Increase of Calcium Concentration in the Testes of Mice Treated with Rare Earth Metals

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(Received April 21, 2000; Accepted May 8, 2000)

Rare earth metals (REMs) are widely used in several emerging technologies, however, little is known about their biological effects. In this study we examined the effects of REMs, including lanthanum (La), neodymium (Nd), gadolinium (Gd), terbium (Tb) and ytterbium (Yb) on the testes of mice. Mice were treated i.v. with a single dose of 20 or 200 μmol REM/kg as chloride. The testicular weights, lipid peroxidation, and alterations such as hemorrhagic inflammation, were examined 5 d after the administration. The concentration of Ca in the testes was also determined by atomic absorption spectrometer. No significant changes in testicular weights, lipid peroxidation, or alterations were observed by the administration of these REMs at either dose. However, the concentration of Ca in the testes was markedly increased at both doses. There was no significant difference in the Ca concentration between dose levels or among the REMs. These results suggest that the REMs induce increased Ca concentration in mice testes, and this might be a significant aspect of their toxic mechanisms.

Key words —— rare earth metal, calcium, testis, mouse

INTRODUCTION

Rare earth metals (REMs), or lanthanides, constitute a series of fifteen metals and are subgrouped as light REMs, medium REMs, and heavy REMs according to their ionic radii. In recent years, the REMs have been used in pioneering technological industries such as basic matter for superconductive materials, ceramics, and amorphous substances.[1,2] Although the use of REMs is increasing, limited information is available on their biological effects. Information on their testicular effects is particularly scarce, though the testis is the major target organ of some heavy metals.[3]

It has been reported that administration of REMs can alter the Ca concentrations in some organs, including liver, kidney, lung, and spleen.[4–8] The effects on the testes, however, are not well known.

Here we examine the testicular effects of lanthanum (La) and neodymium (Nd) (light REMs), gadolinium (Gd) and terbium (Tb) (medium REMs), and ytterbium (Yb) (a heavy REM) in mice, including the effects on testicular weight, lipid peroxidation and Ca concentration.

MATERIALS AND METHODS

Chemicals —— REMs were purchased from the following sources: $LaCl_3$ and $YbCl_3$, Wako Pure Chemicals Co. (Osaka, Japan); $NdCl_3$, $GdCl_3$ and $TbCl_3$, Nacalai Tesque Inc. (Kyoto, Japan). Other chemicals were of reagent grade.

Animals and Treatments —— Male ddY mice, weighing 25–30 g, were purchased from Kyudo Co. (Kumamoto, Japan) and housed in metabolic cages with drinking water and diet (CE-2, Clea Japan Inc.) provided *ad libitum*. The mice were injected i.v. with 5% glucose (10 ml/kg) or REM (20 or 200 μmol/kg) in 5% glucose. Five d after the injection, the mice were killed by decapitation and testes were removed, weighed, and immediately analyzed for lipid peroxidation according to the TBA method.[9]

Testicular Ca Content —— Testicular Ca concentration was measured by flame mode of atomic absorption spectrophotometry with a Hitachi Z-8000 spectrophotometer after tissues were digested with nitric acid. The data was expressed as μg Ca per g wet weight of tissue.

Statistical Analysis —— Data were analyzed by a one-way analysis of variance. When the analysis indicated significant difference, the treated groups were compared to the controls by Duncan's new multiple range test ($p < 0.05$).

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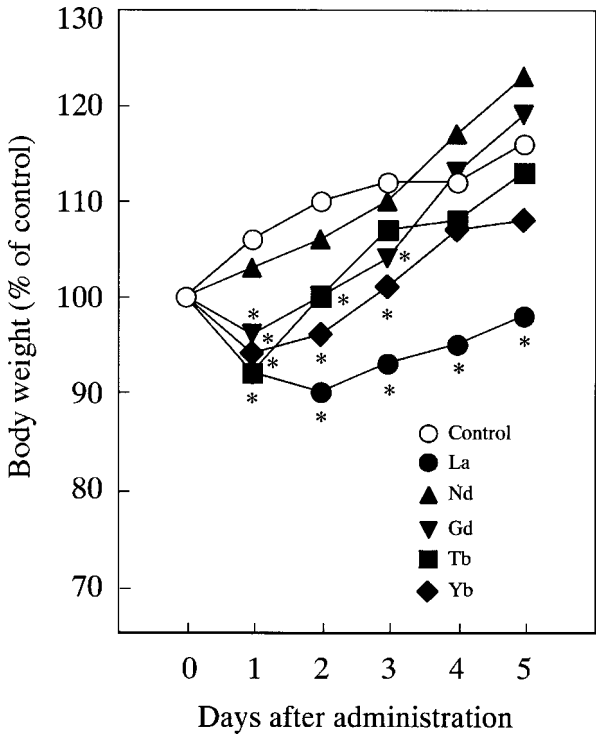

Fig. 1. Changes in Body Weight of Mice after Rare Earth Metal Administration

Mice were administered i.v. with 200 μmol/kg as chloride of rare earth metals. Body weights were determined during the 5 d following administration. The values represent the mean (n = 3 or 6) based on % control with time zero control set at 100%. Asterisks indicate significant differences from control ($p < 0.05$).

