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Removal of radiocesium by Medical Treatment Schedule Using Prussian Blue and Xayexalate in Rats

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INTRODUCTION

Many investigators report that Prussian blue is effective on removing radiocesium from the body. However, we does not agree with the results obtained from the animal experiments, because administration methods on Prussian Blue administration used in these experiments, e.g., dose, route, initial time, resulting in superior effects are marked different from the conditions in the human application (1-6). In fact, it is well known that the Prussian Blue treatment confused in Goiania accident (7-8).

It is necessary to obtain the data based on the following conditions in order to assess the effects of Prussian Blue for humans; (a) the administration should be started after intake of radiocesium, (b) the daily dose is 3 g, and (c) the administration route is by oral.

The purpose of the present study is to confirm the effects of Prussian Blue and Kayexalate in rats, when it is administers by the clinical use applicable to the human treatment.

MATERIALS AND METHODS

Preparation of Prussian blue and Kayexalate: Prussian Blue was purchased from Heyl (Antidotum Thallii-Heyl, 68% Fe4[Fe(CN)6]3). A daily dose of this agent for humans is 3 g by dividing into three times. The solution of Prussian Blue (4 mg of Prussian blue in 0.4 ml of water) was prepared. This is the dose per one time for a rat (mean body weight of 198 g), equivalent to a dose when the body weight of an adult is assumed to be 50 kg. Kayexalate was purchased from Torii Pharmaceutical Co., Ltd. A daily dose for humans is 30 g per day by dividing into 3 times. Based on the same method as that of Prussian Blue, the solution (40mg in 0.4 ml) was prepared.

Radiocesium: Radioactive cesium-137 as chloride was purchased from Amersham Parmacia Biotech UK Lid. (Amersham Place, Little Chalfont, Buckinghamshire HP79NA, England).

Animals and procedure: Male rats, 8 week old, were injected intraperitoneally with a dose of 74000Bq and then allocated to seven groups: the rats of first group were administered orally a dose of Prussian blue equivalent to 1g in humans via a probe into the stomach, simultaneously with radiocesium injection, rats of three groups were administered does of Prussian Blue equivalent to 1, 2, 3 g at 4-h intervals, starting 1h after radiocesium injection on day 1. Rats of five and sixth groups were administered orally Xayexalate simultaneously with, and 1 h after radiocesium injection. The seventh group was kept as a control

The whole body activity was measured immediately after the radiocesium injection. The cesium radioactivity in the whole body of the rats, and in 24-h urine and feces samples, were measured for 7 days. The radioactivity in the whole body and samples was measured by a Ge detector connected to multichannel analyzer with appropriate emulation software.

RESULTS

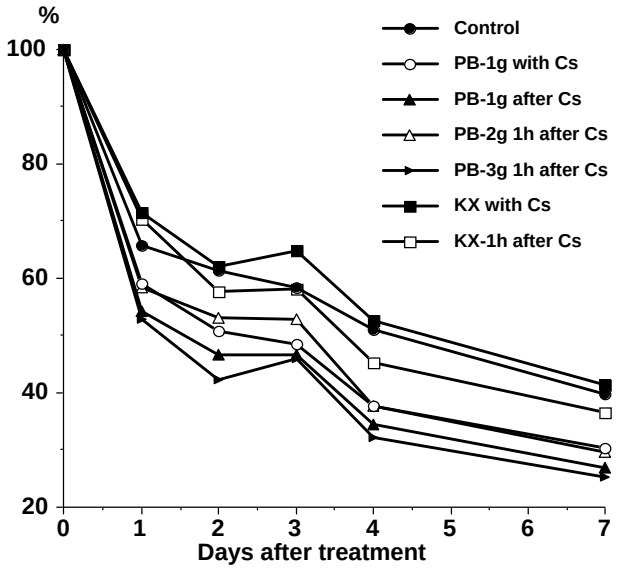

Fig.1 whole body retention in each group

Table 1. Whole body retention in the groups (as percentage of the control group) 7days after treatment

Group	Percentages of control
Control	100.0
PB with Cs	76.0
PB 1g, 1h after Cs	67.6
PB 2g, 1h after Cs	74.3
PB 3g, 1h after Cs	63.5
Xayexalate with Cs	104.8
Xayexalate 1h after Cs	91.9

