

Serum Aluminium in Hyposensitized Allergics

S. VIND JOELT, H.-J. MALLING, U. GERNER SVENDSEN, E. TAUDORF and B. WEEKE

Medical Dept. TA, Allergy Unit, Rigshospital, University of Copenhagen, Denmark

The concentration of serum aluminium was examined in hyposensitized subjects receiving subcutaneous injections of solutions of allergens precipitated with or adsorbed to aluminiumhydroxide and in non-hyposensitized allergics. No correspondence between the serum values and the quantity of aluminium mediated with the injections was found. It was concluded that the investigation did not incriminate this type of treatment in causing rising serum concentrations of aluminium.

Key words: hyposensitization; serum-aluminium.

Accepted for publication 5 February 1985

Aluminium has been established as a potentially poisonous agent (2, 4). An international workshop held in Luxembourg in 1982 (12) decided on plasma levels for normals (below 15 $\mu\text{g/l}$) and for the need of identifying and reducing the sources (above 60 $\mu\text{g/l}$) of potential clinical concern, and close surveillance of the patient (above 100 $\mu\text{g/l}$), and a level that should never be exceeded because of the general implication of clinical symptoms (200 $\mu\text{g/l}$). Many sources of aluminium in the body have been reported ranging from dialysis fluids (2), oral phosphate binders (5) and antacids (10) to chewing gum (7), processed cheese (6), aluminium cookware (6), and domestic water supply (3, 9). Accumulation may be precipitated by treatment with corticosteroids, surgery or immobilization (8). Behavioural deficits have been demonstrated in adult rabbits after repeated subcutaneous injections of aluminium lactate (11). In the management of several allergies hyposensitization by subcutaneous injections of solutions of aluminium precipitated or adsorbed allergen is often administered for years. Accordingly, it was decided to determine whether it was accumulated in the body by examining the serum aluminium in patients hyposensitized with the most commonly used preparations of allergens in Denmark.

MATERIAL AND METHODS

Patients

The study comprised 40 subjects (17 women, 23 men), aged 15 to 71 years (median 34 years) distributed in five groups (Table 1). All had serum creatinine values within the normal range. After questioning the patients and checking their files the following precipitating factors could be ruled out: treatment with dialysis fluid, oral phosphate binders, antacids, corticosteroid, surgery and the domestic water supply judged from the individual residential areas. The individual intake of chewing gum and processed cheese and use of aluminium cookware were not looked into. Group I comprised non-hyposensitized allergics. Group II comprised subjects having received maintenance dose of aluminiumhydroxide adsorbed allergens (Alutard®, Allergologisk Laboratorium, Copenhagen, Denmark) for more than 7 months. Group III comprised patients initially hyposensitized with aqueous solutions of allergen (Aquagen®, Allergologisk Laboratorium, Copenhagen, Denmark) until the maintenance dose had been reached, then the administered preparation was changed to Alutard (2 ml/6-8 weeks). Groups IV and V were based on

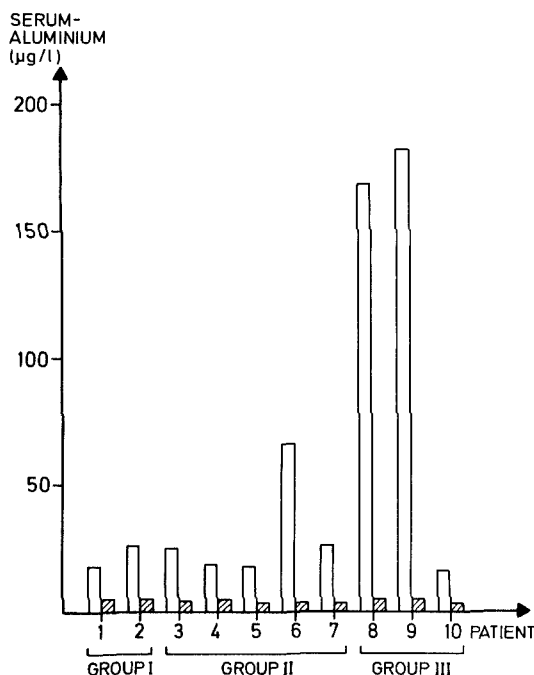


Fig. 1. Serum aluminium of initial (blank column) and renewed (hatched column) blood samples from subjects whose initial values were elevated.

persons having started to receive injections 3 months earlier with allergens precipitated with aluminiumhydroxide (Allpyral®, Dome/Hollister-Stier, England) or aqueous solutions of

allergens (Anjuvac®, Dome/Hollister-Stier, England). Repeated samples were obtained from all persons with elevated values.

