Dosage of DTPA Administration by Inhalation

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INTRODUCTION

In atomic energy facilities, as an emergency medical agents, chelating agent DTPA (diethylenetriaminepentaacetic) have been prepared at risk reduction during inhalation by the accidents of alpha emitting radionuclides. The DTPA is effective when the radionuclides exist in blood before deposition to organs, but that is not effective against the radionuclides deposited to organs. Therefore, the early administration of DTPA after inhalation of the radionuclides is most important.

As an administration method of DTPA to human, a continuous infusion method has been recommended. An advantage of the method is to be able to keep the blood concentration of DTPA stable. However, it is difficult to obtain the effective decontamination, because sending the patient to the hospital, usually takes much time. Simultaneously with the intravenous administration of DTPA, an inhaling administration of DTPA has been recommended. In the case of an immediate inhaling administration of DTPA, the high effectiveness on decontamination due to chelation on the surface of air way is expected. Some problems exist in the inhalation method such as types of equipment's for inhalation, dose of DTPA to air way and the characteristics of DTPA aerosols.

We have investigated the administration methods by the inhalation, inhaled dose and side effects of DTPA[1)~5)、10)]. Based on these investigations and considerations on the practical emergency medical treatments, we selected an ultrasonic nebulizer as the equipment for the inhalation administration, and Ca-DTPA injection solution in ample for human as the chelating agents. In this study, generation performances of DTPA aerosols and quantity of the inhaled DTPA to the air way were investigated by using a human air way model, and then the utility of this inhalation method at the accidents was estimated.

MATERIALS AND METHODS

1. Aerosols generation

A ultrasonic nebulizer (OMRON, NE-U12) was used as the DTPA aerosol generator because of its easy handling and availability on the market. Ca-DTPA(Heyl, 1g/5ml of pure water in ample for human) was used as the chelating agents. Fig. 1 shows the schematic diagram of DTPA aerosols sampling setup. The nebulizer was used at the maximum output of the ultrasonic and the air blast. The Ca-DTPA aerosols were collected in water of a scrubbing bottle and an air filter(TOYO, HE-40T). Ca-DTPA in the scrubbing bottle and washing water of the air filter were measured by chelating titration (standard ; Bi solution, indicator ; Xylenol Orange).

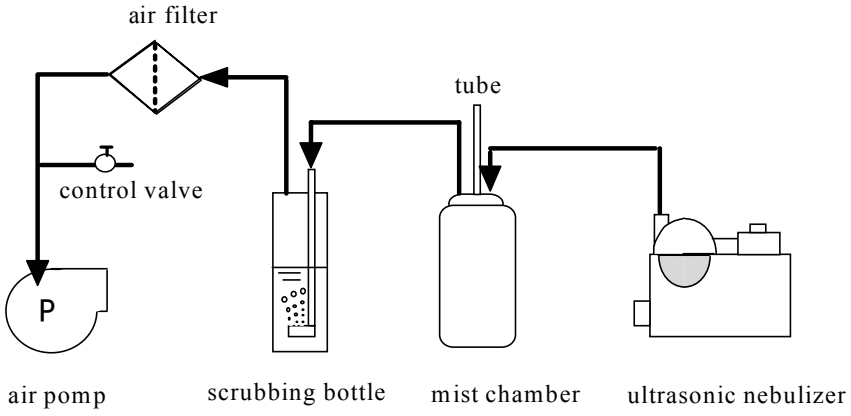

Fig. 1. Sampling setup for measurement of the mist DTPA generated by a ultrasonic nebulizer.

2. Simulative administration examination

Fig. 2 shows a schematic diagram for simulative administration of Ca-DTPA by inhalation using a human air way model(Kokensha). Fig. 3 shows a photograph of the human air way model connected to ultrasonic

nebulizer and ventilator. As a simulative ventilator, an anesthetic machine(Akoma, FO-20) was used. Tidal volume of the simulative breath was 950 ml, speed of breath was 12 times a minute. Ca-DTPA collected in the droplet separator was considered a component which will be swallowed at real inhalation administration to human. Ca-DTPA in the washing water of air filter, droplet separator and the larynx of the human model were measured by chelating titration.

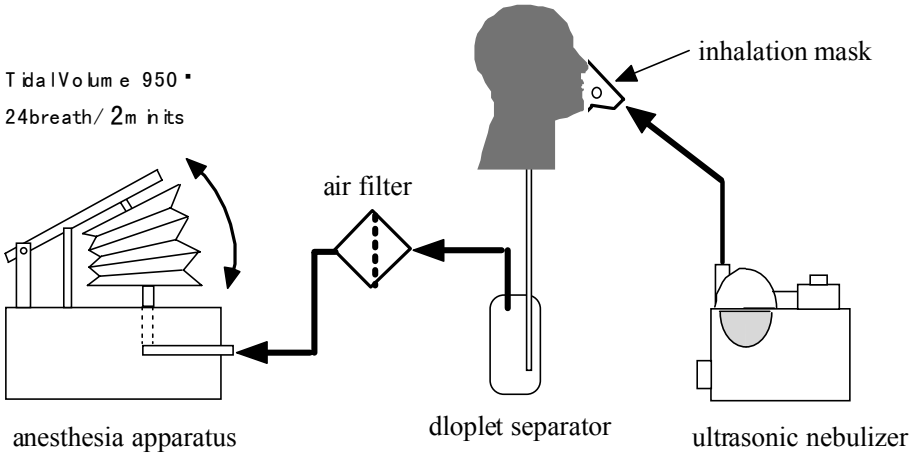

Fig. 2 Sampling setup for sham inharation administration of DTPA mist using a human air way model

