Arch Toxicol (1984) 55: 250–252

Archives of
Toxicology

The effect of 2,3-dimercaptopropane sodium sulfonate on mercury retention in rats in relation to age

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Abstract. The effectiveness of DMPS (sodium 2,3-dimercaptopropane-l-sulfonate) in reducing inorganic mercury retention was studied in 2-, 6-, and 28-week-old albino rats. ^{203}Hg was administered IP. The chelating agent DMPS was administered by IP injection at a dose of 250 μmol/kg body weight three times, 1 day after ^{203}Hg administration and at 24 h intervals thereafter. The whole body retention determined 1, 2, 3, and 6 days after ^{203}Hg administration showed that DMPS decreased the body retention of mercury in all age groups, being about twice as effective in adult compared to suckling rats. The reduced effectiveness was due to the reduced efficacy of DMPS in reducing kidney retention in young animals. In other organs the effectiveness of DMPS was not age dependent. These and previous results obtained with different chelating agents and other metals indicate that age might be an important factor in chelation therapy in general.

Key words: ^{203}Hg – DMPS – Age – Rat

Introduction

DMPS (sodium 2,3-dimercaptopropane-l-sulfonate), the water-soluble derivative of BAL (2,3-dimercaptopropanol) is at present considered to be the most efficient chelator for removal of mercury from the mammalian body (e.g., Planas-Bohne 1981a).

The purpose of this work was to determine whether the efficiency of DMPS is age dependent. In our earlier studies we found that chelation therapy with EDTA (ethylenediaminetetraacetic acid) and BAL was significantly less effective in enhancing the elimination of lead in sucklings compared to adult rats (Jugo et al. 1975). Similar results were obtained with BAL and D-penicillamine in enhancing ^{203}Hg (Jugo 1980) and DTPA (diethylenetriaminepentaacetic acid) in enhancing ^{141}Ce (Kargačin et al. 1983) and ^{115m}Cd (Kostial et al. 1984) elimination in rats of different ages.

The results of our present work in rats show that the effect of DMPS is also age dependent. This finding could therefore be relevant for chelating therapy in general.

Methods

The experiment was performed on albino rats from the Institute's breeding farm. The animals were 2, 6, and 28 weeks old at the beginning of the experiment with average body weights of 37, 140, and 215 g respectively. The 2-week-old rats of both sexes were kept in litters of six (reduced to this number 1 day after birth) in individual cages with their mothers. Three sucklings from each litter were used as controls (received 0.9% saline) and the other three as experimentals (received chelating agent). The 6- and 28-week-old rats were females kept in groups of 10 animals per cage. Radioactive mercury ^{203}Hg (specific activity of about 0.2 mCi/mg Hg; 7.4 MBq/mg Hg) purchased from New England Nuclear, Dreieich-Germany, was administered IP at a dose of 10 μCi (370 kBq)/ml/kg body weight. Therefore each rat received a dose of 50 μg Hg/kg body weight.

Sodium 2,3-dimercaptopropane-l-sulfonate (DMPS; Dimaval, from Heyl and Co., Berlin) was administered intraperitoneally at a dose of 250 μmol/kg body weight (50 mg/kg) three times, 1 day after ^{203}Hg administration and at 24-h intervals thereafter. Control animals received saline solution.

Table 1. Effect of DMPS on whole body retention of ^{203}Hg in rats in relation to age

Days after ^{203}Hg administration	% IP dose		
	Control (C)	Treated (T)	C/T
2-week-old rats			
1	96.1 ± 1.6	86.2 ± 3.0	1.1
2	94.0 ± 1.9	79.6 ± 2.3	1.2
3	91.5 ± 1.9	70.2 ± 2.1	1.3
6	83.6 ± 2.1	52.5 ± 1.9	1.6
6-week-old rats			
1	84.4 ± 1.0	80.5 ± 0.5	1.0
2	74.2 ± 0.9	51.0 ± 0.4	1.5
3	66.1 ± 0.7	33.9 ± 0.4	2.0
6	56.4 ± 0.8	21.7 ± 0.4	2.6
28-week-old rats			
1	88.2 ± 0.9	87.5 ± 1.0	1.0
2	75.2 ± 0.7	51.7 ± 1.3	1.5
3	69.0 ± 1.2	31.4 ± 0.9	2.2
6	55.8 ± 1.1	17.6 ± 0.5	3.2

Control animals (C) received 0.9% saline and treated animals (T) received 250 μmol/kg body wt. DMPS IP three times starting 24 h after ^{203}Hg administration. Results are presented as arithmetic means of 15 animals per group ± SEM

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Table 2. Effect of DMPS on ^{203}Hg organ retention in rats in relation to age (% IP dose 6 days after administration)