Aluminium assay

All blood samples were obtained immediately prior to an injection through disposable single use needles directly into 10 ml glass containers manufactured for the purpose (Medicinsk Laboratorium A/S, Denmark). The samples were left to clot for no more than 4 h before centrifugation and the serum removed to a similar container using disposable plastic pipettes. Subsequently, they were frozen for a maximum of 37 days (range 7-37) before the concentration of aluminium was determined by atomic absorption spectroscopy with a graphite furnace (1) (Medicinsk Laboratorium A/S, Denmark). The test control - a cholinergic aluminium solution (Titrisol, Merck) added to human serum - was analysed after every 4-16 measurements. The variation of the mean values of aluminium determined at Medicinsk Laboratorium was no more than 20 %. Samples of the above-mentioned allergen preparations (Table 2) were obtained and immediately chilled to 4°C. They were analysed on the following day. They were obtained 40-59 days (median 47) after the first samples.

Table 1
Patient distribution

Group	No. of patients	Females/Males	Age (median-range)	Duration of maintenance dose in months (median values, range in brackets)		
				Alutard	Allpyral	Anjuvac
I	10	5/5	29 (15-45)	-	-	-
II	8	5/3	40 (34-67)	15 (7-29)	-	-
III	9	4/5	40 (17-71)	3 (2-10)	-	-
IV	6	1/5	26 (16-37)	-	3 (3)	-
V	7	2/5	28 (17-38)	-	-	3 (3)

Group I: Non-hyposensitized allergics.

Group II: Allergics hyposensitized with approximately 1 ml maintenance dose of aluminium adsorbed allergens for more than 7 months (Alutard).

Group III: Allergics hyposensitized with 2 ml maintenance dose of aluminium adsorbed allergens (Alutard).

Group IV: Allergics having started hyposensitization 3 months earlier with allergens precipitated with aluminium (Allpyral).

Group V: Allergic having started hyposensitization 3 months earlier with aqueous solutions of allergens (Anjuvac).

RESULTS

Seventy-five percent (30/40) of the initial serum samples had normal aluminium concentrations. The remaining 10 samples from Groups I ($n = 2$), II ($n = 5$), and III ($n = 3$) showed elevated values (Fig. 1). Repeated blood samples from these 10 persons were all normal. The aluminium concentrations of the aluminium-based allergen solutions showed rising values with increasing allergenic potency of the preparation (Table 2). The aqueous solution exhibited a negligible content (183 $\mu\text{g/l}$). The maintenance quantity administered per month was determined for each patient from the continuous records of injections. These values were transformed into amounts of aluminium given per month according to the concentrations determined in the allergen solutions (Table 2). The results showed no correspondence between the medians of the serum values and the injected aluminium (Table 3). However, the peak values of serum aluminium were significantly higher with increasing concentrations of aluminium in the administered preparation. The test controls of the analyses stayed within the 20 % variation of the mean throughout the investigation, median 31.6 (27.2–35.5 $\mu\text{g/l}$). The sequence of high and low determinations was distributed at random. There was no correlation between the

Table 2

Aluminium content of some commonly used preparations for hyposensitization in Denmark. Concentrations of allergen used for maintenance injections are 100,000 SQ Alutard and 10,000 PNU Allpyral. The concentration in distilled water was 2.5 $\mu\text{g/l}$

Allergen preparation		Aluminium mg/l
Alutard (wasp)	100 SQ/ml	1
Alutard (wasp)	1000 SQ/ml	15
Alutard (wasp)	10000 SQ/ml	170
Alutard (wasp)	100000 SQ/ml	1260
Allpyral (5-grass)	100 PNU/ml	2
Allpyral (5-grass)	1000 PNU/ml	41
Allpyral (5-grass)	10000 PNU/ml	229

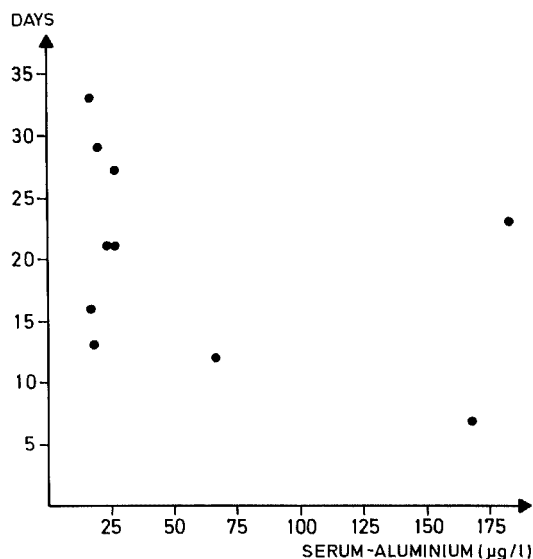


Fig. 2. Time span before analysis of blood samples with elevated serum-aluminium. x): Serum-aluminium of the particular blood sample $\mu\text{g/l}$. y): Number of days between blood sampling and analysis.

range of values and the number of days passing before analysis took place (Fig. 2).

