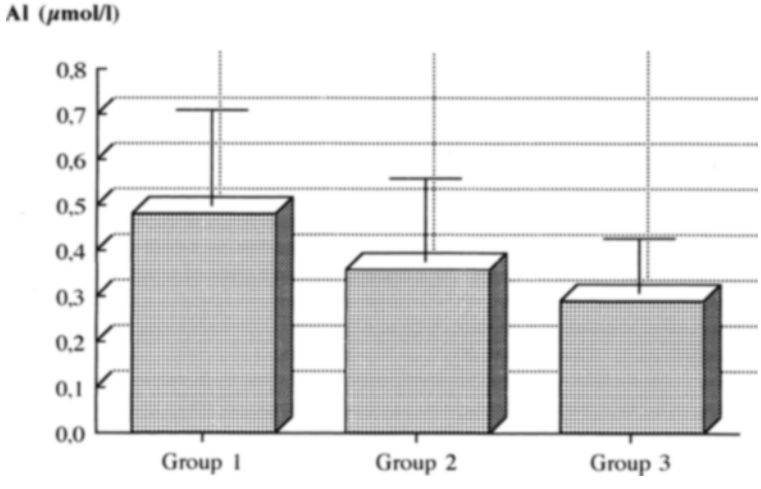

Fig. 3. Mean ± SD serum Al levels from patients with Alzheimer's disease (group 1), patients with senile dementias owing to other causes (group 2), and age-matched controls (group 3).

DISCUSSION

The dangers of Al toxicity were initially recognized in patients with renal failure who were receiving dialysis treatments or dietary Al hydroxide used as a phosphate binder. The question is whether the Al

toxicity was the result of impaired excretion consequent on renal impairment, or of excessive amounts of Al entering the plasma by bypassing the gut barrier, or both.

In a healthy population, renal Al clearance decreases with age, and this is in relation to an increment in urea levels. In this survey, we have observed that serum Al concentration is increased in healthy aging people in relation to age, but it is not the result of the known decline of renal function proportional to age. We suggest that this fact could be associated with an enhanced gastric permeability or by an increase in metal accumulation with age.

Only patients with probable Alzheimer's disease have statistically significant higher serum Al levels than patients with other types of senile dementias (alcoholic, vascular, multi-infartic) and age-matched group controls. When we compare serum Al of patients with senile dementias from other causes with the same age group, we do not find significant differences. We suggest that human exposure to Al should be limited in aging people because of physiological accumulation of the metal during their lifetimes.

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