	2 weeks old			6 weeks old			28 weeks old		
	Control (C)	Treated (T)	C/T	Control (C)	Treated (T)	C/T	Control (C)	Treated (T)	C/T
Liver	14.8 ± 0.7	9.0 ± 0.6	1.6	0.88 ± 0.05	0.51 ± 0.01	1.7	1.19 ± 0.04	0.67 ± 0.03	1.8
Kidneys	21.5 ± 0.6	11.2 ± 0.5	1.9	34.0 ± 0.6	8.8 ± 0.3	3.9	37.7 ± 0.8	8.0 ± 0.2	4.7
Brain	0.91 ± 0.04	0.64 ± 0.02	1.4	0.077 ± 0.003	0.053 ± 0.002	1.5	0.040 ± 0.001	0.028 ± 0.001	1.4
Lungs	1.22 ± 0.04	0.73 ± 0.02	1.7	0.182 ± 0.021	0.100 ± 0.003	1.8	0.194 ± 0.004	0.108 ± 0.008	1.8
Femur	0.27 ± 0.01	0.16 ± 0.01	1.7	0.050 ± 0.002	0.027 ± 0.001	1.9	0.028 ± 0.001	0.014 ± 0.001	2.0
Hair	12.9 ± 0.5	8.8 ± 0.4	1.5	5.9 ± 0.1	4.1 ± 0.1	1.4	4.9 ± 0.2	3.1 ± 0.1	1.6

Control animals (C) received 0.9% saline and treated animals (T) received 250 μmol/kg body wt. DMPS IP three times starting 24 h after ^{203}Hg administration. Results are presented as arithmetic means of 15 animals per group ± SEM

The molar ratio of mercury to chelating agent was 1: 1,000.

The whole body radioactivity measurements were performed immediately after radionuclide administration and were repeated on the 2nd, 3rd, and 6th day of the experiment when the animals were killed and the liver, kidneys, brain, lungs, femur, and hair (including skin) were removed. The radioactivity of the whole body and the skin was determined by the use of a twin crystal scintillation counter (Tobor, Nuclear Chicago) and in other samples in an automatic well type scintillation gamma counter (Nuclear Chicago). The results were corrected for radioactive decay and geometry of the samples. They were expressed as percentage of the administered dose and presented as arithmetic means and standard error of the means.

Results

The age-related differences observed in mercury body retention and distribution in control animals are in general agreement with previously published data (Kostial et al. 1978; Thomas and Smith 1979; Walsh 1982). Sucklings retained a higher fraction of mercury in the whole body (Table 1) but not in all organs. Mercury retention in the kidney was lower in sucklings than in older age groups (Table 2).

DMPS decreased the whole body retention of mercury in all age groups. Differences between control and treated animals increased with time after ^{203}Hg administration. The largest differences were observed at the end of the experiment (6 days after ^{203}Hg administration). DMPS reduced the whole body retention 1.6, 2.6, and 3.2 times more in treated compared to control rats aged 2, 6, and 28 weeks respectively. This indicates an increase in DMPS efficiency with increasing age (Table 1).

DMPS treatment also decreased mercury retention in various organs. The decrease was much higher in the kidney than in other tissues. Kidney retention was 1.9, 3.9, and 4.7 times lower in 2-, 6-, and 28-week-old treated rats than in their respective controls. This indicates that the efficiency of DMPS in reducing mercury retention in the kidney was age dependent. In all other organs DMPS treatment reduced ^{203}Hg retention only by a factor of 1.4–2. This reduction in mercury retention was not age dependent, i.e., it was similar in all age groups of rats (Table 2).

Discussion

In previous experiments the lower efficiency of chelating agents was observed when treating sucklings with chelators immediately after metal administration (Jugo et al.1975; Jugo, 1980; Kargačin et al.1983; Kostial et al. 1984). We therefore assumed that this effect was primarily due to prevention of metal deposition (Kargečin et al. 1983). In our present experiments the first dose of DMPS was administered 24 h after mercury administration. In these experimental conditions lower efficacy of DMPS in immature animals is primarily due to age-related differences in enhancing mercury elimination and not to prevention of metal depositon.

The high efficacy of DMPS in enhancing mercury elimination from the body is known to be due to the ability of this chelating agent to reduce kidney retention (Planas-Bohne 1981b). In pharmacokinetic studies the highest concentration of ^{14}C-labelled DMPS was found in the kidney. In our experiment DMPS had a reduced ability to enhance mercury elimination from the body of sucklings primarily because of its reduced ability to remove mercury from the kidney. This might be explained by the immaturity of the kidney (Wachstein and Bradshaw 1965), which might result in a decreased concentration of DMPS in this organ in sucklings. However in our previous experiments we also found a reduced ability of chelating agents to remove metals from other organs, e.g., ^{141}Ce from the liver (Kargačin et al. 1983) or ^{115m}Cd from the liver and brain in sucklings (Kostial et al. 1984).

Since the age effect in the efficacy of chelating agents was found for different chelating agents (EDTA, BAL, D-penicillamine, DTPA, DMPS) and for different metals (Pb, Hg, Ce, Cd) and at different metal-chelating agent molar ratios, different routes and time of metal or chelating agent administration, we assume that this effect is due to specific features of metal metabolism in young animals. Factors responsible for these specific features, e.g., immaturity of the kidney or biliary transport, differences in binding affinities and/or contents of metal carrier proteins, etc. are discussed in more detail elsewhere (Kostial et al. 1978; Jugo et al. 1975; Kostial 1983).

This finding deserves attention, since chelating agents are the only treatment for metal poisoning in both immature and adult mammals.

Acknowledgement. Our thanks are due to Mrs Marija Ciganović for skilful technical assistance.

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Received March 5, 1984/Accepted April 30, 1984