Effect of Circulating Aluminum on the Biodistribution of Tc-99m-Sn-Diphosphonate in Rats

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The effect of varying plasma aluminum concentrations, ranging from 0 to 60 μg/ml aluminum, on the altered biodistribution of Tc-99m-Sn-diphosphonate was determined experimentally in rats. The results indicate that plasma aluminum levels of 20 μg/ml or greater result in increased soft tissue uptake of the radiopharmaceutical. This soft tissue uptake was predominantly liver and kidney. The higher plasma aluminum levels investigated (20 μg/ml or greater), which can cause an altered biodistribution of Tc-99m-Sn-diphosphonate in rats, can be found clinically in patients in a nuclear medicine department.

The effect of aluminum on the altered biodistribution of Tc-99m radiopharmaceuticals was initially mentioned by Weinstein and Smoak (*1*), who reported a macroaggregation phenomenon when aluminum was added to Tc-99m sulfur colloid. Further evidence of the altered biodistribution of Tc-99m pertechnetate by high plasma aluminum levels was demonstrated by Wang et al. (*2*). Chaudhuri (*3*) observed liver uptake on bone scans when aluminum was added to bone scanning radiopharmaceuticals. Liver uptake was also demonstrated in experimental animals when greater than 20 μg/ml aluminum was added to a Tc-99m-Sn-diphosphonate preparation (*4*). These results prompted us to investigate the effects of circulating plasma aluminum levels on the biodistribution of Tc-99m-Sn-diphosphonate in experimental animals.

Materials and Methods

Six rats, each weighing between 300–500 g, were carefully weighed; the total blood volume was estimated from that weight. A volume of freshly prepared sterile aluminum chloride was then intravenously injected so that the circulating aluminum level in each rat was 0, 5, 10, 20, 40, and 60 μg/ml, respectively.

Following a 30-min delay for complete mixing, 1.0–1.5 mCi of Tc-99m-Sn-diphosphonate (Medi-Physics, Emeryville, CA) was injected intravenously. Whole body rat images were then obtained at 1.5–2.0 hr post diphosphonate injection using a gamma scintillation camera and computer system.

Quantification of soft tissue uptake in experimental rats was performed by obtaining the ratio of counts of an area encompassing the lumbar area of the rats, which would contain liver and kidney, to the counts of an area encompassing the rats' dorsal area. Prior to injection, the radiochemical purity of the Tc-99m-Sn-diphosphonate preparations was evaluated and only preparations having a labeling efficiency greater than 98.0% were utilized in this study.

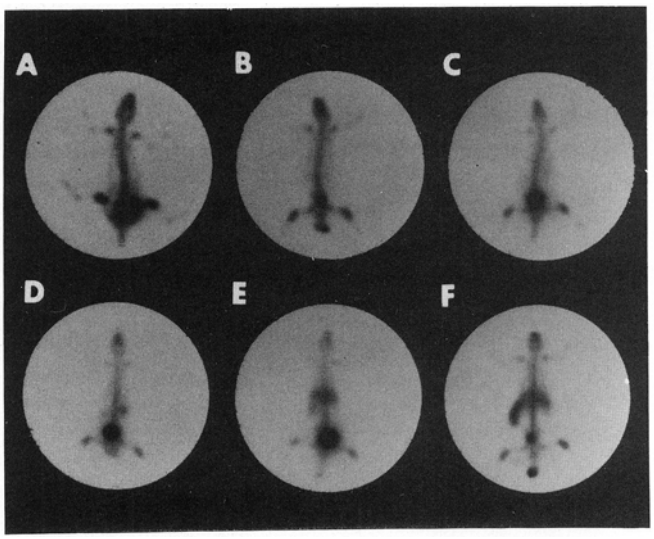

FIG. 1. Whole body rat images show increasing circulating aluminum concentrations: (A) 0 μg/ml Al^{+3}; (B) 5 μg/ml Al^{+3}; (C) 10 μg/ml Al^{+3}; (D) 20 μg/ml Al^{+3}; (E) 40 μg/ml Al^{+3}; and (F) 60 μg/ml Al^{+3}.

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Results and Discussion

Results of the effect of circulating aluminum blood levels on the biodistribution of Tc-99m-Sn-diphosphonate are shown (Fig. 1). Increased soft tissue uptake (kidneys) was observed at a circulating aluminum concentration of 20 μ g/ml and liver uptake was predominant at 40 and 60 μ g/ml. Little altered biodistribution was observed at 5 and 10 μ g/ml circulating aluminum.

Figure 2 expresses the lumbar/dorsal ratio as a function of the aluminum concentration. A ratio of 1.0, observed with no circulating aluminum level, increased to 1.2 and 2.7 at circulating aluminum levels of 5 μ g/ml and 60 μ g/ml, respectively. This signifies increased soft tissue uptake of the radiopharmaceutical. Results of the experiment demonstrate that high blood aluminum levels can alter the biodistribution of bone scanning radiopharmaceuticals. The data indicate that greater than 20 μ g/ml circulating aluminum can cause an altered biodistribution of Tc-99m-Sn-diphosphonate. Other investigators (*2–4*) have also demonstrated that higher than 20 μ g/ml circulating plasma aluminum can cause an altered biodistribution of Tc-99m radiopharmaceuticals. In no case was an altered biodistribution of a Tc-99m radiopharmaceutical observed when the plasma aluminum concentration was less than 20 μ g/ml.

The mechanism by which the altered biodistribution occurs is not yet well understood. However, in all cases of altered biodistribution caused by high plasma aluminum levels, pronounced liver uptake was observed. This suggests the possibility that some type of complexing phenomenon between aluminum and the radiopharmaceutical occurs with the possible formation of colloid particles. Previous investigations, (*4*), however, have shown that if colloid particles are formed, they have a particle size less than 0.2 μ.

Normal plasma aluminum levels in humans are reported to be between 3 and 11 μ g ml (*5*). However, elevated plasma aluminum levels of 30 μ g ml have been observed in selected patients taking aluminum hydroxide antacids (*5*). Even higher plasma aluminum levels have been observed in patients having impaired renal function or undergoing dialysis (*6*). It would certainly appear that these elevated plasma aluminum levels in patients taking antacids, particularly those patients with impaired renal function, could conceivably cause an altered biodistribution upon Tc-99m-Sn-diphosphonate administration.

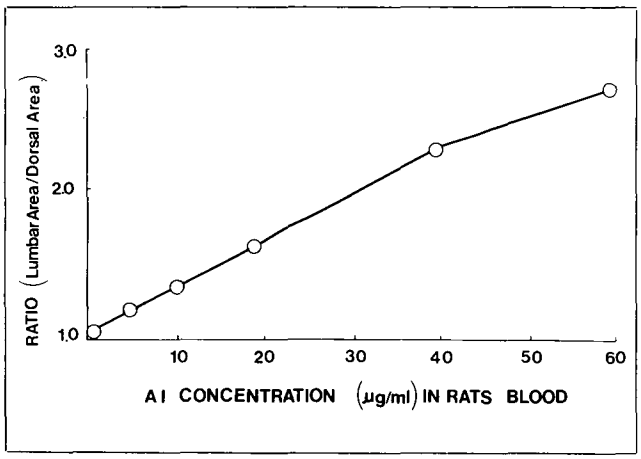

FIG. 2. Lumbar/dorsal ratio in rats with increasing aluminum concentrations is shown.

We are currently investigating the effects of circulating aluminum levels on the biodistribution of other Tc-99m radiopharmaceuticals, including Tc-99m DTPA and Tc-99m glucoheptonate.

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