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THE EVALUATION OF DETOXICATING PROPERTIES OF THE SODIUM SALT OF 2-MERCAPTOETHANOLSULPHONIC ACID [MESNA] IN EXPERIMENTAL MERCURY POISONING IN CHICKEN

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ABSTRACT

The aim of the present investigation was the evaluation of mercury distribution in the chicken tissues in the course of chronic mercury poisoning and the changes of mercury concentrations in the tissues after the administration of antidotum in the form of MESNA preparation.

For the purpose of the experiment 42 chicken were chosen, aged 22 days, with the mean body weight of 688 g which were divided into 4 following groups: Group K_O - control zero (no additives) - 18 birds, Group K_M - control with MESNA added (twice a day 0.1 g for 5 days starting on 22nd day of the experiment) - 6 birds, Group D_{Hg} - experimental (20 days, 0.3 mg Hg every day, 3 mg Hg altogether) - 12 birds and Group D_{Hg+M} - experimental (the same as D_{Hg}, 2 days after the end Hg administration the MESNA was administered twice a day 0.1 g for 5 days) - 6 birds.

An addition of MESNA antidotum in the dose of 1 g after mercury poisoning in the amount of 3 mg does not significantly affect mercury elimination from the organism of chicken and on growth disturbance accompanying the poisoning.
Concluding from the distribution of mercury concentrations in the tissues and organs of chicken after the administration of MESNA preparation its detoxicative action consist in the increase of renal elimination of that heavy metal.

Key words: mercury, MESNA, chicken, detoxification.

INTRODUCTION

From toxicological point of view many poisons act on their proper receptors. The release of poison from such a complex is difficult, however, it decidedly limits its toxic action. The elimination of poison from its specific receptor, with which it had been bound, together with detoxification by its neutralisation lead to poison inactivation. This type of detoxicating action consist in using chemical antidotes which indirectly or directly from with the poison complexes of low toxicity.

As an example one can mention such detoxicating substances as dimercaptopropanol [BAL] and ethylenediamine tetra-acetic acid [EDTA], used in cases of heavy metals poisonings. This group also includes pencylamine which, in view of its very low side-effects, is willingly used in cases of copper, lead, mercury and arsenic poisonings. In the organism metals become bound with the sulphydryl groups of proteins and enzymes thus leading to disorders or inhibitions of the vital cellular metabolic or energetic processes. In these cases the intoxicating action consist in the antidotum forming complexes which are more durable than the protein-metal or enzyme-metal bonds.

Mercury, as a typical heavy metal, binds selectively with the sulphydryl groups of proteins included in the membranes and cellular structures. Since practically all proteins include sulphydryl groups which react with mercury thus the poisoning with that element may disturb all enzymatic reactions and damage cell protein structures.

The source of mercury contaminating the environment is the burning of coal and petroleum products. According to Chmielnicka [3] in the neighbourhood of a coal-burning power station the dustfall may contain about 400 g $Hg \cdot ha^{-1}$ a year. An important source of that element in the agricultural ecosystems were the mercury seed dressings the production of which was discontinued in Poland in 1978 while in the Czech Republic they were still used at the beginning of the nineties [1, 2]. Mercury is a constant component of municipal sewage the use of which for soil fertilization creates a serious danger of introducing this heavy metal into food products and feeds for farm animals.

The problem of intravital reduction of the level of heavy metal contamination of products of animal origin may have practical applications in the regions of ecological hazard and in choosing the product one should consider its detoxicating properties and the lack of side-effects. It seems that all the requirements are met in case of the sodium salt of 2-mercaptoethanolsulphonic acid [MESNA].

First information about the detoxicating properties of this compound are reported by Magos and Butler [6], who demonstrated its liver protective action in case of aflatoxin B_1 poisoning. According to Weinstein [9] MESNA shows protective action for urinary tract in case of treatment with cyclophosphamide and other cytostatic drugs, it acts in a mucolitic way and above all it decreases the concentration of heavy metals in the tissues. Some comprehensive investigations of that compound pharmacokinetics were performed by James at al. [4].

The aim of the present investigation was the evaluation of mercury distribution in the chicken tissues in the course of chronic mercury poisoning and the reactions of mercury concentrations in the tissues after the administration of antidotum in the form of MESNA preparation.