Table 3

Median and range concentration of aluminium in serum (Se-Al) and median and range amount of aluminium mediated from the received hyposensitization (mg Al/month)

	Se-Al g/l	mg Al/month
Group I	7 (2–26)	0
Group II	18 (4–66)	1.0 (0.8–1.7)
Group III	5 (1–182)	2.3 (1.2–2.5)
Group IV	4 (2–6)	0.2 (0–1.4)
Group V	3 (2–4)	0

- Group I: Non-hyposensitized allergics.
 Group II: Allergics hyposensitized with approximately 1 ml maintenance dose of aluminium adsorbed allergens for more than 7 months (Alutard).
 Group III: Allergics hyposensitized with 2 ml maintenance dose of aluminium adsorbed allergens (Alutard).
 Group IV: Allergics having started hyposensitization 3 months earlier with allergens precipitated with aluminium (Allpyral).
 Group V: Allergic having started hyposensitization 3 months earlier with aqueous solutions of allergens (Anjuvac).

DISCUSSION

Twenty-five percent (10/40) of the initial serum samples showed elevated aluminium concentrations. According to the decision of the International Workshop in Luxembourg (12) one of the samples reached the level of the need for identification and reduction of the sources, and two extended into the range of potential clinical concern and close surveillance of the patient. It was considered whether the elevated values of serum aluminium might be due to accumulated aluminium from the injections with aluminium-containing allergen preparations. However, such a dose-dependence was opposed by the results in Table 3, which show no correlation between the levels of median serum aluminium and median allergen-associated aluminium. The repeated blood samples showing normal aluminium concentrations are a further contradiction.

Accordingly, it was concluded that the investigation did not incriminate the administration of subcutaneous injections of aluminium-containing allergen preparations in causing rising serum concentrations of aluminium.

A methodological error was then contemplated. The length of time between blood sampling and analysis did not influence the results. Nor did the sequence of determinations in the analysis reveal any systematics. Finally, the test controls of analysis being within the expected range of variation defies a systematical error in performing the analysis. Therefore, to our knowledge the elevated serum aluminium values cannot be blamed on a methodical error of investigation. We cannot account for the high values as seen in Fig. 1. However, their mere existence calls for further investigation, and we are planning to do this in a prospective study.

REFERENCES

1. Alderman, F. R. & Gitelman, H. J.: Improved electrothermal determination of aluminum in serum by atomic absorption spectroscopy. *Clin. Chem.* 26, 258-260, 1980.
2. Arieff, A. I., Cooper, J. D., Armstrong, D. & Lazarowitz, V. C.: Dementia, renal failure, and brain aluminum. *Ann. Intern. Med.* 90, 741-747, 1979.
3. Davison, A. M., Oli, H., Walker, G. S. & Levine, A. M.: Water supply aluminium concentration, dialysis dementia, and effect of reverse-osmosis water treatment. *Lancet* ii, 785-787, 1982.
4. Drueke, T.: Dialysis osteomalacia and aluminium intoxication. *Nephron* 26, 207-210, 1980.
5. Griswold, W. R., Reznik, V., Mendoza, S. A., Trauner, D. & Alfrey, A. C.: Accumulation of aluminium in a nondialyzed uremic child receiving aluminium hydroxide. *Pediatrics* 71, 56-58, 1983.
6. Lione, A.: The prophylactic reduction of aluminium intake. *Food Chem. Toxicol.* 21, 103-109, 1983.
7. Lione, A. & Smith, J. C.: The mobilization of aluminium from three brands of chewing gum. *Food Chem. Toxicol.* 20, 945-946, 1982.
8. Platts, M. M. & Anastassiades, E.: Dialysis encephalopathy: precipitating factors and improvement in prognosis. *Clin. Nephrology* 15, 223-228, 1981.
9. Platts, M. M., Goode, G. C. & Hislop, J. S.: Composition of the domestic water supply and the incidence of fractures and encephalopathy in patients on home dialysis. *Br. Med. J.* 2, 657-660, 1977.
10. Recker, R. R., Blotcky, A. J., Leffler, J. A. & Rack, E. P.: Evidence for aluminum absorption from the gastrointestinal tract and bone deposition by aluminum carbonate ingestion with normal renal function. *J. Lab. Clin. Med.* 90, 810-815, 1977.
11. Yokel, R. A.: Repeated systemic aluminium exposure effects on classical conditioning of the rabbit. *Neurobehav. Toxicol. Teratol.* 5, 41-46, 1983.
12. International Workshop on The Role of Biological Monitoring in the Prevention of Aluminium Toxicity in Man: "Aluminium analysis in biological fluids", Luxembourg, July 5-7, 1982. Memorandum on the summary and conclusions. *J. Toxicol.: Clin. Toxicol.* 19, 8, 907-910, 1982-83.

Address:

Susanne Vind Joelt, M.D.

Medical Dept. TA 7511

Rigshospitalet

Tagensvej 20

DK-2200 Copenhagen N

Denmark

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.