Table 2 Excreted cesium in the urine and feces (percentages of the administered dose)

Group	Feces			Urine		
	Day 1	Day 3	Day 7	Day 1	Day 3	Day 7
Control	12.5±2.9 %	2.1±0.2	1.3±0.1	14.8±1.2	4.2±0.4	2.2±0.3
PB with Cs	19.2±6.9	3.0±0.3	1.3±0.1	13.5±2.3	3.0±0.5	1.6±0.3
PB 1g, 1h after Cs	43.6±11.0	3.6±0.7	1.9±0.2	11.0±1.2*	3.1±0.5	1.2±0.3
PB 2g, 1h after Cs	23.2±7.1	3.6±0.6	1.8±0.3	12.2±1.4	3.1±0.4	1.14±0.3
PB 3g, 1h after Cs	34.6±8.9	3.7±0.9	1.6±0.3	10.1±1.7*	2.8±0.7	1.4±0.4
Xayexalate with Cs	14.4±5.2	2.4±0.2	1.5±0.1	14.6±1.2	4.7±0.5	2.6±0.4
Xayexalate 1h after Cs	12.1±4.4	2.8±0.2	1.6±0.1	16.4±1.0	4.4±0.2	1.9±0.2

Significantly different from the control ($P<0.05$)

The retention of radiocesium in the whole body of rat in each group was shown in Fig.1. The whole body radioactivity in the groups treated with Prussian Blue and Xayexalate at 7 days was presented as percentages of control group (Table 1). The values of the groups treated with Prussian Blue were 63.5-76.0 % of the control group. There were seen no significant differences between each group. The values of whole body activity in the groups treated with Kayexalate were 104.8 and 91.0 %. The activity excreted in the urine and feces at 1, 3 and 7 days in each group was shown in Table 2.

DISCUSSION

The values of whole body activity in the groups treated with Prussian Blue were examined to decrease compared to that of the control group. However, there were not seen the differences in the values of each groups at 7 days after radiocesium injection, regardless of different doses and initiated time of administration (Table 1). The radioactivity in the groups treated with Prussian Blue reduced to 63.5-74.3% of the control (Table 1). This

values were no differences or high compared to those (1.8~74%) obtained in the previous studies (1- 4). The present study were carried out by the methods based on the simulated schedule of human treatment, however there are marked differences in the experimental conditions used in the previous studies. For example, the daily dose for a rat were 16~60 times (1-3), and 4.2 times (4) more than the dose used in the present study, i.e., equivalent to a human dose. Richmond and Bunde reported that the administration of low dose (0.04~3.8 times) in drinking water reduced to 9-33% of the control groups, by the protracted administration for 60 days (5). In Goiania accident, the daily dose of Prussian Blue for victims was increased from a recommended dose 3g to 10 g. As the result, the side effects were observed and the dose responsible enlargement of removing radiocesium was also not determined, although the tendency to increase it was observed. Therefore, the high doses examined in the previous studies were not applied for the human therapy. The administration methods of Prussian Blue used in the previous studies were by mixing it in the diet or drinking water (1, 2, 6). This means that rats were received almost successive administration of Prussian Blue, resulting in the high removal effects (1-4).

Most unconvincing method is that the initiating time of administration of Prussian Blue was 1-2 days ahead of radiocesium injection. This schedule is a large factor to increase excretion of radiocesium, and means the administration is carried out before the accident occurs. This idea is not used in the human therapy.

Thus, the results indicated in the pervious studies were not always useful to make a treatment schedule for radiocesium contaminated victims. We suppose that such acknowledgements obtained from the animal data may confuse the treatment by Prussian Blue in the Goiania accident. Nigrovic (4) and the present studies indicated that the difference in starting time of Prussian Blue administration did not affect for the removal effects of radiocesium. Melo et al. (6) indicated that the radiocesium activity in the dogs of young to old ages reduced to 49-62% of the control by the dose s of 1.8-2.7 times of Prussian Blue in drinking water in the protracted treatment. Any way, there were not seen the large differences in the effects of oral administration of Prussian Blue between the gathered data and our results. Also, the data obtained from the present study indicated that Xayexalate was not effective on removal of radiocesium in rats as well as in humans. As a result, it is necessary to reassess the effects of Prussian Blue and then to prepare the application forms of treatment for humans by Prussian Blue in a case of accident.

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