MATERIALS AND METHODS

The experiment was performed on broiler cockerels (ROSS) aged 22 days, not showing any disease symptoms. The chicken were kept in groups in cages with constant access to water and feed. They were fed complete ration BR II *ad libitum*. Natural mercury contents in the mixture fed amounted to 0.011 $mg \cdot kg^{-1}$ which in case of the mean feed utilisation of 0.14 $kg \cdot bird^{-1} \cdot day^{-1}$ comprised an additional natural source of that element in the amount of 0.00154 $mg \cdot bird^{-1}$. The supplied water contained less than 0.001 $mg \cdot l^{-1}$ and was not considered as a mercury source.

Mercury was supplied in the form of the seed dressing Agronal containing 2.8% mercury phenylchloride which corresponded to 1.8% pure Hg. The preparation was mixed in a mixer with mixed feed BR II, thus the final mercury concentration in the feed amounted to 0.859 $g \cdot kg^{-1}$ (mean value out of 10 randomly collected samples). The mixture of Agronal with feed BR II was weighed into gelatin capsules in the amount of 0.35 g which corresponded to 0.300 mg Hg.

MESNA antidotum was also administered in gelatin capsules containing 0.1 g preparation.

Mercury was supplied according to the experimental plan always in the morning (between 8 and 9 a.m.) and MESNA preparation twice a day in the morning (8-9 a.m.) and in the afternoon (3-4 p.m.).

For the purpose of the experiment 42 chicken were chosen, aged 22 days with chosen, aged 22 days with the mean body weight of 688 g which were divided into 4 following groups: Group K_O - control zero (no additives) - 18 birds, Group K_M - control with MESNA added (twice a day 0.1 g for 5 days starting on 22nd day of the experiment) - 6 birds, Group D_{Hg} - experimental (20 days, 0.3 mg Hg every other day, 3 mg Hg altogether) - 12 birds and Group D_{Hg+M} - experimental (the same as D_{Hg}, 2 days after the end Hg administration the MESNA was administered twice a day 0.1 g for 5 days) - 6 birds.

In the course of the experiment the following parameters were registered: body weight gains determined by weighing chicken on the 1st, 22nd and 30th day of the experiment, feed utilisation per gain unit and the mercury level in the tissues and organs of the control and experimental chicken after their slaughter.

The chicken were slaughtered on the following days, depending on the group: K_O chicken were slaughtered on the 1st, 22nd and 30th day of the experiment, 6 chicken every time. In the control group K_M 6 chicken were slaughtered on the 30th day of the experiment. In the experimental group D_{Hg} 6 chicken were slaughtered on the 22nd and 30th day of the experiment. In the experimental group D_{Hg+M} 6 chicken were slaughtered on the 30th day of the experiment.

The chicken were slaughtered by means of decapitation. Hg contents was determined in the following samples: liver, kidneys, pectoral muscles, leg muscles, heart muscle, spleen, brain, blood, testes, bills and feather.

Mercury contents in feed, water and biological material was determined with the help of an automatic mercury analyser AMA 254 which is a single-beam atomic absorption spectrometer designed for the direct analysis of mercury in solid or liquid samples not requiring any introductory preparation of the analysed samples. The apparatus is controlled by the computer program AMA-Altec. The sensitivity of the apparatus amounts to 0.01 ng Hg and the repeatability not lower than 1.5%.Accuracy of the method was verified during standard solutions analysis, provided by the Altec company. A detailed description of the method is presented in the earlier papers [10].

The obtained results were subjected to statistical analysis calculating the arithmetic mean, standard deviation, minimum and maximum values. The means were processed statistically with the method of variance analysis. Calculations were performed using the statistical packet Stagraphics 6+.

RESULTS AND DISCUSSION

The body weight of chicken in the control group K_M and experimental D_{Hg} did not differ significantly on the 22nd day of the experiment although the chicken which were administered mercury gained 95 g less than those in the negative control. It is also interesting that a higher equalisation of the body weight was observed in the control group (s-113 g) than in the experimental group D_{Hg} which could point to an individual sensitivity of particular birds to the toxic action of mercury. The administration of mercury finished on the 20th day of the experiment in both experimental groups showed its own successive negative effect on body gains and feed utilisation on the gain unit in the further chicken life (Table 1). From the 22nd to 30th day of the experiment chicken in the experimental groups practically showed growth inhibition while the gains in the control groups were high amounting on the average to about 80 g a day.

