CHELATING AGENT, DTPA, CAN NOT REMOVE EFFECTIVELY INHALED-PLUTONIUM OXIDE IN RATS

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INTRODUCTION

Chelation therapy is a useful method to reduce the cancer risk in the patients contaminated with transuranic elements such as plutonium and americium. Chelating agents, calcium and zinc salt-diethylenetriaminepentaacetic acid (Ca-DTPA and Zn-DTPA) are useful drugs to remove plutonium and americium effectively from the body with almost no toxicity. Although these chelating agents combine with radionuclides of ionic chemical forms such as nitrate and citrate, the effect is not expected for the insoluble form, i.e. oxide. If patients will be contaminated with plutonium oxide through inhalation, it is doubtful whether each DTPA therapy is useful or not. The present study is to clarify whether these DTPAs are useful to remove plutonium oxide from the body or not.

MATERIALS AND METHODS

Twenty female Wistar rats, 3 months of age, inhaled the particles of plutonium oxide generated by the radioactive aerosol exposure system for rodents developed in our institute (1). The inhaled dose was determined by a whole body counter for small animals (2). They were divided into four groups of five each; Group 1(G1): DTPA administration was initiated on 1st day after inhalation, Group 2 (G2): on 7th day, Group 3 (G3): on 14th day and was not administered in the no-treatment group. Chelation therapy was carried out according to the following schedule. Ca-DTPA was injected intraperitoneally with a daily dose of 150 μmol/kg for the first 5 days and subsequently Zn-DTPA was administered orally at the same dose as that of injection in drinking water up to 30 days. The 24-h urine and feces were collected for 1 day after the first Ca-DTPA injection (Table 1). The lung retention in each group was measured using a whole body counter during the experiment period (Table 1).

Table 1 Experimental design

Group	Inhalation 1	7	14	21	30	38	44days
No treatment group	WBC #	WBC	WBC	WBC			WBC+
Group 1	WBC *, #	WBC			WBC+ *		
Group 2		WBC *,#	WBC			WBC+ *	
Group 3		WBC	WBC *,#	WBC			WBC+ *

WBC: whole body count, *: chelation therapy , #: collection of urine and feces, +: sacrifice

The rats in each experimental group were killed after receiving chelation therapy for 30 days and the no treatment group was time-matched to G3. The blood was collected and then the organs such as lung, trachea, liver, kidney and femur were removed. The plutonium concentration in the blood, organs and excreta was measured by a liquid scintillation spectrometry after a wet ashing treatment.

RESULTS

The initial lung burdens in G1-3 were not different from that in the no treatment group. There were no significant differences in the lung retention of plutonium with the group (Fig.1).

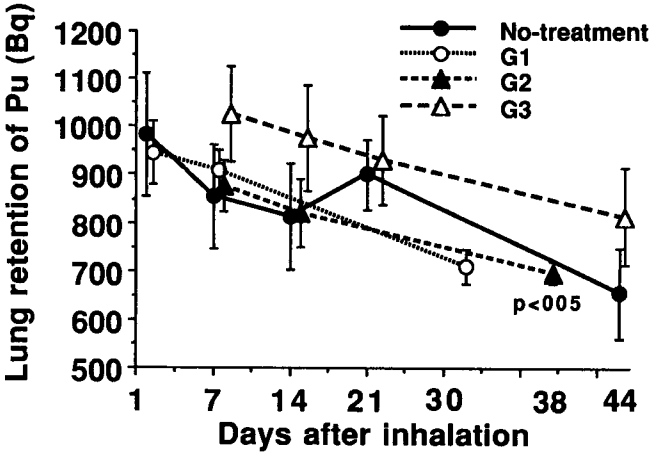

Fig. 1 Lung retention by a whole body counter in each group

The plutonium contents in each organ as well as blood, serum, spleen and ovary were not different between the no-treatment group and each group (Table 2). Also, the excreted plutonium in the urine and feces after first Ca-DTPA injection was not different between the no-treatment group and each treatment group.

Table 2 Plutonium contents (total Bq) in various organs

Organ/Group	No-treatment Group	Group 1	Group 2	Group 3
Lung	772±105	872±50	929±44	1060±144
Trachea	1.20±0.07	1.40±0.25	1.42±0.17	1.12±0.23
Liver	14.1±0.6	17.1±1.0*	15.6±2.5	13.0±1.2
Kidney	2.28±0.25	1.92±0.20	2.04±0.07	1.76±0.12
Femur	0.83±0.02	0.82±0.03	0.88±0.03	0.75±0.04

* significantly different from no-treatment group ($p<0.05$)

DISCUSSION

As an effective method of chelation therapy, Ca-DTPA injection for the first few days after contamination and subsequently the oral administration of Zn-DTPA is generally appreciated. The dose of 150μmol/kg of DTPAs administered here is more than the recommended human dose of 30 μmol/kg/day, but was effective to remove plutonium nitrate with almost no toxicity for rats in our previous study (3). The particles of plutonium oxide deposited in the lung, although insoluble, may change to be soluble, because the activity is determined in the serum, various organs and excreta. Therefore, the chelation therapy for contamination with plutonium oxide of the insoluble form, although slight and gradually,

may be expected to the effectiveness even if the initiation is delayed but the period is long. Although DTPA administration should be initiated immediately after contamination with the soluble form of plutonium to obtain high effectiveness.

We obtained no evidence that chelation therapy using Ca-DTPA and Zn-DTPA can remove plutonium effectively from the body in spite of initiation of chelation therapy and high dose administration for 30 days. Therefore, other treatments such as lung lavage are necessary to decrease the cancer risk with internally contaminated plutonium

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