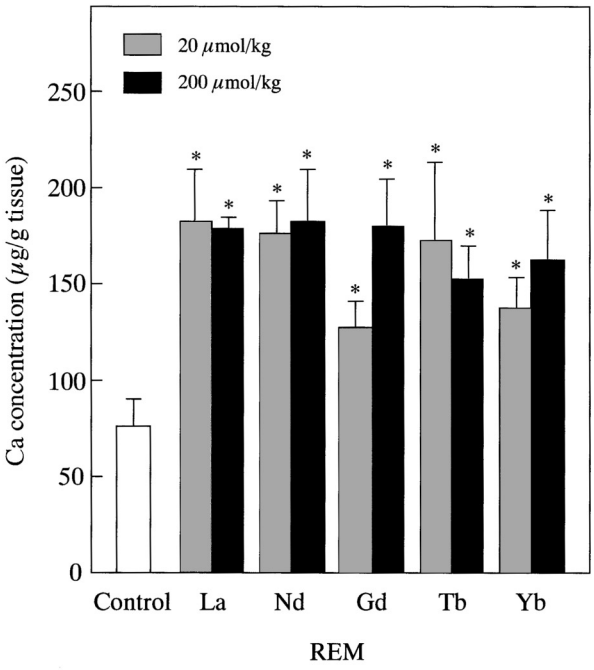

Fig. 2. Calcium Concentration in the Testes of Mice after Rare Earth Metal Administration

Mice were administered i.v. with 20 or 200 μmol/kg as chloride of rare earth metals. The concentration of Ca in the testes was determined 5 d after the administration. The values represent the mean ± S.D. (n = 5). Asterisks indicate significant differences from control ($p < 0.05$).

RESULTS AND DISCUSSION

Figure 1 shows time-course profiles for body weight changes of mice following administration of REMs at a dose of 200 μmol/kg. All the metals except for Nd significantly decreased the body weight at 1 d after the administration. By 5 d post-treatment, this decrease had reached the weight level of control mice. The lower dose of REMs (20 μmol/kg) did not influence body weight (data not shown). Among the metals, La was the most effective in decreasing body weight, and the survival rate of mice treated with La at a dose of 200 μmol/kg was 33% at 5 d after the administration. Mice in the other groups remained alive during the experimental period (data not shown).

The concentration of Ca in the testes of mice at 5 d after the REMs administration is shown in Fig. 2. The concentration of Ca was significantly increased by all the administrations. There was no significant difference in the Ca concentration between dose levels or among the light, medium, and heavy REMs. Nor was any significant change observed in testicular weight, lipid peroxidation, or alteration such as hemorrhagic inflammation at either dose (data not shown). Increase of Ca concentrations in some organs by REMs has been reported. For instance, Shinohara and Chiba found that i.p. injection of Tb to mice induced increase in Ca concentrations in the liver, spleen, pancreas, seminal vesicles, and testes, but not in the kidney, lung, heart, or muscle.[4] Our previous studies showed that i.v. injection of Tb to mice significantly increased Ca concentrations in the spleen,[5] pancreas,[5] kidney,[5] and lung,[6] but not in the liver.[5] Nakamura *et al.*[7] reported that, in rats, i.v. injections of REMs, including yttrium, cerium, praseodymium, europium, dysprosium, Yb, and lutetium, increased Ca concentrations in the liver, spleen, lung, and kidney. In contrast to our present study, Shinohara *et al.*[8] recently reported that i.v. injection of Tb to ICR mice did not alter the testicular Ca concentration, while the Ca concentrations in other organs, including liver, kidney, spleen, and lung, were significantly increased by the metal. This difference may be due to the differences of mouse strain and/or experimental period, although the precise reason has not yet been defined. It has been reported that the toxic metal, cadmium, induces se-

vere testicular damage with increase in the tissue Ca level in rats.[10,11] In this regard, marked increase in the Ca concentration is considered to be closely related to the cadmium-induced cellular damage in the testes. Thus, increased Ca concentration in the testes by REMs may be an important aspect of their toxicity. Further studies are needed to clarify the implications by which REMs induce an increase in Ca concentration in the testes.

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