Table 1. Body weight of chicken and feed utilisation for 1 kg of body weight gain in the control and experimental chicken

Group	Parameters	Experiment days		
		1	22	30
K_O	Body weight (g)			
	$\bar{x}$	688	1 716	2 373 [a]
	s	62	113	326
	min.	624	1 570	2 150
	max.	735	1 990	2 560
	Feed conversion efficiency (kg)			2.49
K_M	Body weight (g)			
	$\bar{x}$			2 466 [a]
	s			277
	min.			2 200
	max.			2 550
	Feed conversion efficiency (kg)			2.36
D_{Hg}	Body weight (g)			
	$\bar{x}$		1 621	1 680 [b]
	s		278	344
	min.		1 100	1 445
	max.		1 995	1 870
	Feed conversion efficiency (kg)			4.23
D_{Hg+M}	Body weight (g)			
	$\bar{x}$			1 662 [b]
	s			363
	min.			1 240
	max.			1 950
	Feed conversion efficiency (kg)			4.31

a,b - differences between values significant at p 0.05.

The administration of antidotum MESNA to chicken subjected to mercury poisoning did not show any positive effect on their gains and feed utilisation.

The natural mercury contents in the tissues of chicken observed prior to the experiment and also at later dates in the control groups was relatively low and similar to the levels reported by other authors [7] in the Czech Republic, although a little higher than in the investigations performed in Poland [11]. It confirms the fact that the chicken used in the experiment had not been earlier exposed to the increased mercury doses (Table 2). The distribution of Hg in particular tissues and organs also agreed with the current knowledge about the cumulation of that element. The highest natural mercury concentration was noted in the kidneys and liver and then in the remaining tissues and organs with the lowest level of that element observed in the blood.

Table 2. Mercury contents in the tissues of the control and experimental chicken with and without the supplement of MESNA preparation (n = 6 for each date of the examination) in mg kg^{-1} fresh tissue

Tissues	Parame-ters	Experiment days						
		1	22	30	30	22	30	30
		Group						
		K_O	K_O	K_O	K_M	D_{Hg}	D_{Hg}	D_{Hg+M}
Liver	$\bar{x}$	0.019	0.022	0.019	0.023	1.228	0.134	0.110
	s	0.007	0.009	0.007	0.006	0.756	0.043	0.045
	min.	0.004	0.013	0.010	0.015	0.478	0.088	0.075
	max.	0.044	0.045	0.034	0.035	2.559	1.990	0.221
Kidneys	$\bar{x}$	0.041	0.034	0.068	0.066	1.318	0.224^{A}	0.148^{B}
	s	0.010	0.007	0.016	0.019	0.239	0.048	0.036
	min.	0.015	0.027	0.054	0.047	1.077	0.129	0.081
	max.	0.083	0.047	0.097	0.105	2.085	0.272	0.205
Pectoral muscles	$\bar{x}$	0.014	0.005	0.002	0.001	0.045	0.007	0.007
	s	0.019	0.003	0.001	0.000	0.052	0.003	0.002
	min.	0.001	0.002	0.000	0.000	0.017	0.004	0.003
	max.	0.068	0.012	0.003	0.002	0.162	0.012	0.100
Leg Muscles	$\bar{x}$	0.020	0.003	0.003	0.003	0.040	0.007	0.005
	s	0.028	0.001	0.004	0.001	0.051	0.003	0.001
	min.	0.001	0.001	0.000	0.000	0.009	0.003	0.004
	max.	0.097	0.004	0.009	0.010	0.149	0.013	0.011
Heart muscle	$\bar{x}$	0.008	0.003	0.002	0.001	0.037	0.004	0.005
	s	0.007	0.001	0.004	0.001	0.054	0.002	0.002
	min.	0.001	0.001	0.000	0.000	0.008	0.002	0.002
	max.	0.042	0.005	0.009	0.003	0.177	0.007	0.010
Spleen	$\bar{x}$	0.022	0.008	0.002	0.004	0.079	0.012	0.010
	s	0.016	0.004	0.001	0.006	0.057	0.004	0.007
	min.	0.005	0.004	0.001	0.001	0.033	0.006	0.005
	max.	0.063	0.025	0.004	0.019	0.203	0.020	0.027
Brain	$\bar{x}$	0.010	0.003	0.004	0.003	0.032	0.010	0.012
	s	0.005	0.000	0.002	0.003	0.013	0.002	0.003
	min.	0.003	0.002	0.002	0.000	0.018	0.005	0.006
	max.	0.024	0.004	0.008	0.009	0.056	0.014	0.019
Blood	$\bar{x}$	0.002	0.005	0.003	0.004	0.040	0.003	0.004
	s	0.002	0.002	0.001	0.003	0.011	0.001	0.001
	min.	0.001	0.003	0.001	0.002	0.021	0.002	0.002
	max.	0.011	0.014	0.004	0.014	0.054	0.005	0.008
Tastes	$\bar{x}$	0.025	0.005	0.012	0.002	0.062	0.012	0.008
	s	0.014	0.006	0.009	0.001	0.006	0.005	0.002
	min.	0.013	0.003	0.003	0.001	0.055	0.005	0.006
	max.	0.059	0.018	0.026	0.008	0.071	0.023	0.011
Bile	$\bar{x}$	0.009	0.021	0.013^{a}	0.028^{b}	0.299	0.055	0.060
	s	0.006	0.001	0.001	0.007	0.049	0.005	0.005
	min.	0.001	0.020	0.011	0.020	0.246	0.051	0,052
	max.	0.021	0.022	0.015	0.037	0.364	0.060	0.065
Feather	$\bar{x}$	0.019	0.021	0.022	0.039	0.211	0.378	0.220
	s	0.011	0.018	0.010	0.012	0.107	0.215	0.015
	min.	0.005	0.015	0.018	0.032	0.085	0.130	0.213
	max.	0.035	0.035	0.033	0.048	0.534	0.776	0.235