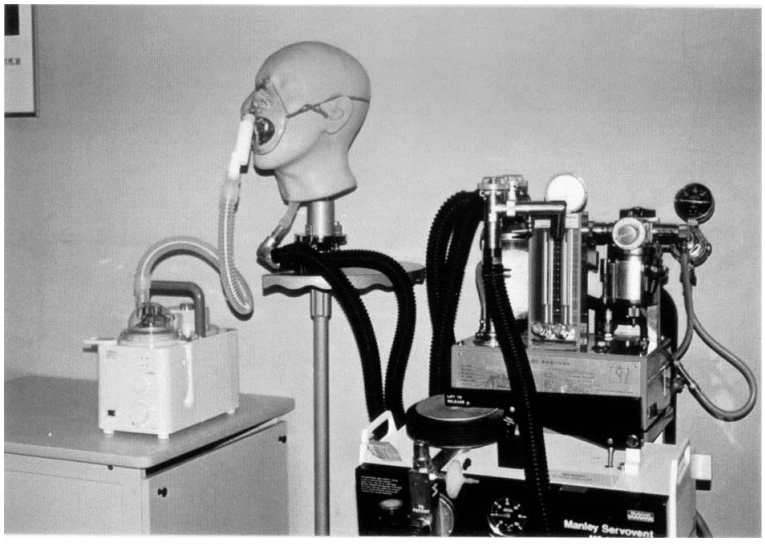

Fig. 3 Photograph showing a human air way model connected ultrasonic nebulizer and ventilator used in the experiment.

RESULTS AND DISCUSSION

1. Performance of the ultrasonic nebulizer

Original solutions of Ca-DTPA in ample have high viscosity, and can not be aerosolized by the nebulizer. Accordingly, the original DTPA solutions were diluted by stages. Fig. 4 shows the relationship between amount of aerosolized Ca-DTPA and dilution time of DTPA original solution in ample. At the 2 times dilution, the highest generation of aerosols was observed. But, the aerosols generation at the 2 times dilution was not stable because the concentration change of DTPA solution. Therefore, it was considered that the 3 times dilution was most optimum in practical use.

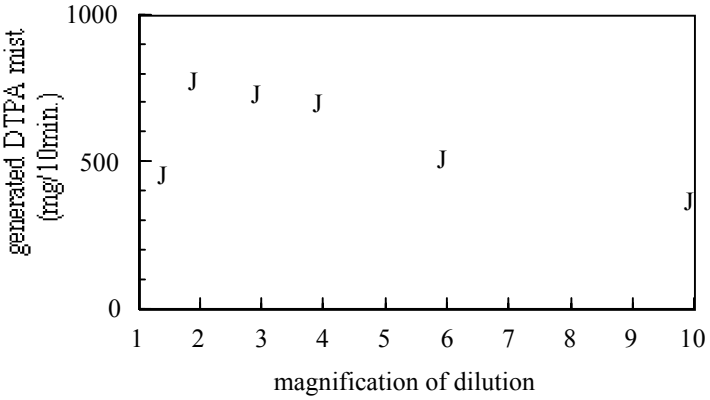

Fig. 4 Yield Change of aerozolised DTPA by a ultrasonic nebulizer at verious dilution magnifications of DTPA solution in ample.

2. inhalation intake of DTPA

Amount of DTPA per minute deposited in the droplet separator and the larynx at the 3 times dilution are shown in Table 1. Total amount of DTPA inhaled to the mouth was 33.3 mg per minute. The aerosols generation rate was 73 mg per minute, so the inhaled DTPA from the mouth was 46% of the aerosolized DTPA. Deposited DTPA in the lung was 26% of inhaled DTPA, and deposition ratio in the oral cavity was 74% of that. From this result, deposition rate of 8.77 mg per minute, that is 26% of inhaled DTPA to the mouth, 73 mg per minute mentioned above, is considered as amount of deposition in the lung, and of amount of DTPA that will make chelation with radionuclides like plutonium on the inner wall of lung.

Table 1 DTPA amounts in cleansing water of the air way model (unit:㎎/min.)

washing water	oral cavity	air filter	total
1st washing water	22.77	8.39	
2nd washing water	2.13	0.26	
3rd cleansing water	1.78	0.02	
total	24.68	8.67	33.3
deposition ratio	74%	26%	100%

ICRP has shown that the ventilation rate at the sitting awake is 12 per minute, tidal volume is 750 m[17]. Comparing with these breathing condition, ventilation rate in this experiment is a little higher, but very lower compared with the breathing condition of the light exercise. Hence the simulative breathing rate and the inhaled amount of DTPA of this experiment is not so far to that of a person in a practical emergency medical treatment.

Deposited DTPA to the larynx , 74% of inhaled DTPA is absorbed from a mucous membrane or swallowed and 3～5%of the swallowed DTPA is although absorbed from the digestive organs[8]. It is reported that DTPA in drinking water for rats was effective to decontamination of inhaled plutonium[9]. From these consideration, DTPA administered by inhalation method is expected to be effective against not only plutonium in lung and larynx, but plutonium in blood.

CONCLUSION

From this study model of inhaling administration of Ca-DTPA using injection solution for human and an ultrasonic nebulizer, it is estimated that inhaled amount of the DTPA is 33.3 mg per minute, and deposition amount of DTPA to lung is 8.5 mg per minute. From these amount, deposition amount of DTPA to lung for 15

minutes inhalation is estimated approximately 130 mg, and this amount of DTPA is expected to be effective on the decontamination.

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