Aluminum Toxicity in Infants and Children

Committee on Nutrition

Although aluminum is the most abundant metal in the earth’s crust and is ubiquitous in its distribution, it has no known useful biological function. Even though the element is present in small amounts in mammalian tissues, its toxic effect on living organisms has become clear only recently. Aluminum is now being implicated as interfering with a variety of cellular and metabolic processes in the nervous system and in other tissues.

ALUMINUM EXPOSURE

Humans are exposed to aluminum from a variety of environmental sources. Because aluminum sulfate (alum) is used as a flocculating agent in the purification of municipal water supplies, drinking water may contain high levels of aluminum. Aluminum cans, containers, and cooking utensils, as well as medications that contain aluminum, are also potential sources of exposure.1 Although an increase in body stores of aluminum as a result of transfer through the skin is probably negligible, exposure is common from the use of deodorants containing aluminum. Aluminum inhaled from dust is retained in pulmonary tissue and peribronchial lymph nodes but is largely excluded from other tissues. The aluminum concentration in pulmonary tissues does not correlate with that in other tissues.

The average dietary intake of aluminum by adults is probably 3 to 5 mg/d, of which about 15 μg is absorbed.2 Most of the aluminum absorbed from the intestinal tract is excreted in urine, leaving total body aluminum stores of less than 30 to 40 mg. Individuals with normal glomerular filtration rates who increase their aluminum intake by ingesting aluminum-containing antacids increase their absorption and urinary excretion of the metal.3 Healthy individuals seem capable of increasing their renal aluminum clearance from approximately 5% to about 50% of the glomerular filtration rate.4 The low aluminum clearance normally present is largely related to the plasma binding of aluminum by a saturable plasma component at blood levels less than 200 μg/L.5

Aluminum levels in tissue are generally low in mammalian tissues, its toxic effect on living organisms has become clear only recently. Aluminum is now being implicated as interfering with a variety of cellular and metabolic processes in the nervous system and in other tissues.

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

PEDIATRICS (ISSN 0031 4005). Copyright © 1996 by the American Academy of Pediatrics.
Aluminum toxicitiy.2,12,15 The precise threshold for toxicity is not known, but it may be lower than 100 μg/L.

Alternatives to treatment with aluminum-containing phosphate binders are available. Calcium carbonate has been shown to be superior to aluminum binders in the control of secondary hyperparathyroidism in adults and children with chronic renal failure.17 Calcium acetate also has been shown to be a safe, effective binder of phosphate.18 Calcium citrate should not be used as a phosphate binder, because citrate enhances aluminum absorption from dietary sources.19

One study has shown that aluminum does not accumulate in infants with chronic renal failure who are not exposed to aluminum-containing antacids or contaminated intravenous solutions.20

**Intravenous Therapy**

High concentrations of aluminum have been found in the bone, urine, and plasma of infants receiving intravenous therapy.21,22 It has been shown that commercial albumin solutions and a number of substances frequently used as additives in the parenteral fluids given to premature infants may have high aluminum concentrations, including intravenous calcium and phosphorus salts as well as dextrose and mixed parenteral nutrition solutions.21-23

Aluminum loading has been observed in patients with normal renal function who receive long-term parenteral nutrition with aluminum-contaminated fluids.24 The Food and Drug Administration has recommended that concentrations of aluminum in parenteral solutions should not exceed 25 μg/L.23

**Infant Formulas**

Data on the aluminum content of human milk and a variety of infant formulas5-29 are shown in the Table. The aluminum levels in all infant formulas are higher than those in human milk. The formulas containing the highest levels of aluminum are those with additives, such as calcium salts and soy protein, which contain aluminum as a contaminant.