a,b - differences significant at p 0.05 ; A,B – differences significant at p 0.01.

After the administration of the mercury preparation in the experimental groups in the dose of 10 x 0.3 mg for 20 days, a significant increase of that element contents was observed in the tissues and organs of the investigated chicken. The highest Hg levels were observed in the kidneys amounting to 1.318 mg·kg^{-1} which 56 times exceeded the value observed in the control group (Table 2) and in the liver where the mercury level amounting to 1.228 mg·kg^{-1} was 39 times higher than in the control. In the remaining material the increase of the Hg level varied in relation to the control from 15 times in the bile to about 10 times in the remaining tissues. These results

are similar to the values obtained by Macek [5] after 28 days period of poisoning pheasants with Argonal in the doses of up to 2.0 $g \cdot kg^{-1}$ feed.

On the 30th day of the experiment, i.e. after 10 days since the end of mercury administration the Hg levels observed in the experimental groups were a few times lower than in the earlier examination as well as in relation to the control group. It is particularly interesting that despite the decrease of mercury concentration in all the investigated tissues the Hg level in the feathers nearly twice increased as compared to the earlier date of examination and was 17 times higher than in the control group. It confirms both the results of our own investigations [8] and those of other authors which show that the accumulation of Hg in the feathers is one of the mechanisms of natural detoxification in birds resulting from the presence in that tissue of proteins with many thiol groups.

A higher level of that element in the bile points to a lower but always active mechanism of mercury elimination from the organism as a result of hepatic detoxification.

The lowest mercury level was observed in the heart muscle which confirms the results by Magos and Butler [6] that this tissue shows the shortest period of mercury biological half-life.

The administration of MESNA preparation showed lesser effect on mercury elimination than the natural mechanisms. However, one could observe a significantly lower Hg level in the kidneys of chicken which were administered the antidotum as compared to the birds which did not receive it, amounting to 0.224 and 0.148 $mg \cdot kg^{-1}$, respectively and in the feathers to 0.378 and 0.220 $mg \cdot kg^{-1}$, respectively. In chicken which were not given mercury the administration of the MESNA preparation did not cause any significant differences in the distribution of that element concentrations as compared to the control group except its concentration in the bile which was higher than in the control (Table 2).

The above presented fact seem to demonstrate that in the mechanism of detoxification connected with the administration of MESNA antidotum the renal elimination and hepatic detoxification with some part played by metaloproteins predominate. Natural detoxification is additionally supported by the accumulation of mercury in the dead tissues of feathers [8].

CONCLUSIONS

1. The administration of mercury in the dose of 3 mg during 20 days leads to growth inhibition and increased feed utilisation for a body weight gain unit in young growing broiler chicken.
2. The highest mercury accumulation after a prolonged oral poisoning takes place in the kidneys and liver and the lowest in the muscles and brain.
3. A ten day's period after the end of mercury administration both in groups with and without the addition of MESNA preparation significantly affected mercury elimination from the tissues and organs of chicken.
4. Feather creatine containing large amounts of sulphuric amino acids comprise an important element in natural processes of detoxification after mercury poisoning in poultry.
5. An addition of MESNA antidotum in the dose of 1 g after mercury poisoning in the amount of 3 mg does not significantly affect mercury elimination from the organism of chicken and on growth disturbance accompanying the poisoning.
6. Concluding from the distribution of mercury concentrations in the tissues and organs of chicken after the administration of MESNA preparation its detoxicative action consist in the increase of renal elimination of that heavy metal.

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