Bull. Environ. Contam. Toxicol. (1988) 41:185–188

Environmental Contamination and Toxicology

2,3-Dimercaptopropane-1-sodium Sulfonate for Reducing Retention of Ingested ^{203}Hg in Suckling Rats

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It was recently suggested that oral chelation therapy might be used for reducing the body burden of ingested metals or radionuclides in sucklings. Sullivan and Ruemmler (1986) showed that oral administration of diethylenetriaminepentaacetic acid (DTPA) reduced ^{238}Pu and Kostial et al. (1987) that it reduced ^{141}Ce retention after ingestion in suckling but not in older rats. This effectiveness of oral DTPA treatment in reducing the retention of ingested radioisotopes is an exception. It is known that oral chelation therapy is not indicated while the metal is still in the gastrointestinal tract. Chelated cations are better absorbed and therefore such treatment might increase the body burden of metals (IAEA 1978).

The purpose of this work was to determine the efficiency of treatment with 2,3-dimercaptopropane-1-sodium sulfonate (DMPS) for reducing retention of ingested mercuric chloride in suckling rats. We wanted to estimate whether the previously mentioned efficacy of oral chelation therapy is related to DTPA only or also applies to other chelating agents. This might be important for establishing treatment for ingested metals and radionuclides in the youngest age group.

MATERIALS AND METHODS

The experiment was performed on six-day-old suckling rats of both sexes (body weight about 11 g) and six-week-old female rats (body weight about 140 g) from the Institute's breeding house (outbred rats). Litters were reduced in number to six within one day after birth. They were kept with their dams. Older rats were kept in macralon cages (10-12 animals in each) and fed standard rat diet. All animals received ^{203}Hg from the Radiochemical Centre Amersham, England (as chloride, specific activity 323 MBq/mg Hg) - about 100 kBq/rat. Sucklings were artificially fed (Kostial et al. 1971)

cow's milk (0.3 ml) labelled with ^{203}Hg through a dropper during an 8-hours period. They were divided into five groups according to the time of starting the DMPS treatment: one group received DMPS by a dropper 32.3 mg/kg (150 µmol/kg) in 0.1 ml i.e. four drops per day during the artificial feeding period and four times during the second day of the experiment; the second group received the same dose of DMPS during the second and third day; the third received the DMPS treatment during the third and fourth day; the fourth received DMPS during the artificial feeding period and 24 and 48 hours thereafter; a fifth served as control receiving distilled water by the same method as was used for DMPS (in group four). Sucklings were returned to their dams each day after the end of artificial feeding or DMPS treatment. Older rats received ^{203}Hg by stomach tube. They were divided into two groups: one group received DMPS (same dose per kg body weight as in sucklings) by intubation immediately after ^{203}Hg administration; the other group served as control receiving distilled water in the same way as DMPS.

Whole body radioactivity was determined after the end of the artificial feeding period in sucklings and after gavage in older rats. This value was taken as 100% of the dose. The same measurements were performed six days later in a double crystal scintillation counter (Tobor, Nuclear Chicago). All results were corrected for radioactive decay, expressed as percentage of oral dose and presented as arithmetic means and one standard error of the mean. Differences between groups were evaluated by Student's t-test.

RESULTS AND DISCUSSION

The much higher retention values of ingested ^{203}Hg in sucklings than in older rats (Table I) are in agreement with previously published data (Kostial et al. 1978) on high absorption of metals in the youngest age group. Treatment with DMPS decreased the whole body retention of ^{203}Hg in suckling rats about two times. This effect was practically independent of the time of starting the treatment. It was only slightly more effective in conditions of early DMPS administration than after delayed administration (24 and 48 h after ^{203}Hg). However, in older rats the same treatment (early administration) caused a two times higher whole body retention of ^{203}Hg. All differences between treated and untreated suckling and older rats were statistically significant ($P<0.001$).

DMPS is a chelating agent used orally for enhancing mercury elimination from the body (Planas-Bohne 1981). However, it has not been used previously as an immediate treatment for decreasing body retention of inges-

ted mercuric chloride. Our results with DMPS confirm earlier findings with DTPA that oral chelation therapy can be used for reducing retention of ingested metals or radionuclides but only in suckling and not in older rats. Although the mechanism of this action is not clear these preliminary results indicate that chelating agents (DTPA, DMPS) influence metal absorption and retention in sucklings in a different way than in older rats.

More work should be performed to estimate the usefulness of oral chelation therapy for reducing the body burden of ingested metals or radionuclides in the youngest age group.

Table I. The effect of oral DMPS therapy on whole body retention of ingested ^{203}Hg in suckling and older rats (% oral dose six days after radionuclide administration)

	n	6-day-old rats	Control/experimental ratio
Control	(9)	67.8 ± 2.6	
DMPS[a]	(11)	32.2 ± 2.0	2.1
DMPS[b]	(11)	39.8 ± 2.9	1.7
DMPS[c]	(10)	40.8 ± 2.9	1.7
DMPS[d]	(10)	28.0 ± 1.8	2.4
		6-week-old rats	
Control	(12)	0.72 ± 0.03	
DMPS[a]	(10)	1.42 ± 0.14	0.5

Results presented as arithmetic means ± SEM; number of rats in brackets.

[a]DMPS administered orally with ^{203}Hg and 24 hours thereafter

[b]administered 24 and 48 hours after ^{203}Hg

[c]48 and 72 hours after ^{203}Hg

[d]administered orally with ^{203}Hg and 24 and 48 hours thereafter

Acknowledgments. Our thanks are due to Mrs M. Ciganović for excellent technical assistance and Mrs M. Horvat for preparing the manuscript.

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Received October 13, 1987; accepted March 3, 1988.