There have been conflicting reports on the possibility of aluminum accumulation from infant formulas. One group of investigators have proposed that the aluminum present in infant formulas played a role in the development of aluminum toxicity in two neonates with renal failure.25 Later, the authors conceded that other unrecognized sources of aluminum, such as intravenous fluids, may have contributed to the excessive aluminum loading in these infants.26

Other investigators20,28 have found no evidence of aluminum accumulation from infant formulas. Formulas for premature infants seem to contain higher levels of aluminum than do standard formulas for term infants.27,28 Therefore, there is a slightly higher aluminum intake and plasma aluminum concentration in premature infants than in term infants.29 A provisional tolerable intake recommended by the Food and Agriculture Organization of the United Nations and the World Health Organization30 is 1 mg/kg per day. Infants fed formulas with even the highest levels of aluminum, 2.35 mg/L, at intakes as high as 200 mL/kg per day would receive an aluminum dose of less than 0.5 mg/kg per day.26-28 Currently, the data are insufficient to recommend against the use of specialized formulas in premature infants; on the contrary, the nutritional advantages of premature infant formulas clearly outweigh the concern about the higher concentrations of aluminum in these products. However, it seems prudent to seek further reduction in the aluminum levels of infant formulas and to investigate whether aluminum accumulates in the tissue of premature infants fed formulas.

**TREATMENT OF ALUMINUM TOXICITY**

Deferoxamine administered intravenously has been shown to reduce the body aluminum burden and to ameliorate injury to the bone and brain in adults receiving hemodialysis and peritoneal dialysis.32 Deferoxamine also has been used successfully to treat aluminum toxicity in children.33,34 Although new cases of aluminum intoxication should be preventable in most instances, deferoxamine therapy seems beneficial for those with established aluminum toxicity; however, this therapy is not without hazards. It may cause a number of allergic reactions, including pruritus, wheals, and anaphylaxis. Other adverse effects include dysuria, abdominal discomfort, diarrhea, fever, leg cramps, and tachycardia. Cataracts and neurotoxicity also have been described.35

**CONCLUSIONS**

Dialysis encephalopathy and fracturing osteomalacia, which occur in hemodialysis units that use dialysis fluid contaminated with aluminum, have largely disappeared. This has been accomplished by establishing standards for safe concentrations of aluminum in dialysates. Infants, children, and adults with chronic renal failure who are not receiving dialysis have been shown to be at risk for aluminum intoxication from the oral administration of aluminum-containing phosphate binders. This complication should be avoided with the use of phosphate binders that do not contain aluminum and the use of other measures to control hyperphosphatemia.

A number of substances commonly administered intravenously, including calcium and phosphorus salts and albumin, have high levels of aluminum. Premature infants receiving intravenous fluid therapy may accumulate aluminum and show evidence of aluminum toxicity. Efforts are being made to reduce the levels of aluminum in

<table>
<thead>
<tr>
<th>Feeding</th>
<th>Aluminum Content (μg/L)</th>
</tr>
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<tbody>
<tr>
<td>Human milk</td>
<td>4-65</td>
</tr>
<tr>
<td>Standard cow milk-based formulas, 20 or 24 calories/oz</td>
<td>15-400</td>
</tr>
<tr>
<td>Soy-based formula</td>
<td>500-2400</td>
</tr>
<tr>
<td>Premature infant formula</td>
<td>100-900</td>
</tr>
</tbody>
</table>

* Based on previously published data.25-29
products added to intravenous solutions; these efforts must continue.

Some infant formulas may contain relatively high concentrations of aluminum. The reported concentrations of aluminum in soy formulas and premature infant formulas are higher than those in other infant formulas. The potential impact of these formulas on the aluminum intake of premature infants and infants with impaired renal function should be recognized, although it is not clear that toxic effects result from the use of the formulas in these situations.

RECOMMENDATIONS

1. Aluminum-containing phosphate binders should not be administered to infants and children with renal failure.

2. Continued efforts should be made to reduce the levels of aluminum in products that are added to intravenous solutions that are used for premature infants and infants and children with renal failure.

3. Continued efforts should be made to reduce the aluminum content of all formulas used for infants, but especially soy formulas and formulas tailored specifically for premature infants.

4. In infants at risk for aluminum toxicity (renal failure and prematurity), attention should be paid to the aluminum content of the water used in reconstitution of infant formulas.

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